Pulmon

The Journal of Respiratory Sciences

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Guidelines for authors

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Pulmon
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Editorial

Pleural Effusion in Patients with End-Stage Chronic Kidney Disease: Causes and Concerns

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Chronic kidney disease (CKD) is a global health concern. Worldwide, increasing incidence of CKD is a major concern for healthcare and the economy. In India, the age-adjusted incidence rate of end-stage renal disease (ESRD) has been estimated to be 229 per million population[1]. More than 100,000 new patients enter renal replacement programs annually in India[2]. In a recent cross-sectional study (n=5588) conducted at 13 academic and private medical centres all over India, the prevalence of CKD was observed to be 17.2% with about 6% having CKD stage 3 or worse[3].

Pleural effusion is a common perplexing diagnostic problem for which nephrologists refer patients to pulmonologists. Common causes of pleural effusion in patients with CKD include fluid overload, cardiac failure, hypoproteinaemia, tuberculosis (TB), bacterial infection, and even inadequate dialysis[4]. Many patients with CKD with exudative pleural effusion get empirically treated with anti-TB drugs in India[5]. Further, there are sparse published data in India on the aetiological causes of pleural effusion in patients with CKD[5,6].

In this background, the cross-sectional study reported by Laila et al[7] published in the current issue of the journal (n=38) attempts to detail the demographic characteristics of patients with end-stage CKD who developed pleural effusion and document the nature and size of pleural effusion and the aetiological causes. The authors documented that most of the patients were men aged over 40 years; more than half had duration of CKD over one year and had presented with right sided pleural effusion most frequently. Transudates and exudates were equally distributed. The common aetiological causes were cardiac failure, renal failure and TB.

In a cross-sectional study[6] in adult patients with CKD (stages 3 to 5) from Eastern India, pleural effusion was found in 29 out of 430 patients with CKD (6.7%) and in two out of 34 post-renal transplant recipients (5.9%). Exudates and transudates were found in equal frequencies. The authors reported that heart failure was the most common cause of pleural effusion in CKD (13/31; 41.9%); TB (n = 8, 25.8%) and uraemic effusions (n = 6, 19.4%) were responsible for the majority of exudative pleural effusion. The author has observed an interesting finding that several transudative effusions secondary to congestive heart failure in his series were misclassified as exudative effusions emphasizing the Roth.BJ.et.al observations that although Light's criteria for exudates are sensitive, albumin gradient of ≤ 1.2gm/dl tends to be more specific especially in cases of congestive heart failure on diuretic therapy. On the other hand, Porcel JM in his review article titled 'Identifying transudates misclassified by Light's criteria stated that, the accuracy of a pleural fluid to serum albumin ratio less than 0.6 proved much more superior when compared with albumin and protein gradients in identifying the exudates. On the basis of Light's criteria, transudative effusions are classified as pseudo exudates following diuretic therapy because of increase in the non-albumin fraction of protein in the pleural fluid.

Unilateral effusion with a normal heart size had a positive predictive value of 83.3% for non-heart failure aetiology. In another study from Chandigarh[5] (n=107), 45 and 62 patients were diagnosed to have transudative and exudative pleural effusions, respectively. TB pleural effusion was diagnosed in 6 patients and uraemic pleuritis was diagnosed in 20 subjects. The sensitivity and specificity of pleural fluid adenosine deaminase (ADA), 65 kDa gene polymerase chain reaction (PCR), and multiplex PCR were 66.7% and 90%, 100% and 50%, and 100% and 100%, respectively. The authors concluded that Multiplex PCR and thoracoscopy are useful investigations in the diagnostic work-up of pleural effusions complicating CKD while the sensitivity and/or specificity of ADA and 65 kDa gene PCR is poor. In a study from USA, non-infectious causes were more frequently encountered compared to infectious aetiological causes like TB[8].

CKD is a predisposing cause for the development of active TB disease and pleural effusion is one of the common forms of extrapulmonary TB (EPTB) in these patients. Diagnosing TB as the aetiological cause of pleural effusion in patients with end-stage CKD is difficult. Given the low yield of pleural fluid smear and mycobacterial culture in pleural fluid[9], search of alternative diagnostic modalities is ongoing.The diagnostic performance of Xpert/MTB RIF in pleural fluid specimens has also been disappointing[10]. Invasive procedures like, blind, radiologically guided, video-assisted thoracoscopic surgery (VATS) or medical thoracoscopic pleural biopsy is often required for the diagnosis of TB in this scenario. In the present study, Laila et al[7] had used high pleural fluid ADA in 6, pleural biopsy in 1 and TB PCR positivity in 2 patients for confirming TB as the aetiology. Further, from the report by Laila et al[7], it

is not possible to know the yield of pleural biopsy histopathology/culture/ PCR in the diagnosis of TB as the aetiology. The utility of ADA in the setting of CKD is low and it is also known that haemodialysis reduces the levels of ADA[11].

The sample size in this study[7] is small which limits the generalization of these results. The author should have subjected every case of CKD to chest roentgenography for the detection of asymptomatic minimal and moderate effusions, which might have enabled to enhance the sample size. Still, given the paucity of published data on this topic from India, the clinical information is useful. There is a need for multicentric, prospective studies with a large sample size to delineate the aetiological spectrum of pleural effusions in patients with CKD. Guidelines need to be evolved for defining the role of pleural fluid ADA, molecular diagnostic tests and pleural biopsy histopathology, mycobacterial culture and molecular testing in the diagnosis of TB pleural effusion in this setting.

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Review Article

Arterial Blood Gas Analysis : The Essentials

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Introduction

Arterial blood gas (ABG) analysis plays a decisive role in the management of critically ill patients. Unless a logical and systematic approach is followed, ABG interpretation becomes a formidable task.Moreover, an improper report undermines the clinical utility of the test.ABG analysis remains the definitive method to diagnose, categorize and quantitate respiratory failure. It is also the only clinically applicable method of assessment of acid-base status.

Indications for Arterial Blood Gas Sampling

1. To evaluate the adequacy of ventilatory, acid-base and oxygenation status, and the oxygen-carrying capacity of blood.
2. To quantitate the patient's response to therapeutic interventionand/or diagnostic evaluation (e.g., oxygen therapy, exercise testing).
3. To monitor severity and progression of a documented disease process.
4. To perform co-oximetryin order to assess for methemoglobinemia and carboxyhemoglobinemia[1].

The indications for ABG analysis should be guided by clinical circumstances. Previously, ABGs were drawn after every ventilator change and with each step of the weaning process; such an approach is no longer recommended. As a "general rule" all patients should have an ABG performed on admission to the Intensive Care Unit and/or following (10-15 minutes) endotracheal intubation. Patients with respiratory failure should have an ABG performed at least every 24 to 48 hours. Patients with complex acid-base disorders and those undergoing permissive hypoventilation will require more frequent ABG sampling[2].

Obtaining an arterial sample

Points to be considered before obtaining a sample

- Obtain a relevant clinical history.
- Always note the fraction of inspired oxygen (FiO_2).
- Allow a steady state after initiation or change in oxygen therapy before obtaining a sample (in patients without overt pulmonary disease, a steady state is reached between 3 and 10 minutes and in patients with chronic airway obstruction, it takes about 20-30 minutes)[3].

The ABG samples may be obtained from an indwelling arterial catheter or by direct arterial puncture. The order of preference is radial artery > brachial artery > femoral artery. The radial artery at the wrist is the best site for obtaining an arterial sample for the following reasons:

- It is superficial and relatively easy to palpate and stabilize.
- Effective collateral circulation normally from the ulnar artery.
- The artery is not near any large veins[4].

A modified Allen test can be performed to assess the adequacy of the collateral circulation to the hand. To

perform the test, occlude both the ulnar and radial arteries. Instruct the patient to make a fist to drain the blood from the hand; this should be done for approximately 30 seconds. Instruct the patient to unclench the fist. The patient's palm should appear blanched or pale. Now, release pressure only from the ulnar artery. Adequate collateral circulation is indicated by the return of normal colour within 10 seconds[4].

Procedure

The arm of the patient is placed palm up on a flat surface, with the wrist dorsiflexed at 30°. A rolled towel is helpful in positioning the wrist. The puncture site should be cleaned with alcohol or iodine (allow the alcohol to dry before puncture as alcohol can cause bronchospasm).A local anaesthetic can be injected subcutaneously.Flush the syringe with liquid heparin or use preheparinised syringes. Only 0.05 mL heparin is required to anticoagulate 1 mL of blood. Filling the dead spaceof a standard 5 mL syringe with heparin provides sufficient volume to anticoagulate a 4 mL blood sample. The syringe with a 23- or 25-gauge needle should be inserted, bevel up, at a 45-degree angle just distal to the palpated pulse[4,5,6].

Allow at least 2 to 4 ml of blood to fill the syringe. Apply firm pressure to the puncture site with sterile gauze until the bleeding stops.Expel any air bubbles from the sample, and cap the syringe. Mix the sample by inverting the syringe and rolling it between the palms to prevent stacking of red blood cells.The sample should be analyzed within 20 minutes at room temperature. When analysis is expected to be delayed, use of glass syringes and ice slurry is recommended; iced samples can be processed up to one hour after collection[4,5,6].

Common Preanalytical Errors[7,8]

Errors can occur at any stage of ABG analysis, but the most common ones occur before analysis. These include:

Accidental venous sampling : The following points may help in recognize inadvertent venous sampling:

- Failure to observe a flash of blood on entry into vessel or pulsation during syringe filling
- Incompatibility of values with clinical condition
- Low PaO_2(partial pressure of oxygen in blood) and high $PaCO_2$(partial pressure of carbon dioxide in blood)
- SpO_2 by pulse oximetry more than SaO_2 by ABG analysis

The colour of blood is not a reliable indicator because severe hypoxemia can cause dark, "venous - appearing" arterial blood. When in doubt, arterial and venous samples can be sampled simultaneously to solve this problem.

Table 1 :

Arterial versus venous blood gas – Normal values[7]

Value	**Arterial Blood**	**Mixed Venous Blood**
pH	7.40 (7.35-7.45)	7.36 (7.31-7.41)
PaO_2	80-100 mm Hg	35-45 mm Hg
Oxygen saturation (SaO_2)	95%	70-75%
$PaCO_2$	35-45 mm Hg	41-51 mm Hg
Bicarbonate (HCO^{3-})	22-26 $mEqL^{-1}$	22-26 $mEqL^{-1}$

Excess Anticoagulant : Liquid heparin dilutes the plasma. Excess heparin can cause spuriously low $PaCO_2$ and plasma electrolytes.

Air bubbles in the sample : An air bubble whose relative volume is up to 1% of the blood in the syringe can cause significant error and falsely elevate PaO_2.

Delay in processing the sample : This can increase the $PaCO_2$ and decrease the pH.

Interpretation of the Arterial Blood Gas report

A structured approach should be followed to ensure that nothing is missed. The authenticity of the ABG report should be checked first. The arterial oxygenation should be assessed next. The $PaCO_2$ and pH are then analyzed to assess the ventilatory state and acid-base balance.

Assessment of the validity of the ABG report

The bicarbonate value from the blood gas report (a calculated value) can be compared with the bicarbonate from a simultaneously drawn chemistry panel (a measured value). Both the values should be close to each other.

A better method to check the consistency between the blood gas report and the chemistry panel is to calculate the hydrogen ion concentration $[H^+]$ using the modi-

fied Henderson-Hasselbach equation[8].

$[H^+] = 24 \times PaCO_2 / HCO^{3-}$

The calculated $[H^+]$ is used to determine what the pH should be.

$pH = -\log [H^+]$

The pH thus calculated is compared with the pH in the ABG report.

The following table can also be used to find the pH from the $[H^+]$.

Table 2

$[H^+]$ in mmol/L	pH
100	7.00
89	7.05
79	7.10
71	7.15
63	7.20
56	7.25
50	7.30
45	7.35
40	**7.40**
35	7.45
32	7.50
28	7.55
25	7.60
22	7.65

Assessment of oxygenation status

The arterial blood gas report provides information about the severity and cause of hypoxemia as well as adequacy of gas exchange. The PaO_2 is primarily used for assessment of oxygenation status. The PaO2 is always interpreted in conjunction with FiO_2 and age.

As a rule of thumb:
Expected PaO_2 $\approx FiO_2$ (%)× 5
Age predicted PaO_2 = Expected PaO_2 – 0.3(age - 25)
[Expected PaO_2 at sea level is 100 mm Hg]

Hypoxemia is defined as a PaO_2 of less than 80 mm Hg at sea level in an adult breathing room air. The concomitant decrease in cell / tissue oxygen tension is called **hypoxia**.

Table 3 :

Grading of hypoxemia

Grade of hypoxemia	PaO_2 (in mm Hg)
Mild	60-79
Moderate	40-59
Severe	< 40

The **alveolar-arterial oxygen difference** (AaO_2D) has to be calculated in patients with unexplained hypoxemic respiratory failure to ascertain the probable cause for hypoxemia. For this purpose, the alveolar PO_2 (PAO_2) is first determined using the alveolar gas equation.

$PAO_2 = PiO_2 - PaCO_2/R$
$= FiO_2 (PB - PH_2O) - PaCO_2/R$

[PiO_2, partial pressure of inspired oxygen; R, respiratory quotient assumed to be 0.8; PB, barometric pressure (760 mm Hg at sea level); PH_20, water vapour pressure (47 mm Hg)]

Thealveolar-arterial oxygen difference can be calculated as follows:

$AaO_2D = PAO_2 – PaO_2$

The normal value for AaO_2D is 10 -15 mm Hg. If the AaO_2D is normal, then hypoxemia can be due to hypoventilation or a low inspired partial pressure of oxygen. If the AaO_2D is elevated, then hypoxemia is due to shunt or low ventilation relative to perfusion (V/Q). The AaO_2D also increases with age. The upper limit of normal for AaO_2D = 2.5 + (0.21×age).Larger values imply a lower V/Q and/or shunt, but do not distinguish between the two. Supplemental oxygen will raise PaO_2 and reduce the AaO_2D in patients with low V/Q as the primary cause of hypoxemia, whereas in shunt, supplemental oxygen does not improve PaO_2[8].

Calculating the AaO2D as well as the PaO_2/FiO_2 ratio can assess the adequacy of gas exchange. The normal PaO_2/FiO_2ratio is between 400 and 500 mm Hg. The smaller the value, the worse the gas exchange.

