Review Article

Brittle Asthma

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Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity ,together with variable expiratory airflow limitation[1]. Asthma has a very wide clinical spectrum, at one end of which is the patient with mild intermittent symptoms and at the other extreme the patient whose symptoms are difficult to control despite the best all-round efforts. This reflects in clinical practice where the physician finds it difficult to control asthma in spite of the optimized treatment. The term "brittle asthma" was first used in 1977 to describe patients with asthma who maintained a wide variation in peak expiratory flow (PEF) despite high doses of inhaled steroids[2]. Based on the PEF variability different asthma phenotypes are described. Asthmatics were labeled as 'morning dippers' if they had an early morning fall in their PEF, 'double dippers' if the PEF dipped twice in a day or 'chronic persistent' if their PEF showed low values with less variability[3]. The brittle asthmatic pattern of PEF variability was identified as a separate group, being described as 'chaotic' showing no such obvious repeating pattern. The significance of the brittle pattern is that these patients had more severe asthma that was difficult to control and could lead to a sudden attack and death. Brittle asthma is a rare disease and the prevalence of brittle asthma is of the order of 0.05% of all asthmatics[4].

Definitions :

Brittle asthma is defined as a diurnal PEF variability of > 50% on at least three days per week despite maximal medical treatment including high doses of inhaled corticosteroids with repeated doses of inhaled bronchodilator and maintenance or courses of oral corticosteroids[5].

Type 1 brittle asthma is characterised by a maintained wide PEF variability (> 40% diurnal variation for > 50% of the time over a period of at least 150 days) despite considerable medical therapy including a dose of inhaled steroids of at least 1500 μg of beclomethasone or equivalent.

Type 2 brittle asthma is characterised by sudden acute attacks occurring in less than three hours without an obvious trigger on a background of apparent normal airway function or well controlled asthma[6].

Risk Factors :

The risk factors for Type 1 brittle asthma are atopy, impairment of local immunity, increasing susceptibility to respiratory infections and psychological factors. About 60% of patients are allergic to dairy products, wheat, fish, citrus, egg, potato, soya, peanut and yeast which are the most common food triggers for brittle asthma[7]. Psychosocial factors play an important role; depression, broken relationships and physical and sexual abuse are often seen in type 1 brittle asthma. Women are more prone to develop type 1 brittle asthma although the reason is not known.The male-female ratio is 1:2.5 most being aged between 15 and 25yrs[8]. Some women with brittle asthma show typical exacerbations in relation to

menstruation[9]. The risk factors for type 2 brittle asthma are exposure to aeroallergens such as fungal spores and poor perception of the disease. Whether the impaired perception is inherited or acquired is not known[10].

Possible underlying mechanisms:

Brittle asthma patients are difficult to investigate because of the potential danger of invasive investigations. Even the measurement of bronchial reactivity may be contraindicated in such patients. Many patients find that more than one forced expiratory manoeuvre is enough to cause significant worsening of their condition without adding a further bronchoconstricting stimulus[6].

On bronchoscopy patients with severe brittle asthma had atrophic alterations, inflammatory mucosal infiltration, marked bronchial remodeling in spite of therapy with high doses of inhaled corticosteroids[11]. It remains, however, of particular importance to determine whether the inflammatory pattern is the same in brittle asthma as in the other types of asthma.

Clinical features and Diagnosis:

Brittle asthma is recognised by sudden life threatening attacks on the background of a wide PEF variability or apparent normal airway function and significant difficulties to manage the disease[12]. Type 1 brittle asthma is common in women but type 2 brittle asthma is equally prevalent in men and women. Diagnosis of brittle asthma involves careful exclusion of all the factors that may be