The PaO_2 in the ABG report should be interpreted with caution in certain situations. In a **hypothermic** patient, PaO_2 will be overestimated when the blood samples are warmed to 37°C before analysis. So correction formulae for temperature have to be applied in such cases. **Leukocyte larceny** is a situation seen in patients with

extremely high white blood cell counts. The measured PaO_2 is lower than the expected PaO_2 because of oxygen consumption by the white blood cells. Placing the sample on ice and adding potassium cyanide to halt oxygen consumption can avoid this error. In **methemoglobinemia**, the patient has a low SpO_2 (usually 87-88%) because the oxygen will not bind to the abnormal hemoglobin but the PaO_2 will be much higher than expected.

Assessment of acid-base balance

The normal pH of blood is maintained within a narrow range through a complex interaction between the lungs, kidneys and blood buffers. To sustain life, the body must maintain the pH of fluids within a narrow range, from 7.35 to 7.45 (corresponding of to a $[H^+]$ of 45 to 35 nmol/L. Normally, the kidneys maintain an arterial bicarbonate concentration of approximately 24 mEq/L, whereas alveolar ventilation maintains an arterial $PaCO_2$ of 40 mm Hg. These normal values produce an arterial pH of 7.40, as shown by the Henderson-Hasselbach equation as follows:

$pH = 6.1 + \log [HCO^{3-}] / (PaCO_2 x 0.03)$

$= 6.1 + \log 24 / 1.2$

$= 6.1 + \log 20 = 7.4$

The pH remains normal, or 7.40 as long as the ratio of $[HCO^{3-}]$ to dissolved CO_2 is 20:1.

Primary Acid-Base disorders

According to the equation $[H^+] = 24 \times PaCO_2 / HCO^{3-}$, a change in either the $PaCO_2$ or the HCO^{3-} will cause a change in $[H^+]$. When a change in $PaCO_2$ is responsible for the change in H^+, the condition is a respiratory acid-base disorder. When a change in HCO^{3-} is responsible for the change in H^+, the condition is a metabolic acid-base disorder.

Table 4 :

Primary acid-base disorders and secondary responses

Primary Disorder	Primary change	Secondary response
Respiratory acidosis	$\uparrow PaCO_2$	$\uparrow HCO^{3-}$
Respiratory alkalosis	$\downarrow PaCO_2$	$\downarrow HCO^{3-}$
Metabolic acidosis	$\downarrow HCO^{3-}$	$\downarrow PaCO_2$
Metabolic alkalosis	$\uparrow HCO^{3-}$	$\uparrow PaCO_2$

Secondary responses are always in the same direction as the primary change

Secondary responses tend to limit the change in $[H^+]$ produced by the primary disorder. This is accomplished by changing the other component of $PaCO_2$ / HCO^{3-} ratio in the same direction. The secondary responses usually do not completely correct the change in $[H^+]$ produced by the primary acid-base disorder. Overcompensation never occurs.

The secondary response to a metabolic acid-base disorder involves a change in minute ventilation to increase or decrease the $PaCO_2$. This is mediated by peripheral chemoreceptors located in the carotid body. The secondary response to metabolic acidosis appears in 30-120 minutes and can take 12 to 24 hours to complete. However, the secondary response to metabolic alkalosis is not so vigorous because the peripheral chemoreceptors are not active under normal conditions; they are easier to stimulate than inhibit.

When a respiratory acid-base disorder occurs acutely, hemoglobin and other nonbicarbonate buffers are responsible for immediate restoration of pH to normal. This early response is less effective than renal compensation.For example, the compensatory response in acute respiratory acidosis produces only 1 mEq increase in HCO^{3-} for every 10 mm Hg rise in $PaCO_2$. Therefore even extreme hypercarbia will not push bicarbonate over 32 mEq/L acutely. After 6-12 hours, the kidneys adjust the HCO^{3-} reabsorption in the proximal tubules to produce the appropriate change in plasma HCO^{3-}. This renal response is relatively slow, and can take 3 to 5 days to reach completion.[9,10,11,12]

Step-wise approach to acid-base analysis

If the $PaCO_2$ and/or pH are outside the normal range, there is an acid-base disorder.

1. Identify the primary acid base disorder

a. Check if acidosis (pH<7.35) or alkalosis (pH>7.45) is present.

b. If pH indicates **acidosis**, then look at $PaCO_2$ and HCO^3.

- If $PaCO_2$ is increased, then it is primary respiratory acidosis. Primary respiratory acidosis is classified further based on $\Delta H^+/\Delta PaCO_2$.

$\Delta H^+/\Delta PaCO_2 < 0.3$ – chronic

> 0.8 – acute

0.3 to 0.8 – acute on chronic

[Example: pH = 7.24, $PaCO_2$ = 95, HCO^{3-} = 45

$H^+ = 24 \times 95/45 = 50.6$ mmol/L

$\Delta PaCO_2 = 95 - 40 = 55$

$\Delta H^+/\Delta PaCO_2 = 50 - 40 / 55 = 0.18$

So this is a case of chronic respiratory acidosis.]

- If HCO^{3-} is decreased, primary metabolic acidosis is present.

c. If pH indicates **alkalosis**, then look at $PaCO_2$ and HCO^3.

- If $PaCO_2$ is decreased, then it is primary respiratory alkalosis. Primary respiratory alkalosis is classified further into acute and chronic based on $\Delta H^+/\Delta PaCO_2$.
- If HCO^{3-} is increased, primary metabolic alkalosis is present. Based on the urinary chloride, metabolic alkalosis is classified further into chloride responsive (urinary chloride < 20) and chloride resistant (urinary chloride > 20) alkalosis.

2. Evaluate the secondary responses

Table 5 :

Compensation formulae for simple acid-base disorders[12]

Acid-base disorder	Compensation formula
Metabolic acidosis	$\Delta PaCO_2 = 1.2 \times \Delta HCO^3-$
Metabolic alkalosis	$\Delta PaCO_2 = 0.6 \times \Delta HCO^3-$
Acute respiratory acidosis	$\Delta HCO^3- = 0.1 \times \Delta PaCO_2$
Chronic respiratory acidosis	$\Delta HCO^3- = 0.4 \times \Delta PaCO_2$
Acute respiratory alkalosis	$\Delta HCO^3- = 0.2 \times \Delta PaCO_2$
Chronic respiratory alkalosis	$\Delta HCO^3- = 0.5 \times \Delta PaCO_2$

3. Use the "gaps" to evaluate metabolic acidosis

a. Anion gap (AG)

Anion gap is the difference between the plasma cations and measurable plasma anions.Because electrical neutrality must be maintained, the difference reflects the unmeasured anions. Normally, this gap is filled by the weak acids, principally albumin, and to a lesser extent phosphates, sulfates, and lactates. Anion gap is calculated as **$[Na^+] - ([Cl]+[HCO^3]$**.

The normal reference range for AG is 12± 2mEq/L.A high anion gap metabolic acidosis occurs when there is an accumulation of fixed or non-volatile acids (e.g., lactic acidosis, diabetic ketoacidosis), while a normal anion gap or hyperchloremic metabolic acidosis occurs when there is a primary loss of bicarbonate (e.g., diarrhoea)[13].It is possible to have an acid base disturbance with normal values for pH, $PaCO_2$ and HCO^{3-}, the only clue being a raised anion gap.

Albumin corrected anion gap (AGc)

Hypoalbuminemia will lower the AG. Hence the corrected AG has to be estimated to include the contribution of albumin[12,14].

AGc = AG + 2.5 x (4.5 – [albumin in g/dL])

(4.5 represent the normal plasma albumin concentration)

e.g., for a patient with an AG of 10 mEq/L and a plasma albumin of 2.5 g/dL, the AGc is 10 + 2.5 x (4.5 – 2.5) = 15mEq/L, which represents a 50% increase from the initial value.

b. Osmolal gap (OSM gap)

Osmolal gap is calculated in patients with unexplained high AG metabolic acidosis to exclude toxic ingestion like ethylene glycol or methanol toxicity.

OSM gap = measured OSM – (2[Na^+] – glucose/18 – BUN/2.8).

The OSM gap should be < 10.

4. The Gap-Gap ratio[12]

If increased AG is present, assess the ratio of the change in AG to the change in HCO^{3-} **($\Delta AG/\Delta HCO^{3-}$= [AG – 12] / [24 – HCO^{3-}]**). This ratio should be between 1.0 and 2.0 if an uncomplicated anion-gap metabolic acidosis is present.

If $\Delta AG/\Delta HCO^{3-} < 1.0$ – Concurrent normal AG metabolic acidosis (e.g., A diabetic ketoacidosis patient treated with aggressive isotonic saline infusion)

If $\Delta AG/\Delta HCO^{3-} > 2.0$ – Concurrent metabolic alkalosis(e.g., Uremia with frequent use of nasogastric suction and diuretics)

5. Identifying other mixed acid-base disorders

A mixed acid-base disorder should be suspected if the actual response deviates from the expected compensatory response to the primary abnormality. It is

possible to have two or even three acid-base disorders simultaneously. The only combination which is not possible is a combined respiratory alkalosis and respiratory acidosis as it is impossible to hyper- and hypoventilate at the same time.

If $PaCO_2$ and HCO^{3-} are abnormal and change in opposite directions, then there is a mixed disorder (either metabolic + respiratory acidosis, or metabolic + respiratory alkalosis). Identification of the dominant disorder requires the calculation of the percent difference of the change in $PaCO_2$ and HCO^{3-} (ΔHCO^{3-} / HCO^{3-} and $\Delta PaCO_2$ / $PaCO_2$).

[Example: pH = 7.25, HCO^{3-} = 16, $PaCO_2$ = 60. Here pH is acidotic and both raised $PaCO_2$ and reduced HCO^{3-} can cause acidosis: so look at the % difference.

HCO^{3-} % difference = (24-16) / 24 = 0.33

$PaCO_2$ % difference = (60-40) / 40 = 0.5

Therefore, respiratory acidosis is the dominant disorder.]

If only the pH or $PaCO_2$ is abnormal, the condition is a mixed metabolic and respiratory disorder (equal and opposite disorders). The following combinations are possible : **- Normal pH + abnormal $PaCO_2$**

a. Primary respiratory disorder with metabolic compensation, **OR**

a. Two opposing primary acid-base disorders (one respiratory+ one metabolic).The directional change in $PaCO_2$ identifies the type of respiratory disorder (e.g., high $PaCO_2$ indicates a respiratory acidosis), and the opposing metabolic disorder.

-Abnormal pH+"normal" $PaCO_2$

Always represent two primary acid-base disturbances. The directional change in pH identifies the type of metabolic disorder (e.g., low pH indicates a metabolic acidosis) and the opposing respiratory disorder[12].

Clinical case : An 18 year old female was found in a semi-comatose state at home and admitted to hospital. On examination, she was found to be hyperventilating. Her plasma concentrations of sodium, potassium, urea and creatinine were normal, but plasma anion gap was found to be 23 mmol/L and plasma HCO^{3-} was 12 mmol/L. Further investigations revealed a plasma salicylate concentration of 350 mg/L. Her blood gas values were as follows:

pH – 7.43, PaO_2 – 105 mm Hg, $PaCO_2$ - 20mm Hg, HCO^{3-} - 12mmol/L

Diagnosis : Mixed acid-base disorder – a high anion gap metabolic acidosis caused by salicylate poisoning and acute respiratory alkalosis caused by salicylate-induced hyperventilation.

Three factors suggest that this is a mixed acid-base disorder, rather than a compensated primary metabolic acidosis or a compensated primary respiratory alkalosis. First, chronic hyperventilation can instigate a compensatory metabolic acidosis, which can result in a blood pH within the normal range. However, the respiratory alkalosis in this patient was acute, and thus it would be unlikely for her to have a "normal" pH or a compensatory decrease in blood bicarbonate to 12mmol/L [in acute respiratory alkalosis the plasma HCO^{3-} rarely falls below 18 mmol/L]. This suggests an element of primary metabolic acidosis. Second, if this patient had a simple primary metabolic acidosis, the expected compensatory level of $PaCO_2$ would be 40- [1.2 x (24-12)] = 26 mm Hg. This patient's $PaCO_2$ of 20 mm Hg thus suggests primary respiratory alkalosis. Finally, the high value for the anion gap indicates the presence of a primary high anion-gap metabolic acidosis[15].

To conclude, medical personnel managing the critically ill patient need to master the skill of arterial blood gas sampling. Accurate interpretation of the ABG report requires a thorough understanding of the basic physiological processes involved in oxygenation, ventilation and acid-base balance. The combination of clinical assessment and a systematic approach to interpretation will help in arriving at the correct diagnosis.

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Review Article

HRCT Imaging of Diffuse Lung Diseases - A Pattern Based Approach

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Abstract : Diffuse lung diseases is a group of conditions with varying aetiologies. High resolution computed tomography (HRCT) has become the imaging modality of choice for evaluation of diffuse lung diseases. Secondary pulmonary lobule is a key anatomic structure, in relation to which the HRCT findings are described. Lung diseases present with predominantly four HRCT patterns – reticular pattern, nodules, increased lung attenuation and decreased lung attenuation. By identifying the dominant pattern or combination of patterns and associated imaging findings it is possible to arrive at a diagnosis or to a list of differential diagnosis. Correlation of HRCT features with clinical features and biochemical investigations is also crucial in many situations.

Key Words : HRCT, CT, Diffuse lung diseases

Abbreviations used in the article :

HRCT – High resolution computed tomography
MDCT – Multidetector computed tomography
ECG – Electrocardiogram
GGO – Ground glass opacity
NSIP – Non-specific interstitial pneumonia
LIP – Lymphocytic interstitial pneumonia
OP – Organising pneumonia
DLDs –Diffuse lung diseases
HU – Hounsfield Unit
ILD – Interstitial lung disease
UIP – Usual interstitial pneumonia
DIP –Desquamative interstitial pneumonia
RB-ILD – Respiratory bronchiolitis associated interstitial lung disease

Introduction

Clinical presentations of diffuse lung diseases (DLDs) show significant overlap and histopathology findings are not always reliable due to heterogeneity of lung parenchymal involvement. High resolution computed tomography (HRCT), by providing global anatomic assessment of the lung parenchyma, is a problem solving tool in the evaluation of patients with suspected DLD[1].

Imaging Technique

Several HRCT techniques have been described in the evaluation of DLDs. Axial acquisition is performed with 10 mm interslice gap and thin collimation of approximately 0.6-1.5 mm thickness, reconstruction is done with sharp bone algorithm. Axial mode cannot be used for evaluation of pulmonary nodules as there will be significant data loss due 10 mm gap. Volume acquisition of HRCT can be done by modern multidetector computed tomography scanners (MDCT). Advantages of this acquisition are that there is no interslice data loss, increased speed of acquisition- so less motion artefacts and volume rendering can be performed, using which, especially ground glass opacification and architectural distortion can be depicted with greater confidence. Minimum intensity projection is very helpful for identifying associated airway disease and subtle attenuation difference while maximum intensity projection can help us detect otherwise obscure subtle

nodules. As radiation is the prime concern in MDHRCT, recently low dose technique has been developed. After acquisition HRCT images should be interpreted with proper window level (- 600 / - 900 HU). Expiratory HRCT is important to detect air trapping, which is seen in airway diseases. Prone HRCT plays an important role in differentiating dependent densities and gravitational atelectasis from early interstitial lung disease. Dependent densities seen in supine HRCT disappear on prone CT[2].

Anatomy

Before going into the pathology of diffuse lung disease, it is important to understand the anatomy of secondary pulmonary lobule. As defined by Miller, secondary pulmonary lobule is the *"smallest unit of lung structure marginated by connective tissue septa"*[2].

On HRCT, three anatomical components of the secondary pulmonary lobule can be identified - the interlobular septa and septal structures, the centrilobular region and centrilobular structures, and the lobular parenchyma[3] (Fig 1). The interlobular septa contain the pulmonary veins and lymphatics. Contents of centrilobular region are pulmonary artery, bronchiole and lymphatics. Lobular parenchyma surrounds the centrilobular region and consists of alveoli, capillary bed and supporting interstitium or intralobular septae[3].

Figure- 1 : Schematic diagram of secondary pulmonary lobule showing lobular artery (red), lobular vein (dark blue) and lymphatics (yellow). Centrilobular area is represented as sky blue area and perilymphatic area as yellow

Pattern Identification and Approach

HRCT findings in DLDs can be grouped into four general patterns – reticular opacities, nodules, increased lung attenuation and decreased lung attenuation. Duration of symptoms is important as the differential diagnosis for a particular pattern varies based on Acute/ Subacute/ Chronic presentation. After identifying the dominant pattern, distribution is studied in relation to secondary pulmonary lobule and in cranio-caudal directions. Associated parenchymal abnormalities and pleura/ mediastinal/ chest wall abnormalities can help in further narrowing the differential diagnosis. Laboratory investigations can sometimes offer specific clues –for example Eosinophil count in patients with suspected Eosinophilic lung diseases.

Reticular Pattern

Definition "On chest radiographs, a reticular pattern is a collection of innumerable small linear opacities that, by summation, produce an appearance resembling a net "[4]. HRCT can clarify whether the reticular pattern is due to interlobular septal thickening or intralobular septal thickening or honeycombing.

Approach to differential diagnosis on HRCT

Reticular pattern can be due to interlobular septal thickening or honey combing. If the pattern is due to interlobular septal thickening, then we have to see if the septal thickening is smooth, nodular or irregular and formulate a differential diagnosis list accordingly[5].

Interlobular septal thickening

Smooth interlobular septal thickening is due to fluid or tumour infiltration of the interlobular septal lymphatics. Most common causes are pulmonary edema and lymphangitic spread of tumour. Symmetrical involvement favors pulmonary edema (Fig 2), whereas asymmetric involvement and history of a primary tumour with associated findings like lymphadenopathy favour a diagnosis of lymphangitic spread[5].

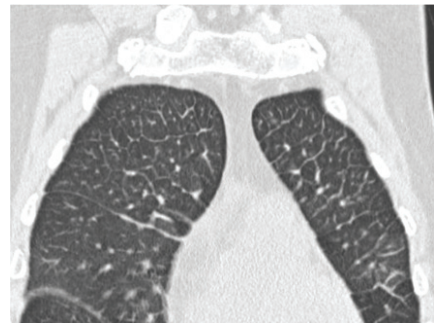

Figure-2 : Coronal HRCT image showing smooth interlobular septal thickening outlining the secondary pulmonary lobules.Bilateral involvement favour pulmonary edema. Patient was in renal failure.

Nodular interlobular septal thickening suggests involvement of the lymphatics, with the nodularity either due to granulomas or tumour nodules. The differentials in this type of septal thickening are sarcoidosis or lymphangitic spread of tumour[1].

Irregular interlobular septal thickening is secondary to fibrosis with associated architectural distortion.

Honey combing

Pathological honey combing is seen in the late stage of various lung diseases, when fibrosis causes parenchymal destruction and architectural distortion resulting in multiple cystic spaces with thick walls[4]. On HRCT, it is seen as clustered or layers of air spaces measuring 3 to 10mm in diameter in sub pleural region with well-defined wall. The cysts have attenuation equal to air and have common walls. Associated findings are traction bronchiectasis and irregular septal thickening [4 5]. Though honey combing is most commonly seen in UIP, it can be seen in other conditions like connective tissue disease associated ILDs, drug related fibrosis, hypersensitivity pneumonitis, etc.[5] (Fig 3).

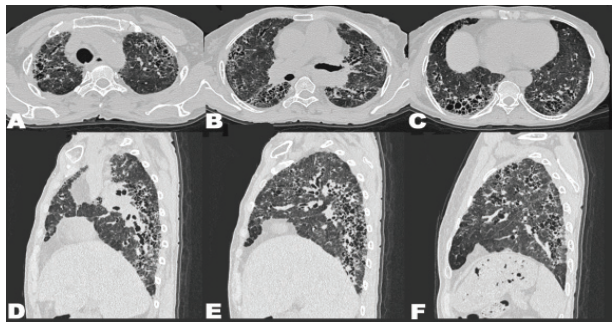

Figure – 3 : Axial CT images lung window (A, B, C) and sagittal images (D, E, F) showing irregular interlobular septal thickening, honeycombing with traction bronchiectatic changes. There is temporal heterogeneity and apico basal gradient (evident on sagittal images). Also note the interface sign (Irregular mediastinal borders) suggestive of fibrosis

Nodular Pattern

Definition

On HRCT a nodule appears as "a rounded or irregular opacity, well or poorly defined, measuring up to 3 cm in diameter". Based on attenuation the nodules can be divided into ground glass and solid nodules[4].

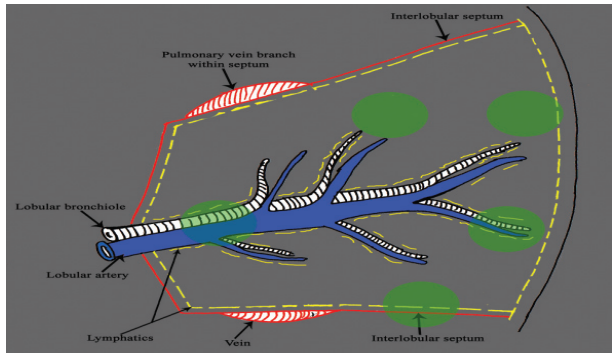

Figure -4 : Schematic diagram showing perilymphatic distribution of the nodules.

Approach to differential diagnosis on HRCT

When nodules are the predominant pattern, the differential diagnosis is based on a) Distribution of nodules in relation to secondary pulmonary lobule b) Craniocaudal distribution and c) Attenuation. Of these, distribution in relation to secondary pulmonary lobule is the most important feature[5]. There are three patterns of distribution with respect to the secondary pulmonary lobule– perilymphatic, centrilobular and random patterns.

Perilymphatic nodules

These are seen in conditions which involve the lymphatics. Distribution of nodules follows the location of lymphatics and are seen in four locations -(1) the parahilar peribronchovascular interstitium, (2) the centrilobular peribronchovascular interstitium, (3) the interlobular septa, and (4) the subpleural interstitium[5] (Fig 4). On HRCT, these are seen as nodular thickening of peribronchovascular interstitium, centrilobular cluster of small nodules, nodular interlobular septal thickening along the fissures and beneath the pleural surfaces. Common conditions with perilymphatic distribution of nodules are sarcoidosis, lymphangitic spread of tumor and pneumoconiosis (Fig 5).

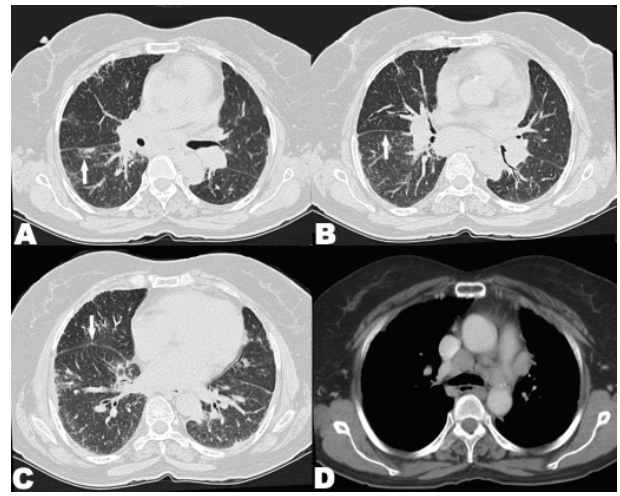

Figure - 5 : Known patient of sarcoidosis. Axial CT sections lung window (A,B,C) showing perilymphatic nodules (white arrows) along the fissure, pulmonary fibrosis, thickening of peribronchovascular interstitium. Axial CT section mediastinal window (D) showing right paratrcheal lymphadenopathy

Centrilobular nodules

These are seen in conditions which involve the centrilobular bronchiole, artery or lymphatics. Cluster of nodules are seen around the centrilobular bronchovascular

bundle with two specific features – there is distinct sparing of the subpleural interstitium and equal spacing between the clusters of nodules[5] (Fig 6). Centrilobular nodules when associated with linear opacities , produce tree in bud pattern. Though initially described in endobronchial spread of tuberculosis, this pattern is seen in a wide variety of conditions such as viral, bacterial and fungal infections, immunologic disorders, idiopathic conditions, connective tissue disorders, etc.[6] (Fig 7)

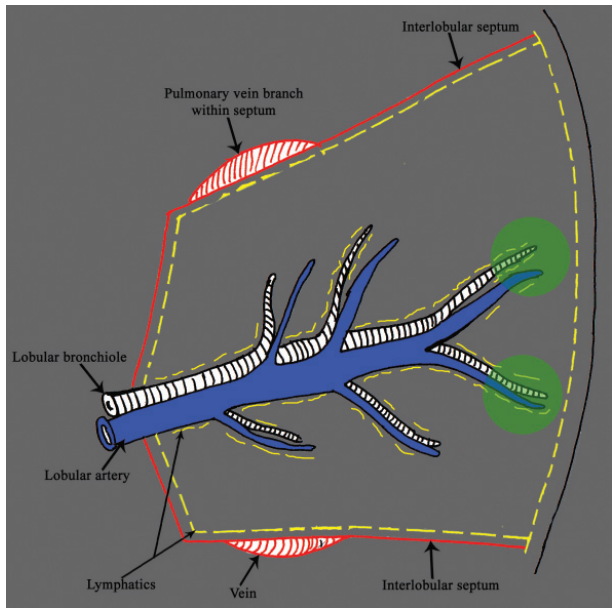

Figure - 6 : Schematic diagram of showing centrilobular distribution of the nodules

Random nodules

In conditions with random nodules, there is no particular relation of the distribution to structures of secondary pulmonary lobule (Fig 7). Depending on the size random nodules can be divided into fine random nodules and medium sized random nodules. Fine random nodules produce miliary pattern and the differentials are miliary tuberculosis, fungal infection and metastasis. Medium sized random nodules are usually seen in metastases[7].

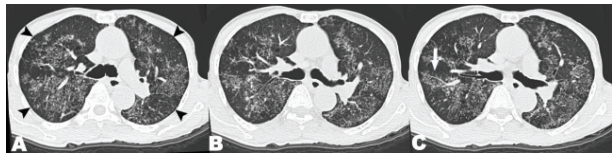

Figure – 7 : Centrilobular nodules, Axial CT sections lung window (A, B) showing nodules involving the centrilobular portion of secondary pulmonary lobule in both lungs. Tree in bud pattern, indicating endobronchial spread of the disease is seen in right lung (white arrow). Note subpleural sparing of the disease (Black arrowheads).

Differential diagnosis based on Craniocaudal distribution -

Conditions like Tuberculosis and sarcoidosis are more likely to present with nodules in upper lobes than in lower lobes. Since there is significant overlap among different conditions in the Craniocaudal distribution, correlation with other features is always recommended to arrive at a differential diagnosis

Increased Lung Attenuation

Normal average lung attenuation is around -950HU. Increased lung attenuation can be either due to ground glass opacification or consolidation.

Ground-glass opacity (GGO)

Definition- GGO is defined as "increased attenuation of the lung parenchyma without obscuration of the pulmonary vascular markings on CT images[8]".

Approach to differential diagnosis on HRCT-

Ground glass opacification results from partial filling of air spaces, interstitial thickening due to any cause or a combination of these. Often ground glass opacity is patchy in distribution and easily recognised. It is difficult to recognise, when the involvement is diffuse. In such situations the dark bronchus appearance, where the airways appear too black compared to adjacent lung, can be used to identify the GGO[2].

It is important to identify ground glass opacification, as it often signifies the presence of an active disease[2]. Also it can act as a guide to target areas with active disease process, during lung biopsy. On HRCT, GGO can be seen when there is active inflammation and also when there is fibrosis below the resolution of HRCT. It is important to look for signs of fibrosis, such as traction bronchiectasis and honey combing as these point towards fibrosis as the cause of GGO.

Since there is a long list of causes for ground glass opacification, it is essential to approach this finding taking into consideration the duration of clinical symptoms(acute, subacute or chronic), distribution of ground glass opacities and associate findings.

Ground glass opacity in acute clinical setting is seen in infections (especially viral pneumonia and pneumocystis jiroveci pneumonia), pulmonary oedema(hydrostatic and increased permeability oedema),

hypersensitivity pneumonitis and acute eosinophilic pneumonia[5]. In hydrostatic pulmonary edema, GGO is associated with smooth septal thickening. In Pneumocystis pneumonia, it is associated with cysts.

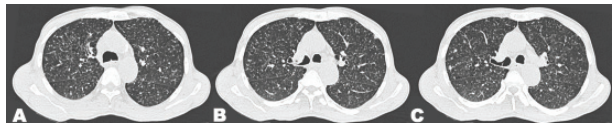

Figure - 8 : Randomly distributed nodules in a case with disseminated tuberculosis.scattered discrete varying sized nodules in both lungs. There is no particular anatomical pattern of distribution in relation to the secondary pulmonary lobule; A few nodules are abutting the pleura, in contrast to centrilobular pattern.

In chronic clinical setting, GGO is seen in NSIP, DIP, RB-ILD, LIP, organising pneumonia, chronic eosinophilic pneumonia and alveolar proteinosis. Peripheral distribution is seen in NSIP, DIP, organising pneumonia and eosinophilic pneumonia. In alveolar proteinosis, there is association with septal thickening producing crazy paving pattern. Crazy paving pattern, though initially described in alveolar proteinosis, can be seen in many conditions presenting with GGO. GGO associated with air trapping or mosaic perfusion is seen in hypersensitivity pneumonitis[5].

Consolidation

Definition- Consolidation is homogenous increase in lung attenuation resulting in obscuration of the vessels. The airways are often spared and appear lucent against the increased attenuation of lung parenchyma, resulting in air bronchograms.

Approach to differential diagnosis

Most of the conditions which produce ground glass opacities, can also present with consolidation. Sometimes both the findings can coexist. Similar to ground glass opacification, consolidation has a long list of differentials and the approach is based on duration of symptoms and distribution of findings.

Consolidation in the acute clinical setting – Most common conditions are pneumonia and aspiration. Other differentials are pulmonary oedema, diffuse alveolar damage, haemorrhage and acute eosinophilic pneumonia. Among these, conditions which can produce diffuse consolidation are viral pneumonias, pneumocystis pneumonia, pulmonary oedema and haemorrhage. Bacterial pneumonia and aspiration typically produce focal consolidation, especially aspiration where consolidation is seen in lower lobes or posterior segments of upper lobes[5].

Consolidation with chronic symptoms- Conditions producing consolidation with chronic symptoms are organising pneumonia, chronic eosinophilic pneumonia, lymphoma, mucinous adenocarcinoma and sarcoidosis. Peripheral distribution of consolidation is typically seen in OP and chronic eosinophilic pneumonia (Fig 9). Focal consolidation in chronic setting is seen in lymphoma, lipoid pneumonia and mucinous adenocarcinoma. Diffuse consolidation is seen in mucinous adenocarcinoma or OP[5].

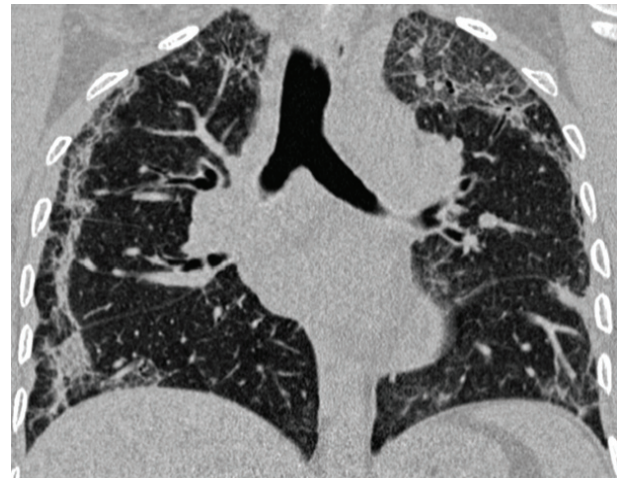

Figure- 9 : Peripheral patchy areas of consolidation in both the lungs, more on right side, in a patient with chronic eosinophilic pneumonia

Identifying some specific signs can sometimes help in further narrowing the list of differentials. Atoll sign or reverse halo sign is used to identify perilobular pattern of consolidation seen in OP. In conditions with focal consolidation, low attenuation area of consolidation favours a diagnosis of lipoid pneumonia.

Decreased Lung Attenuation

Decreased lung parenchymal attenuation can be due to emphysema, cystic lung disease, bronchiectasis and mosaic perfusion

Emphysema is of three types- centrilobular, panlobular and paraseptal. Centrilobular emphysema, as the name states, involves the central portion of secondary pulmonary lobule. It is classically seen in smokers with upper lobe predominance. On HRCT it presents as areas of low attenuation measuring upto 10mmwithout a wall and surrounding the centrilobular artery, producing the

central dot sign (Fig 10). Panlobular emphysema involves the entire secondary pulmonary lobule. Because of its tendency for diffuse involvement, diagnosis in early stages can be difficult. Paraseptal emphysema is seen along the periphery or along fissures. Paraseptal emphysema is seen in smokers, along with centrilobular emphysema. It is important to differentiate paraseptal emphysema from honeycombing. In paraseptal emphysema the cysts are usually arranged in a single row, thin walled and larger in size, in contrast to honeycombing, where the cysts are relatively thick walled, arranged in multiple layers and smaller in size. Findings of fibrosis such as traction bronchiectasis and septal thickening are seen in honeycombing only[5].

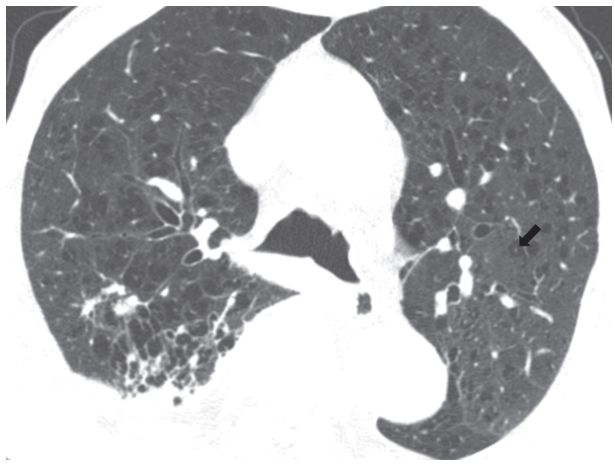

Figure – 10 : Axial HRCT section in lung window shows well defined lucent areas with no definite wall. Central dot sign(black arrow) is seen in some of the areas in left lung, suggesting centriacinar emphysema

Cystic lung disease- Cyst is defined as round, lucent areas of air attenuation with a thin wall. Wall thickness is usually <2mm. Though usually cyst content is air, it can have fluid or solid components also[4]. In the differential diagnosis of lung cysts, distribution of the cysts, morphology of cysts and associated findings are important[9].

When cysts are diffusely seen in lungs the common differentials are Langerhans cell histiocytosis and Lymphangioleiomyomatosis. Langerhans cell histiocytosis is seen in smokers. Cysts are bizzare shaped and spare the lung bases. LAM occurs in young women. There is no sparing of basal regions and the cysts are thin walled and round (Fig 11). When a few scattered cysts are seen associated with ground glass opacities and nodules, lymphocytic interstitial pneumonia has to be suspected[9].

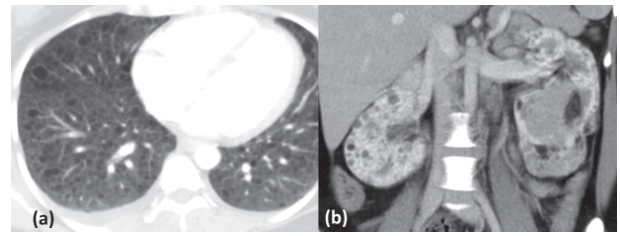

Figure – 11 : (a) Axial CT section in lung window shows multiple cystic lesions in both lungs. The lucent areas are having a well-defined wall, favouring a diagnosis of cyst. There was no sparing of costophrenic angles (b) Coronal contrast section of abdomen shows multiple angiomyolipomas in both kidneys. A diagnosis of Tuberous sclerosis is made and Lung involvement is diagnosed as Lymphangioleiomyomatosis

Mosaic perfusion – Mosaic perfusion is due to regional differences in lung perfusion either because of airway pathology or vascular pathology. On HRCT it is seen as areas of differential attenuation. Involved areas are of low attenuation with small size of vessels, as compared to uninvolved areas. In mosaic perfusion due to airway causes like bronchiolitis, air trapping is seen in expiratory scans. Mosaic perfusion due to vascular cause is seen in chronic pulmonary thromboembolism and is associated with features of pulmonary arterial hypertension. Mosaic perfusion has to be differentiated from patchy ground glass opacification, where involved parenchyma is of higher attenuation. In this situation, there is no difference in vessel size, between the low and high attenuation areas[5]. Head cheese sign is used to describe the presence of Ground glass opacification and air trapping in the same patient. This is commonly seen in patients with Hypersensitivity pneumonitis (Fig 12).

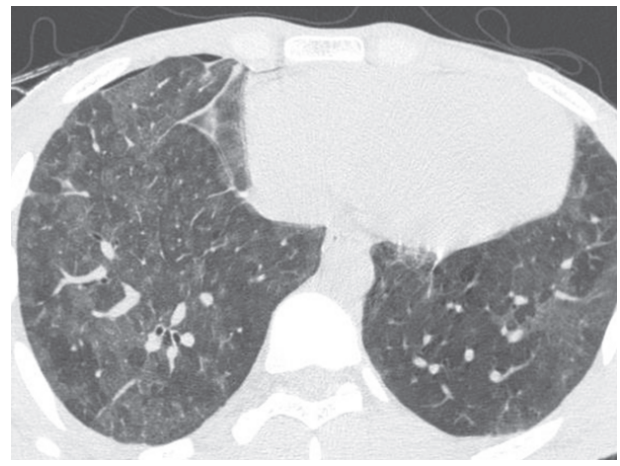

Figure -12 : Axial HRCT section in lung window shows Head cheese sign(patchy areas of ground glass opacification and air trapping) in a patient with suspected Hypersensitivity pneumonitis

Conclusion

Diffuse lung diseases can show significant overlap in the clinical symptomatology. HRCT has become the imaging modality of choice in evaluation of these entities. Management implications of the information provided by HRCT chest can be profound. Identification of the predominant pattern or combination of patterns often helps in coming to a diagnosis and avoids invasive methods of diagnosis like lung biopsy. Where a single diagnosis is not possible, differential diagnosis based on HRCT helps in targeting biochemical investigations to particular entities.

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Original Article

Pattern of Pleural Effusion in End Stage Renal Disease

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Abstract

Introduction : End stage Chronic Kidney Disease (CKD) is characterized by decreased glomerular filtration rate. Most pleural effusions occurring in CKD is attributed to renal failure and heart failure and left alone. But there are other diseases responsible for many of the effusions such as parapneumonic effusion, atelectasis, tuberculosis, other infections and malignancies due to immunosuppression and deserves further evaluation.
Aim of the study : To find the demographic characteristics of patients with end stage chronic kidney disease developing pleural effusion, the nature and size of effusion and their etiology.
Methodology : The Study was conducted in CKD patients attending Govt. Medical College, Kozhikode. 38 patients with CKD Stage 4 & 5 who developed pleural effusion from January 2012 to September 2013 were included in this study. The clinico- radiological course, biochemical characteristics of the pleural fluid and other relevant investigations were done to come to an etiological diagnosis .
Study design : Cross Sectional Study
Results : Of the 38 patients, there were 31 males and 7 females, 81.57% were above 40 years of age. Dyspnea (100%), Cough(44.7%) and chest pain (31.5%) were the main presenting symptoms. Comorbidities included hypertension(60.5%), diabetes(42.1%), anemia(71%). Majority were on hemodialysis(63.1%). Radiologically, 34.2% had right sided, (26.3%) had left sided and 39.47% had bilateral effusion, majority being moderate in amount. There were equal number of transudates and exudates. Cardiac failure (28.9%), renal failure and tuberculosis (21.05%) were the most common etiological reasons for the same.
Conclusion : Majority of patients were males above 40 years of age, with dyspnea, cough and chest pain as main presenting symptoms. Over a half had duration of CKD over one year and many had right sided effusion. Most of the effusions were moderate in amount. There were equal number of transudates and exudates, the most common etiology being cardiac failure, renal failure and tuberculosis.
Key words : CKD, Pleural effusion

Introduction

Chronic Kidney Disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). The prevalence and the incidence of CKD are increasing.

Table 1 :

Classification of Chronic kidney disease

Stage	GFR (mL/min per 1.73 m2)
1	>90
2	60-89
3	30-59
4	15-29
5	<15

Diseases of the kidney may involve the pulmonary system also in the form of pulmonary edema, pulmonary infections, pulmonary hemorrhage and / or pleural diseases, many of which gets alleviated by dialysis and or renal transplantation

There are several reasons for pleural and pulmonary complications happening in chronic kidney disease which includes:

1. Increased risk for ischemic heart disease and potential for dilated cardiomyopathy making these patients especially prone to problems with fluid balance.
2. Virtually all of these patients are oliguric or anuric.
3. Diseases, such as SLE are associated with renal and pleural manifestations.
4. Patients with end stage renal disease (ESRD) are immunocompromised, and some studies have suggested that this population may be at increased risk for certain malignancies, such as non-Hodgkin's lymphoma, renal, prostate, and uterine cancer. All of these malignancies can involve the pleura.
5. Comorbid conditions associated with or contributing to ESRD may indirectly cause pleural abnormalities.
6. Uremia per se has been shown to cause a pleuritis by an unknown mechanism.

Aetiology of pleural effusion in patients with chronic kidney disease include :

- Heart failure
- Fluid overload
- Hypoalbuminemia
- Uremic pleurisy
- Parapneumonic effusion
- Atelectasis
- Malignancy
- Uremic pericarditis
- Pancreatitis
- Hepatic hydrothorax
- Bacterial peritonitis
- Lupus pleuritis
- Unknown

Why is it important to establish an etiology for pleural effusion in CKD patients?

Patients with CKD have immune dysfunction manifested by depressed cell-mediated immunity (CMI). This impairment of CMI makes infection with M.Tuberculosis more difficult to detect and more likely to progress to TB disease than in immune competent individuals. This will increase the morbidity, duration of hospital stay and requirement for prolonged hemodialysis.

Aim of the study :

This study was conducted to find out-

1. The demographic characteristics of patients with end stage renal disease developing pleural effusion
2. The nature and size of pleural effusion in CKD patients.

Materials and methods :

A cross sectional study was conducted in CKD patients with Pleural Effusion attending the Nephrology OP and Pulmonology OP, Government Medical College, Kozhikode. 38 patients with Stage 4 & 5 CKD who developed either unilateral or bilateral pleural effusion from January 2012 to September 2013 were included. The clinico- radiological course and biochemical characteristics of the pleural fluid were studied and other relevant investigations were done to reach an etiological diagnosis.

Patients with CKD stage <4, patients not willing for thoracentesis and those with severe comorbidities like

recent myocardial infarction, sepsis or bleeding disorders were excluded from the study.

A suspected pleural effusion in a chronic kidney disease stage 4 or 5 patient was diagnosed by Chest X-ray after proper clinical evaluation. Complete blood count, ESR, blood sugar, renal function tests, Liver function tests and urine routine examination were done. Sputum samples were sent for AFB smear and routine culture and sensitivity.

Thoracocentesis was performed using a 20 Gauge needle with syringe, and the fluid was studied for the gross appearance, total count, differential count, haematocrit, protein, sugar, ADA, LDH, cytology, routine culture and AFB culture.

Chest radiograph was classified according to the size of effusion. The size of the effusion was assessed on the posteroanterior radiograph by visually estimating the area of the hemithorax occupied by pleural fluid. Pleural effusions were deemed to be *small, medium or large if* it occupied less than one third, between one third to two third, and more than two third of the hemi thorax respectively.

Pleural biopsy and other relevant investigations such as thoracic ultrasound (TUSG), ultrasound abdomen, echocardiography and CT Thorax were performed to establish the etiology. Pleural biopsy was performed with an Abrams or Cope needle.

GFR was calculated using Crocroft-Gualt equation,

GFR= (140-age) x (weight in kg) / 72 x creatinine, multiply by 0.85 if female.

The causes of pleural effusions were diagnosed in accordance with the following criteria :

1. **Congestive heart failure (CHF):** Compatible clinical and radiologic findings, remission upon appropriate treatment, and absence of pulmonary infiltrates, chest pain, and purulent sputum.

2. **Tuberculosis**: 1) An exudative lymphocytic effusion with an ADA level of > 40 U/L, along with a positive tuberculin skin test (2) Presence of a granuloma in a pleural biopsy specimen after excluding other causes of granulomatous pleuritis; or (3) Positive results for AFB culture of pleural fluid, sputum, or pleural biopsy specimens; and exclusion of any other potential causes of pleurisy.

3. **Parapneumonic**: Associated with pneumonia, lung abscess, or bronchiectasis

4. **Malignant:** A pleural effusion was categorized malignant, if pleural fluid cytology or pleural biopsy findings were positive for malignancy (*ie*, *true malignant*), or if the patient had a known cancer with no other explanation for the effusion (*ie*, *paramalignant*).

5. **Renal failure**: Patient with chronic kidney disease with fluid overload in the absence of cardiac failure, after ruling out other possible etiologies.

6. **Pulmonary thromboembolism**: Angiographic evidence or ventilation-perfusion scan showing deficient perfusion affecting at least the whole lobe.

7. **Idiopathic:** If the aetiology could not be established by any of the diagnostic tests (including pleural biopsies)

Data was analysed using standard statistical methods.

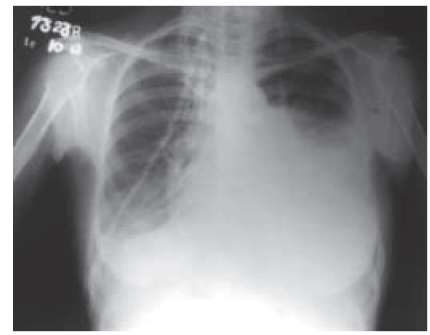

Figure 1: Chest X Ray of a CKD patient with bilateral pleural effusion

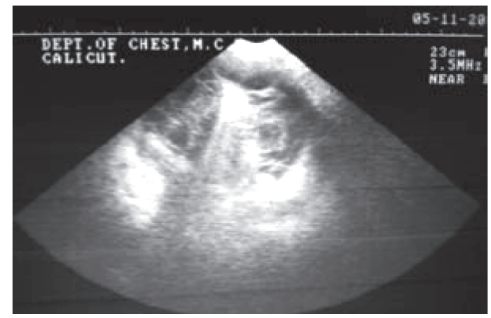

Figure 2: USG Thorax showing multiple encystments in an exudative effusion

Observations :

A total of 38 patients were included in our study, which included 31 males and 7 females. 31 (81.57%) patients were above 40 years of age and the rest 7 (18.42%) were below 40 years of age.

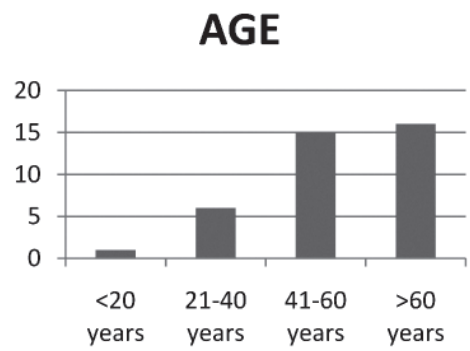

Chart 1: Age distribution

All of them complained of dyspnea on exertion, 12 (31.5%) had chest pain, 17(44.7%) had cough, 14 (36.8%) had fever and 9 (23.68%) had significant loss of appetite and loss of weight. There were 9 (23.6%) current smokers, 15(39.4%) ex-smokers and 14 (36.8%) non smokers. Comorbidities included - Diabetes mellitus in 16 (42.1%), 23(60.5%) with hypertension, 13 (34.2%) had Coronary heart disease, 27 (71%) had anaemia, 12 (31.5%) had previous history of tuberculosis, 10 (26.3%) had other comorbidities- like asthma, parkinsons disease and chronic liver disease .(Chart 2)

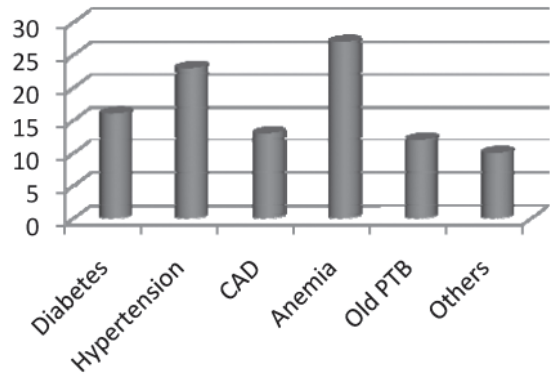

Chart 2: Co Morbidities

Duration of CKD less than one year was present in 17 (44.7%) patients and more than one year in 21(55.2%).

Medical management was taken by 10 (26.3%) patients, 24(63.1%) were on haemodialysis, none were undergoing peritoneal dialysis, one had history of Renal transplantation, 3 patients were not taking any regular medication for their kidney disease. (Chart 3)

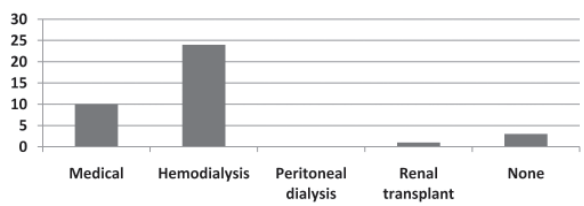

Chart 3 : Treatment taken for Kidney disease

Radiologically, 13 (34.2%) had unilateral right sided effusion, 10 (26.3%) patients had unilateral left sided effusion, 15 (39.47%) patients had bilateral effusion.

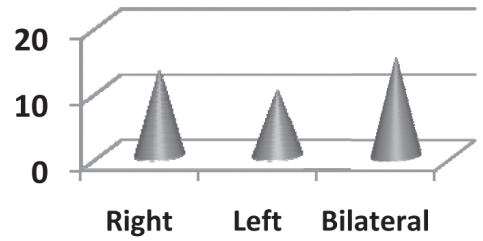

Chart 4 : Pleural effusion in Chest X Ray

Amongst the right sided effusions,7 (18.4%) had small effusion, 19(23.6%) had moderate effusion, 2(5.26%) had large effusion. In the left sided effusions- 6(15.78%) were small, 15(39.47%) were moderate and 4(10.52%) had large effusion.

There were equal numbers of patients having transudative and exudative pleural effusions in our study. Of the total 38 pleural fluid aspirated- 9(23.68 %) had clear pleural fluid, 16 (42.41%) were straw coloured, 10 (26.31%) were blood tinged or hemorrhagic, 3 (7.89%) were turbid/ purulent.(Chart 5)

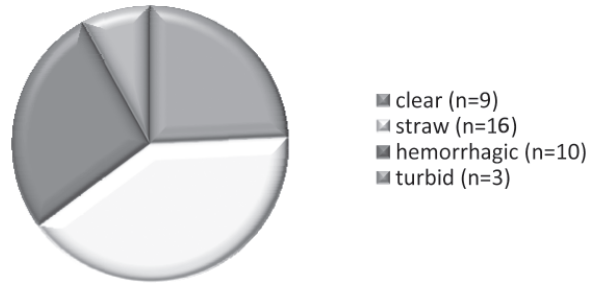

Chart 5 : Pleural fluid appearance

Pleural effusion was attributed to cardiac failure in 11 (28.94%) cases, to renal failure in 8(21.05%) cases, 5 (13.15%) were malignant/ para malignant effusions, 9 (23.68%) were due to tuberculosis as obtained from high pleural fluid ADA in 6, pleural biopsy in 1 & TB PCR positivity in 2 patients. One was due to hypoproteinemia (2.6%), and the cause of one was unknown (2.6%).(Chart 6)

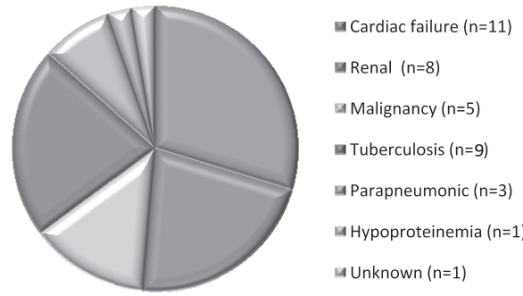

Chart 6 : Etiology of Pleural effusion

Of the total 8 patients whose pleural effusion was attributed to renal failure, 75% were transudative and 25% were exudative. Majority were straw colored (62.5%) and the rest hemorrhagic (37.5%). (Chart 7 &8)

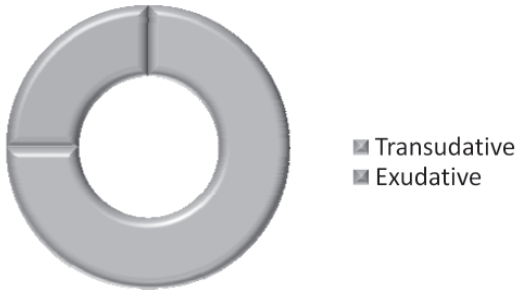

Chart 7: Pleural effusion in Renal Failure

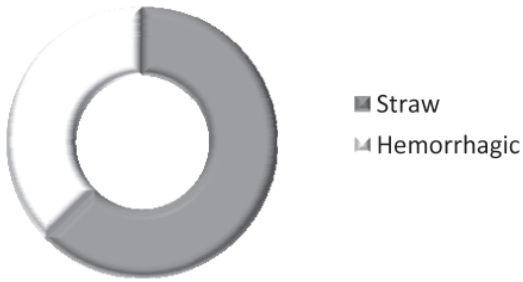

Chart 8 : Appearance of pleural effusion in Renal Disease

Discussion :

Chronic kidney disease is becoming a major global health problem. It is estimated that 1, 00,000 new patients of end stage renal disease enter renal replacement programs annually in India[1]. In a community level survey by Mani et al [2], in Chennai, the evidence of CKD was 0.7%. In a population based study from Bhopal[3], Modi GK reported the average crude and age adjusted incidence rates of stage 5 CKD (ESRD) as 151 and 232 per million population. Prevalence and incidence of tuberculosis as per WHO global report on Tuberculosis in India is 211 and 172 per lakh population respectively. Tuberculosis (TB) among patients with compromised kidney function is an important cause of concern as they have immune dysfunction manifested by depressed cell-mediated immunity (CMI). This impairment of CMI makes infection with M. tuberculosis more difficult to detect and more likely to progress to TB disease than in immune competent individuals.

Multiple studies have demonstrated cutaneous anergy rates of 30 to 80% in patients with ESRD. The risk of active TB in hemodialysis (HD) patients is 7-52 times higher than in the general population. HD units located in countries with high background TB prevalence have reported that up to 23% of their HD populations eventually develop active TB. Further complicating detection and treatment, only a minority of ESRD patients with active TB will present with typical pulmonary disease as a large majority of them may often have extra pulmonary disease or an atypical pulmonary presentation. The most common forms of extra pulmonary disease are pleural and lymph node TB. Tuberculous peritonitis can occur in PD patients. Patients with CKD or ESRD often have false negative TST (Tuberculin Skin test) or indeterminate QFTs due to anergy.

Mortality rates of patients with ESRD developing tuberculosis are much more than other TB patients. Many patients with CKD have additional risk factors for progression to active TB disease. The most prevalent risk factor is diabetes, but the use of immunosuppressive drugs to treat rheumatologic disorders and to maintain kidney transplants is also common. Prevention of progression to active TB among those patients with latent TB infection (LTBI) and early detection of active TB disease are a high priority because of the grave consequences of the disease and the difficulty in treating TB in CKD patients.

Pleural effusion is a common complication occurring in patients with renal failure. Most of which are attributed to the primary disease and fluid overload. But a detailed examination and evaluation may reveal another underlying etiology. According to the 2003–2006 NHANES study, the prevalence of Stage 3 CKD in people aged <40 years was 0.2% and for those 60 years and above, it was as high as 26% [4]. According to the statistics of number of ESRD patients by treatment modality in the US, more than 10 times as many ESRD patients receive hemodialysis (HD) treatments as those who do peritoneal dialysis (PD) and other treatment modalities combined [5]. A study by Bakirci T, et al in Turkey, in patients with CKD on long term hemodialysis , unilateral effusion was found in (48%), the most frequent cause of unilateral effusion were hypervolemia and para pneumonic effusion. Of the transudative effusions, 85.7% were bilateral. The most common cause of exudative effusion was uremic pleuritis which occurred in 40% patients[9].

In our study there were equal numbers of transudative and exudative pleural effusions. Initially when only Lights criteria was applied, 26 out of the 38 patients were classified as exudates, with 8 of them satisfying the Lights criteria by a narrow margin. So when the Serum -Pleural fluid protein gradient was assessed, 7 out of the 8 borderline exudates turned out to be

transudates; all these 7 patients were on diuretics as a part of their treatment. Most of the CKD patients are on long term diuretics and hence this fact should be kept in mind while interpreting the pleural fluid results.

According to a report by Stevenson et al. in 2007[6], patients with Diabetes mellitus (DM) are 1.5–8.0 times more at risk to develop TB than those without DM. DM, old age, male sex, malnutrition, iron overload, and inadequacies in dialysis are major risk factors for TB in dialysis patients (Ahmed et al., 2003; Christopoulos et al).[7,8] In study by Andrew P. Lundin, Et al [10],TB was diagnosed in eight patients in those CKD patients undergoing maintenance hemodialysis and there were seven extra pulmonary cases out of the eight cases under follow up. Hence active case of tuberculosis was difficult to be established for the fact that most of them had smear negative extra pulmonary disease.

The study by Bakirci T, et al in Turkey, in patients with chronic renal failure on long term hemodialysis the incidence of pleural effusion was 20.2%, with 61.5% developing effusion due to hypervolemia, and was bilateral in 68.8% [9]. Data from a similar larger multicentre study over longer study duration may give us a more accurate picture of the same. Thus from the above data it is suggested that all patients who are known to have advanced CKD, those who are on dialysis, and those with a transplant should be screened actively for TB. If we fail to establish a proper etiological diagnosis in patients with chronic renal failure developing pleural effusion despite proper antibiotics, a trial of anti tuberculous chemotherapy is justified especially in tuberculosis endemic country like India. One drawback of our study was that X-ray was taken only in those patients suspected to have pleural effusion clinically, so a lot of patients with minimal effusion might be missed.

Conclusion :

Our study on pleural effusion in advanced chronic kidney disease revealed equal number of transudative and exudative effusions. It was interestingly observed that several of them were misclassified as exudates overlooking the fact that many were on long term diuretics.

The effusions were predominantly unilateral, with right sided effusions more than left, and majority were moderate in amount. Though establishing the diagnosis with utmost certainty is a tough challenge to the treating physician, cardiac failure, fluid overload in renal failure and tuberculosis were found to be the most common etiologies of pleural effusion in patients with advanced Chronic Kidney Disease. Further studies and scoring systems to come to a firm diagnosis of each reason cited above have to be developed in future prospective studies planned in these patients.

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Radiology Quiz

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A 68 year old lady with history of progressive shortness of breath for the last 5 years presented with acute worsening of her respiratory symptoms coupled with weakness and anorexia for 2 weeks. Her past symptoms was punctuated by recurrent similar episodes associated with wheezing. The episodes had no relation with dust exposure or changes in environment. She was hypoxic at admission with a SpO2 of 91% on room air. The chest was clear to auscultation this time and cardiovascular examination revealed a loud P2 with pan systolic murmur at right sternal border. The chest radiograph obtained at admission is shown below. An emergency computerised tomographic evaluation of the thorax was performed, the representative images of which are exhibited along with the chest roentgenogram. What is the diagnosis?

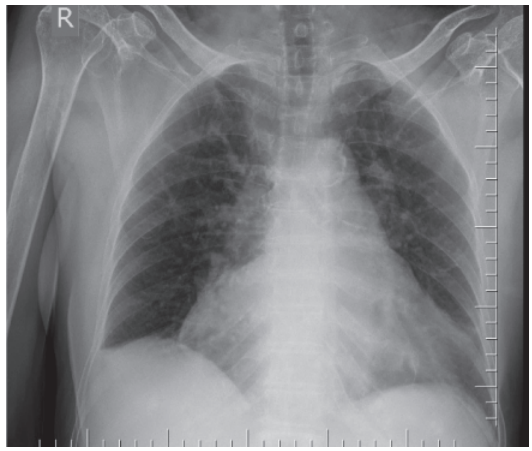

Image 1 - Chest Radiograph

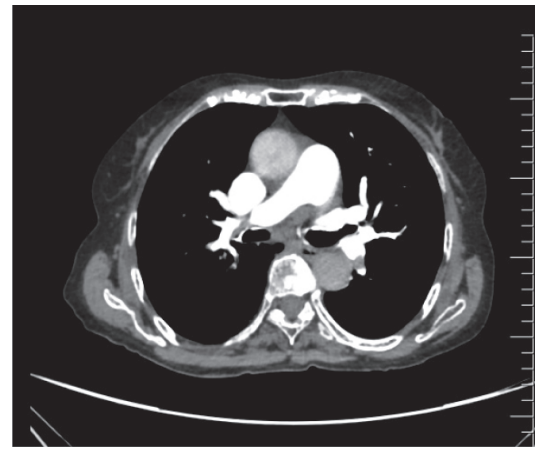

Image 2

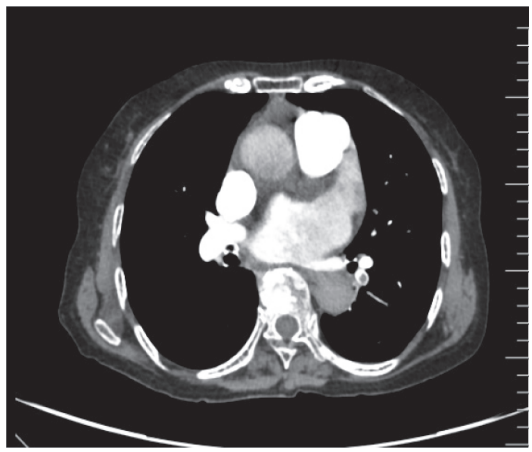

Image 3

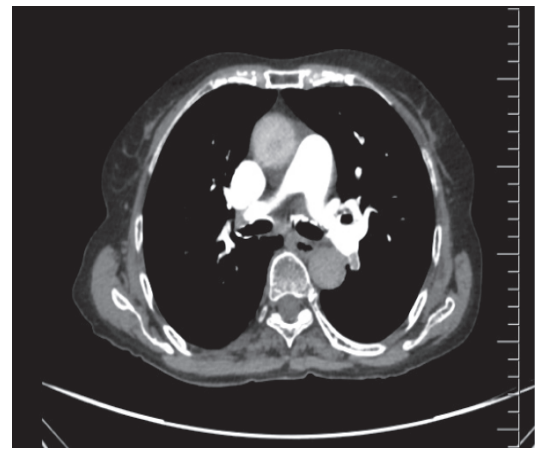

Image 4

ANSWER

Chronic thromboembolic pulmonary hypertension with acute embolism of left Lower lobe pulmonary artery

Discussion

Chronic thromboembolic pulmonary hypertension (CTEPH) results from an extension of the natural history of acute pulmonary embolic disease, although it occurs only in a minority of subjects who survive an acute pulmonary embolism event[1]. Some authors estimate that 0.1% to 0.5% of survivors of an acute embolic event later develop symptomatic CTEPH[2]. History of multiple pulmonary embolic events, younger age at presentation, larger perfusion defects at diagnosis, and idiopathic pulmonary embolic disease were found to be significant risk factors for the development of CTEPH[3]. Upto one-third to half of patients who have CTEPH may not provide a history of prior acute symptomatic pulmonary embolism or deep vein thrombosis and this makes the diagnosis challenging. They present with insidious shortness of breath, lethargy and giddiness similar to idiopathic PAH.

Advances in computerised tomographic imaging has allowed for better detection rates of CTEPH and distinguishing this entity from acute pulmonary thromboembolic episodes. Organized thrombus apparently lines the larger pulmonary vessels in either a concentric or eccentric manner. Abrupt narrowing and tapering of pulmonary arteries, web-like strictures, pouch defects, and other irregularities of the intimal surface may also be appreciated. These findings should be distinguished from the intraluminal filling defects and abrupt vessel cutoff seen in acute thromboembolic disease[4]. Acute embolus also tends to have an acute angulation between the filling defect and vessel wall.

In the present case, image 2 and 4 show the dilated pulmonary trunk, abrupt narrowing and tapering of the right main pulmonary artery with organised thrombus lining the vessel wall consistent with CTEPH. Image 3 and 4 show a central filling defect in the left lower lobe pulmonary artery making an acute angulation with the vessel wall consistent with an acute embolus of the left lower lobe artery. Echocardiography revealed severe PAH (PA pressures of 85 mm of Hg) with severe tricuspid incompetence. She was initiated on therapeutic anticoagulation with reasonable symptomatic resolution and improvement in gas exchange over the next 2 weeks. A work up for occult neoplasm and other hypercoagulable states were unrewarding. She is being continued on therapeutic anticoagulation.

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Radiology Pearl

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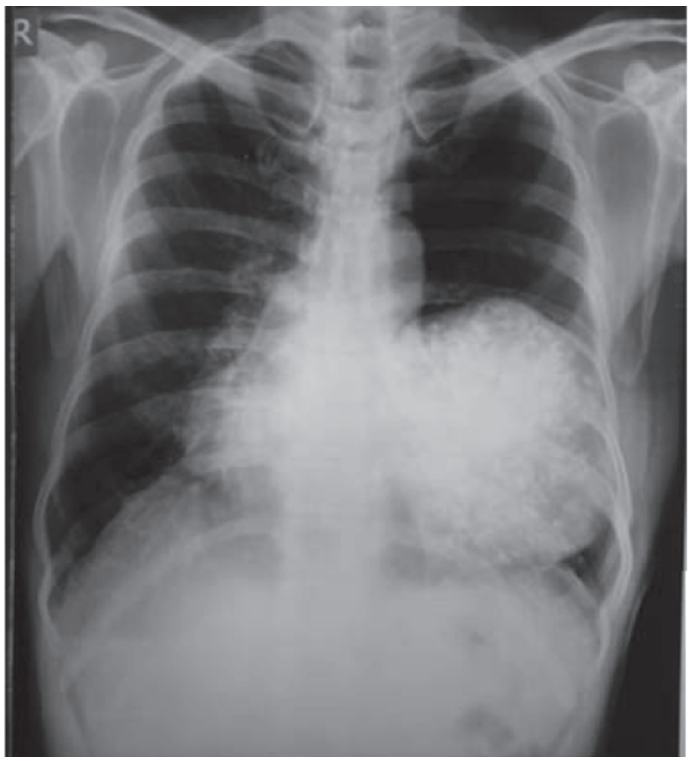
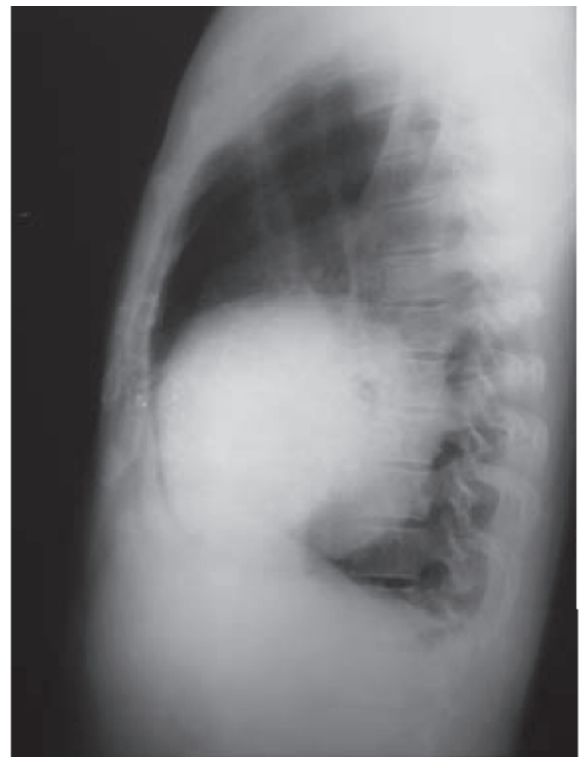
A 53 year old male smoker presented with progressive exertional dyspnea. He did not give history of recent worsening of symptoms. He did not have any previous Chest X-ray with him. His Chest X-ray PA and Left lateral view is shown below.

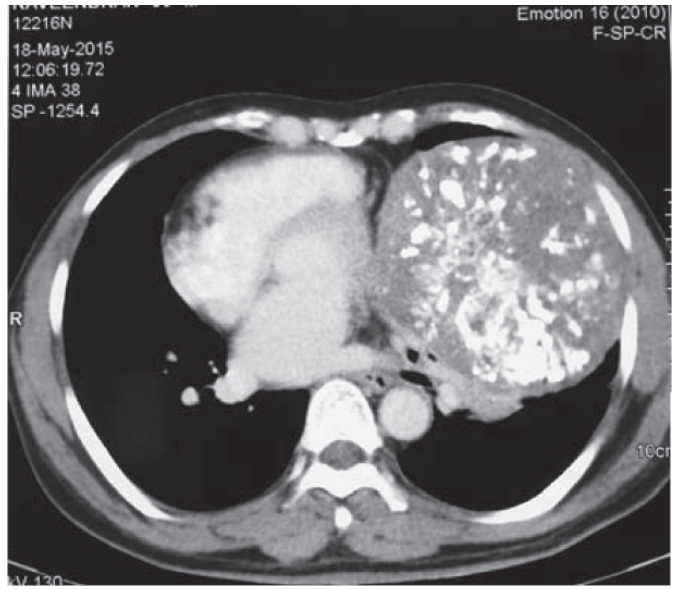


Chest X - Ray PA



Left Lateral View

What is the possible diagnosis?



CECT Chest

Answer :

Giant Pulmonary Hamartoma

Discussion :

Spot diagnosis is the charm of radiology. This is such a situation where the presence of popcorn pattern of calcification seen in the large left lower lobe mass suggests the possibility of a benign lesion, pulmonary hamartoma, which is well seen in the lateral projection also. There is evidence of considerable mass effect owing to the fact that the heart shadow is grossly shifted to right. The contrast enhanced CT section shows a giant 11x10x12 cm large non enhancing fat density lesion with chunks of calcification medially abutting the heart and pulmonary vessels and causing compression of left upper lobe segmental bronchi.

Pulmonary hamartomas are the most common benign pulmonary parenchymal neoplasm composed of mixed mesenchymal elements and hence also known as mesenchymomas[1]. Commonest subtype chondromatous hamartomas are parenchymal in 80 % cases and endobronchial in 20 % cases. The clinical presentation in this patient is suggestive of chronic obstructive pulmonary disease. However owing to the large size and compression of adjacent structures surgical resection is the best possible management strategy in this patient.Though hamartomas are common, giant pulmonary hamartomas(>9 cm) are extremely rare and only about 15 cases are published in English literature so far[2].

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Case Report

An Unusual Cause of Chronic Cough

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Abstract

Chronic cough is a common problem with which patients present to medical and respiratory outpatient clinics. Although there are very few causes of chronic cough, in some instances multiple aetiologies and sometimes even rare causes could add to the clinical dilemma. Here in we present the case of a 76 yr old lady with persistent cough ,who on evaluation was found to have tracheobronchomalacia in addition to laryngeopharyngeal reflux disease as causes for her intractable cough.

Key words : Chronic cough, tracheobronchomalacia, laryngeopharyngeal reflux disease

Introduction

Chronic cough is defined as cough lasting for > 8 weeks. Prevalence of cough in the population is estimated to be 40 % [1]. Various Indian studies show a prevalence of 2.5 to 5.8% [2]. Most common causes include upper airway cough syndrome (previously referred to as post nasal drip syndrome), asthma, non asthmatic eosinophilic bronchitis and GERD.

A 76 year old lady presented with history of cough since 10 years. It was a non productive cough with no diurnal, postural or seasonal variation. The cough was not associated with wheeze, dyspnea, chest pain or hemoptysis. There was no history of skin rashes, joint pains or recurrent fever. She did not have history of weight loss. She had symptoms suggestive of gastro oesophageal reflux disease. There was a family history of asthma. She was a house wife and there was no significant exposure to birds, pets, biomass fuel or passive smoking.

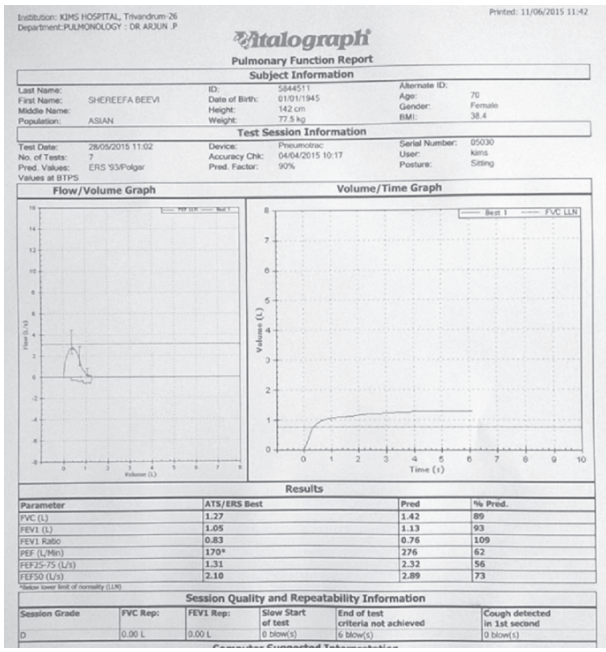
Four years back she presented with these symptoms to an ENT surgeon and on evaluation she was detected to have a retrosternal goiter which was presumed to be the cause of cough. This was later surgically removed and she was started on supplementary thyroxine. But her nagging cough persisted and hence she presented to a chest physician. Correlating her family history and cough she was started on a combination of long acting inhaled bronchodilator and steroids. Although she continued these medications for one year regularly, her symptoms did not have any respite.

At this juncture, she presented to our respiratory clinic.Her general examination and respiratory system examination were unremarkable. Her routine blood investigations as well as the chest radiograph were normal. Our evaluation mainly targeted the sinuses, the airway and gastrointestinal tract.

Her para nasal sinus imaging was normal. Her upper gastro intestinal endoscopy revealed antral gastritis. Nasal endoscopy revealed laryngeal pachydermia, suggesting GERD as a potential cause of cough. Although she was on long term PPI for more than an year, the cough

was persisting. Hence it was assumed that she had more than one cause for her cough.

With the past history of long standing goiter, the possibility of an acquired tracheomalacia was considered. She was evaluated with a spirometry, which revealed variable extrathoracic obstruction (fig 1). A computed tomogram of the thorax was showing evidence of tracheomalacia with more than 50% narrowing of the tracheal lumen during expiratory phase (fig 2 & 3). This narrowing was found extending to the main bronchi on both sides as well. She was advised for a bronchoscopic assessment also, but she declined the same.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Vitalograph

Pulmonary Function Report

Subject Information

Last Name:		ID:	5844511	Alternate ID:	
First Name:	SHEREEFA BEEVI	Date of Birth:	01/01/1945	Age:	70
Middle Name:		Height:	142 cm	Gender:	Female
Population:	ASIAN	Weight:	77.5 kg	BMI:	38.4

Test Session Information

Test Date:	28/05/2015 11:02	Device:	Pneumotrac	Serial Number:	05030
No. of Tests:	7	Accuracy Chk:	04/04/2015 10:17	User:	kims
Pred. Values:	ERS '93/Polgar	Pred. Factor:	90%	Posture:	Sitting
Values at BTPS					

Flow/Volume Graph

Volume/Time Graph

Results

Parameter	ATS/ERS Best	Pred	% Pred.
FVC (L)	1.27	1.42	89
FEV1 (L)	1.05	1.13	93
FEV1 Ratio	0.83	0.76	109
PEF (L/Min)	170*	276	62
FEF25-75 (L/s)	1.31	2.32	56
FEF50 (L/s)	2.10	2.89	73

*Below lower limit of normality (LLN)

Session Quality and Repeatability Information

Session Grade	FVC Rep:	FEV1 Rep:	Slow Start of test	End of test criteria not achieved	Cough detected in 1st second
D	0.00 L	0.00 L	0 blow(s)	6 blow(s)	0 blow(s)

Fig 1 : Spirometry showing presence of variable extra thoracic obstruction.

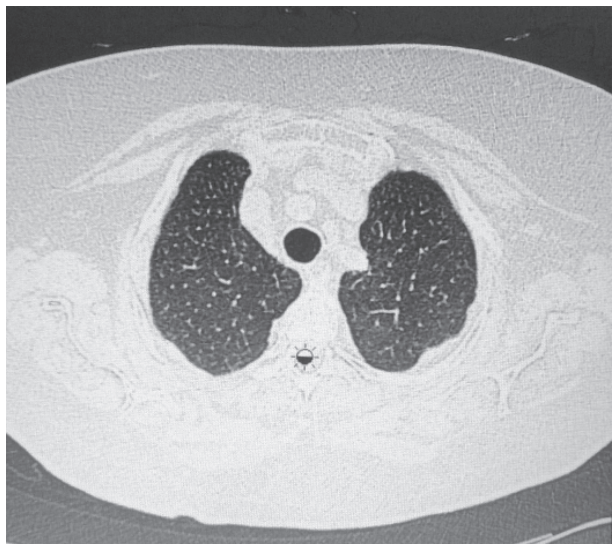

Fig 2 : CT thorax taken in inspiration, showing the tracheal lumen to be of normal caliber.

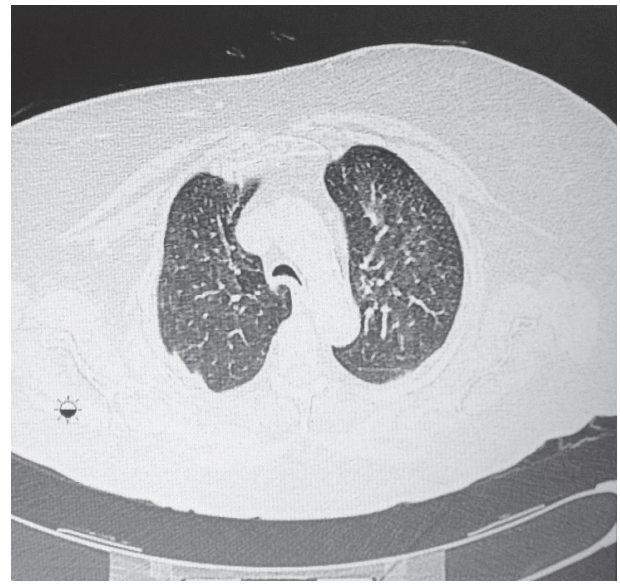

Fig 3 : Expiratory CT thorax showing > 50% reduction in tracheal lumen

A final diagnosis of a combination of tracheobronchomalacia with laryngopharyngeal reflux disease as the aetiologies for her cough was made. She was referred to thoracic surgeon for possible tracheobronchial stenting. As a stop gap treatment, she was managed with cough suppressants and proton pump inhibitors.

Discussion

The most common causes of chronic cough include - Upper airway cough syndrome (UACS) due to a variety of rhinosinus conditions, previously referred to as postnasal drip syndrome, asthma, nonasthmatic eosinophilic bronchitis (NAEB), and gastroesophageal reflux disease (GERD) . Each of these diagnoses may be present alone or in combination and may be clinically silent apart from the cough itself.[1]

Our lady was investigated for rhinosinusititis with nasal endoscopy and sinus imaging which turned out to be normal. Hence we proceeded to rule out other causes. The causes left were asthma, nonasthmatic eosinophilic bronchitis (NAEB), and gastroesophageal reflux disease (GERD). Next we planned a spirometric and upper GI endoscopic evaluation. The spirometry showed variable extrathoracic obstruction. Hence the possibility of asthma and NAEB were ruled out. Non asthmatic eosinophilic bronchitis is defined as a chronic cough in patients with no symptoms or objective evidence of variable airflow obstruction, normal airway hyperresponsiveness (ie, a

provocative concentration of methacholine producing a 20% decrease in FEV1 of 16 mg/ml), and sputum eosinophilia.[2]

Further she was evaluated with CT thorax with expiratory and inspiratory films which revealed the presence of tracheobronchomalacia

Tracheomalacia refers to diffuse or segmental weakness of trachea[1]. It is classified according to the etiology as congenital or acquired, according to the distribution as segmental or diffuse and according to the appearance as scabbard and saber sheath[2].

There are many causes for tracheomalacia. The most common acquired causes include tracheostomy and endotracheal intubation. Other eitiologies include chronic compression of the trachea most commonly due to a benign mediastinal goiter, malignancy, vascular compression, an abscess, a cyst or another benign lesion[3]. Relapsing polychondritis leads to the destruction of cartilage and trachoemalacia. Recurrent infections like cystic fibrosis and chronic bronchitis, cigarette smoke, exposure to mustard gas and gastroesophageal reflux disease (GERD) are the other causes[4].

The most likely etiologies in our patient could be attributed to long standing goiter and GERD.

The diagnosis of tracheobronchomalacia is by bronchoscopy, CT scan thorax and spirometry[5]. Bronchoscopic visualization of dynamic airway collapse during forced expiration is characteristic of the disease. CT thorax shows more than 50% expiratory collapse of the posterior wall. The treatment of choice is surgical repair – Tracheobronchoplasty[6]. It is usually not done since the expertise is available only in very few centres. The most commonly tried therapeutic option is tracheal stenting. Although this is a less invasive option, the chances of stent migration should always be kept in mind, which would require removal of stent and repositioning it. CPAP therapy also has been tried as a stop gap therapy as it is partially successful in preventing the expiratory collapse[7].

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Case Report

Partial Anomalous Venous Drainage of Lung (Scimitar Syndrome)

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Abstract : Presenting a case of partial anomalous venous drainage of lung (Scimitar syndrome). Importance of radiological imaging and clinical history is highlighted.

Introduction

Scimitar syndrome, or pulmonary venolobar syndrome, is a rare congenital heart defect characterized by anomalous venous return from the right lung (to the systemic venous drainage, rather than directly to the left atrium).[1] This anomalous pulmonary venous return can be either partial (PAPVR) or total (TAPVR). The syndrome associated with PAPVR is more commonly known as Scimitar syndrome after the curvilinear pattern created on a chest radiograph by the pulmonary veins that drain to the inferior vena cava.[2] This radiographic density often has the shape of a scimitar, a type of curved sword.[2]

Case Report

A 65 year old female, known case of hypothyroidism, hypertension on expectoration and breathlessness to our OPD with complaints of fever, cough, expectoration and breathlessness on exertion of 1 week duration of Grade 2 MMRC (Modified Medical Council Research) which was not progressing. She had cough with scanty mucoid expectoration of 1 week duration. There was no history of haemoptysis or purulent sputum production. History of recurrent respiratory infections was present. On examination she was afebrile and not tachypnoeic. Respiratory system examination showed no abnormality. Other system examination were normal. Routine blood investigations were normal except for hypothyroidism. Cardiology evaluation showed evidence of mild PAH(Pulmonary Artery Hypertension).

Chest radiography (Fig 1)showed a well defined homogenous opacity near the right paracardiac border silhoutting the lower right cardiac border.

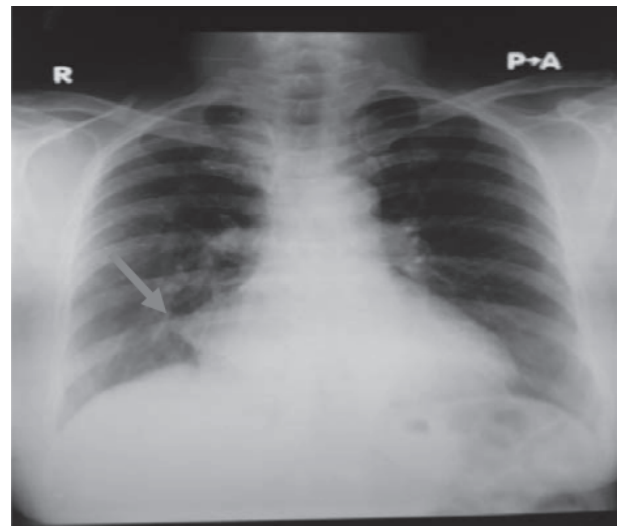

Fig 1 : Chest Xray showing a well defined homogenous opacity near the right para cardiac border silhouetting the lower right cardiac border.

A CT Thorax (Fig 2) with contrast (Fig 3) was taken which showed a well defined lesion near the right cardio phrenic angle.

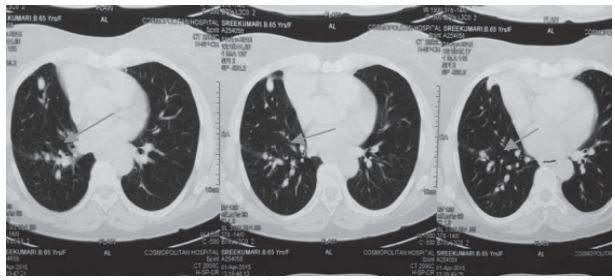

Fig 2 : CT thorax showing a well defined lesion near the right cardiophrenic angle.

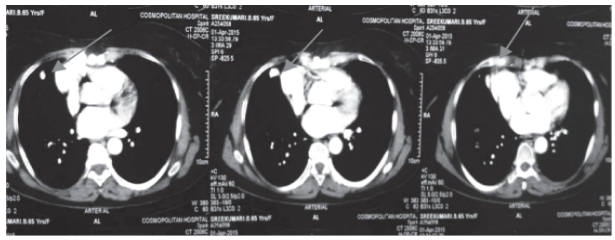

Fig 3 : CT Contrast showing a well taken contast lesion near the right cardiac phrenic angle.

The CT reconstructed image (Fig 3, 4) clearly depicted the abnormal pulmonary vein draining into the inferior venaca, thus arriving at a diagnosis of Scimitar Syndrome.

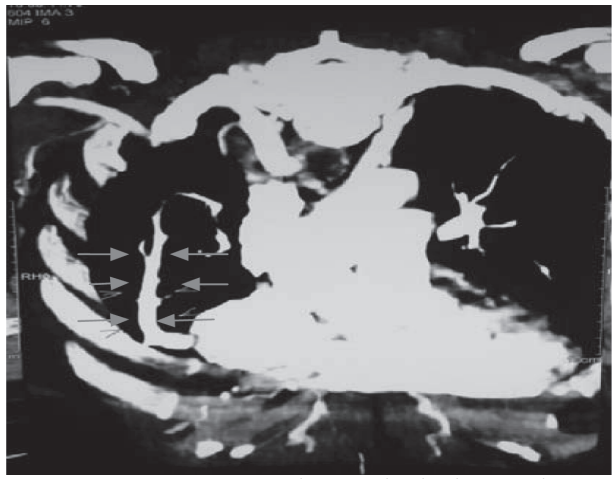

Fig 4 : CT reconstructed image clearly showing the abnormal right pulmonary vein draining into the inferior venacava , the characteristic 'scimitar sign'.

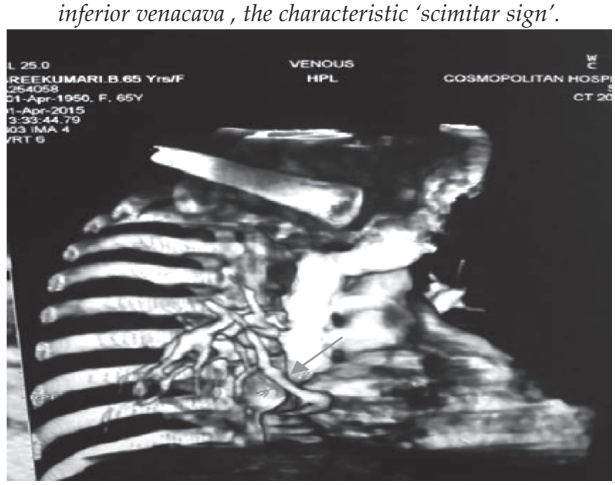

Fig 5 : CT reconstucted image showing the abnormal right pulmonary vein draining into the inferior venacava.

Case Discussion

Scimitar syndrome (also known as **pulmonary venolobar syndrome** or **hypogenetic lung syndrome**)[4] is characterised by a hypoplastic lung that is drained by an anomalous vein into the systemic venous system. It is a type of partial anomalous pulmonary venous drainage.

Pathology

It is essentially a combination of pulmonary hypoplasia and partial anomalous pulmonary venous return (PAPVR). It almost exclusively occurs on the right side.

Haemodynamically, there is an acyanotic left to right shunt. The anomalous vein usually drains into

- inferior vena cava - most common
- right atrium
- portal vein

The lung is frequently perfused by the aorta, but the bronchial tree is still connected and thus the lung is not sequestered.

Associations

- congenital heart disease (e.g. ASD, VSD, tetralogy of Fallot, PDA)
- ipsilateral diaphragmatic anomalies (e.g. accessory diaphragm, diaphragmatic hernia)
- localised bronchiectasis
- horse shoe lung
- vertebral anomalies (e.g. hemivertebrae)[4]
- genitourinary tract abnormalities[4]

Radiographic Features

The diagnosis is made by transthoracic or transesophageal echocardiography, angiography, or by CT or MR angiography[7,8].

Plain Film

Chest radiographic findings are that of a small lung with ipsilateral mediastinal shift, and in one third of cases the anomalous draining vein may be seen as a tubular structure paralleling the right heart border in the shape of a Turkish sword ("scimitar"). The right heart border maybe blurred.

Complications

The presence of a left-to-right shunt may lead to development of pulmonary hypertension and Eisenmenger physiology.

Treatment

Surgical correction should be considered in the presence of significant left to right shunting and pulmonary hypertension. This involves creation of an inter-atrial baffle to redirect the pulmonary venous return into the left atrium. Alternatively, the anomalous vein can be re-implanted directly into the left atrium[9].

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Case Report

An Unusual Cause for Recurrent Haemoptysis and Pneumothorax

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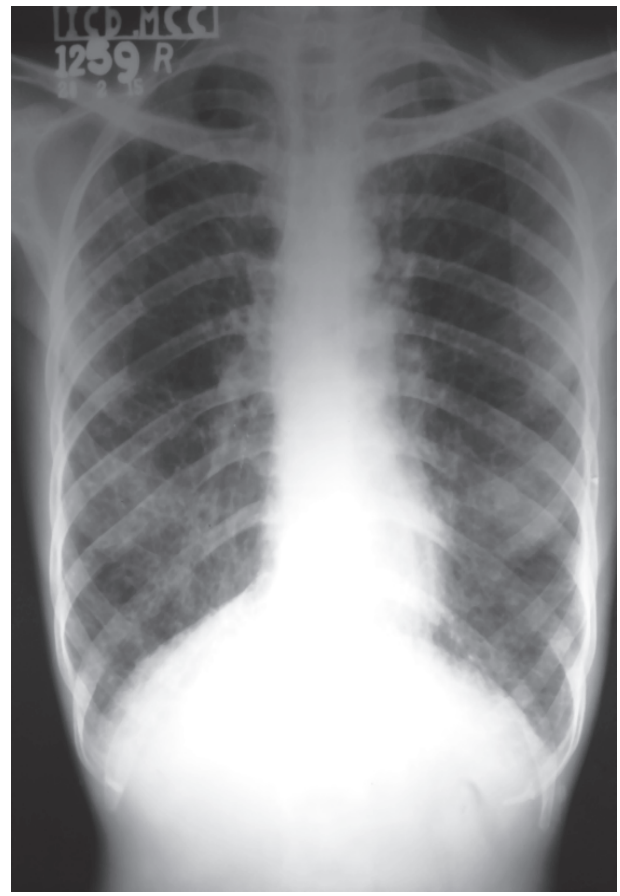
Abstract : Lymphangioleiomyomatisis (LAM) is a rare cystic lung disease of unknown cause that usually affects young women of reproductive age. Here we present a case of 48 year old nulliparous female with progressive dyspnoea and recurrent pneumothorax who was diagnosed to have LAM based on typical HRCT findings of thin walled cystic lung lesions. This article briefly describes on the etiology, pathology, diagnosis and treatment of LAM.

Key words : LAM, recurrent pneumothorax

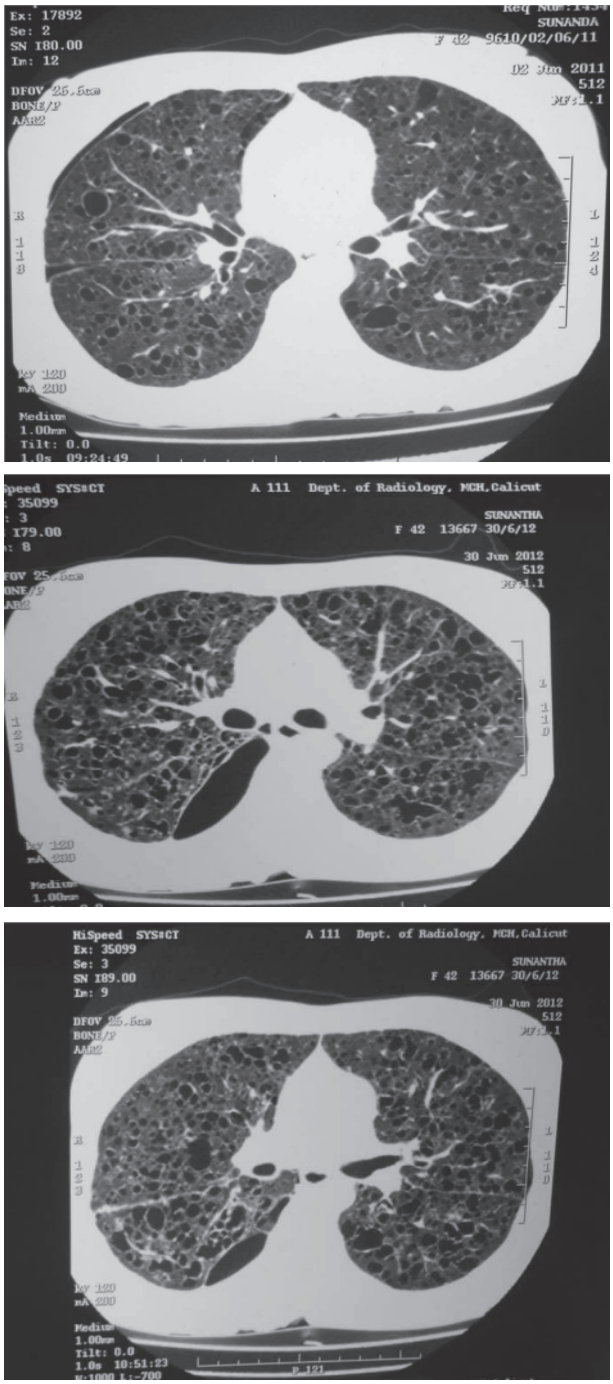
A 48 year old female, nonsmoker, presented with progressive dyspnoea, dry cough and streaky haemoptysis of 5 years duration.There was no history of wheeze or chest pain. There was history of recurrent bilateral pneumothorax for 5 years and all episodes were managed conservatively. There was no family history of similar illness. She was married and on treatment for infertility for past 3 years. There was history of myomectomy 8 years back.

On examination there was tachypnoea and tachycardia. There was no clubbing or lymphadenopathy. On respiratory system examination, trachea and mediastinum were central, upper border of liver dullness was in right 7th inter costal space in mid clavicular line, breath sounds were bilaterally equal and there were no added sounds. Other systems examination was normal.

Her routine haematological investigations were normal. ANA profile, Rheumatoid factor were negative. Chest xray showed hyper inflated lungs with bilateral diffuse cystic shadows. HRCT thorax showed bilateral numerous thin walled cystic lesions throughout the lung fields with evidence of pneumothorax on right side suggesting lymphangioleiomyomatosis. USG abdomen was normal. Spirometry showed obstructive pattern and DLCo was reduced.



Chest X ray shows hyperinflation and multiple cystic shadows throughout the lung fields predominantly in the midzone



CECT Thorax shows bilateral thin walled cystic lesions of varying sizes and pneumothorax on right side.

Discussion

Lymphangioleiomyomatosis (LAM) is a multisystem disorder, predominantly affecting women, which is characterized by cystic lung lesions, abdominal angiomyolipomas (AML) and lymphatic abnormalities, like lymphatic tumours and chylous effusions. Inherited and sporadic forms of LAM have been described[1]. Sporadic LAM is caused by somatic mutations in an unknown susceptible cell of the tuberous sclerosis complex (TSC)2 (TSC2) gene[2]. LAM also occurs in TSC, an autosomal dominant disorder resulting from germline mutations in the TSC1 or TSC2 genes that is characterized by widespread hamartomas in several organs including the brain, heart, skin, kidney, eyes, lung, and liver, and occurs in 1 of 6000 livebirths. Sporadic LAM is an uncommon disease occurring in approximately 4.9/1,000,000 women[3].

LAM is now best defined as a chronic disease of post- and premenopausal women with a life expectancy spanning decades. Patients with LAM often present with a history of progressive dyspnea and recurrent pneumothorax. The other modes of presentation include chylothorax, abdominal lymphangioleiomyomas, chylous ascites, hemoptysis, chyluria, chyloptysis and hemorrhage caused by renal AML. The physical examination of LAM patients may disclose wheezing, pleural effusions, ascites or intra-abdominal masses. In patients with TSC, typical skin lesions or signs of brain involvementmay be evident.

Sporadic LAM is caused by proliferation of neoplastic LAM cells that have mutations or deletions in the TSC2 (16p13) gene. The mechanism by which interstitial LAM cell proliferation causes lung cyst formation is unknown. It has been proposed that compression of the airways by LAM cells leads to distension of the terminal airspaces and cyst formation.It has also been proposed that degradation of lung elastic fibers is a major cause of the cystic lesions. Matrix metalloproteinases, which play a role in lung remodeling and lymphangiogenesis, are associated with LAM[4]. Airflow obstruction was seen in approximately 61% of patients with sporadic LAM, normal spirometry was present in about 31%. The remaining patients had restrictive disease[5]. Most patients have both decreased FEV1 and DLCO.

Chest radiographic findings in LAM range from being normal, to showing a reticular or nodular irregular shadowing or, in advanced stages, severe cystic changes. Computed tomography (CT) demonstrates diffuse, well-defined, round thin-walled cysts scattered throughout the lungs. Cysts vary in size from a few millimeters to up to 2 cm[6]. HRCT is highly distinctive and cardinal feature is nuerous thin walled cysts[<20 mm diameter] distributed diffusely throughout both lungs with normal intervening parenchyma. Usually, nodules are absent in HRCT. Abdominal CT and ultrasonography studies may show renal AML, abdominal lymphadenopathy, lymphangioleiomyoma, ascites, and dilatation of the thoracic duct.

The diagnosis of LAM should be strongly suspected in any woman who presents with progressive dyspnea, recurrent pneumothorax, or a chylous pleural effusion.The differential diagnosis includes pulmonary emphysema, asthma, chronic extrinsic allergic alveolitis, Langerhans cell histiocytosis, sarcoidosis, Birt–Hogg–Dubé syndrome, and follicular bronchiolitis

Definite LAM may be diagnosed in the presence of a characteristic HRCT and a lung biopsy showing the pathologic features of LAM or a characteristic lung HRCT and 1) angiomyolipoma, 2) chylous effusion, 3) lymphangioleiomyoma or lymphadenopathy, and 4) TSC. A diagnosis of probable LAM may be established in the presence of a characteristic HRCT and a compatible clinical history or a characteristic HRCT and angiomyolipoma or chylous effusions.

Possible LAM may be diagnosed in the presence of a characteristic or compatible HRCT.

The clinical course of LAM is highly variable.The estimated 10-year transplant-free survival is 86%. Age appears also to affect survival, as rapid decline in lung function is more common in younger premenopausal patients. The severity of lung involvement in LAM may be assessed in patients who had a lung biopsy using the LAM Histology Score (LHS), which grades the extent of replacement of normal lung tissue by cystic lesions and LAM cell infiltrates. The severity of lung disease in LAM can also be graded by HRCT. HRCT findings correlate with lung function tests, gas exchange, and exercise performance. HRCT computer analysis can quantify the percentage of lung volume affected by cysts and evaluate the texture of areas not involved with cysts. Other prognostic indicators include spirometry and DLCo[7]. VEGF-D, a lymphangiogenic factor, is increased in the serum of patients with LAM compared to normal individuals[8].

Treatment options of LAM include antiestrogen therapy, mTOR inhibitors, matrix metalloproteinase inhibitors, statins, and inhibitors of autophagy. Antioestrogen therapies include Oophorectomy, progesterone, and gonadotrophin-releasing hormone (GnRH) analogs . Based on the findings in the MILES trial it is recommend that sirolimus (mTOR inhibitors) may be given to patients in whom lung function is declining rapidly and also recommend sirolimus therapy for LAM patients with symptomatic lymphangioleiomyomas and chylous pleural effusions or ascites[9]. A potential role of doxycycline in the treatment of LAM was suggested by a report of one patient with LAM in whom treatment with doxycycline decreased urinary MMP levels and improved lung function. A decrease in serum and urine levels of MMP-9 and MMP-2 in 34 patients treated with doxycycline has been reported. A controlled study showed that it is unlikely that doxycycline has a useful effect in LAM. Autophagy is a mechanism by which cells maintain energy homeostasis and recycle proteins and organelles. Hydroxychloroquine and its analogs inhibit the growth of cancer cells and induce cell death by blocking autophagy A current study (SAIL trial) testing the effects of sirolimus and hydroxychloroquine is ongoing .Lung transplantation be considered when FEV1 and DLCO are less than 30% predicted, and the patient is on continuous supplemental oxygen and unable to carry out activities of daily living.

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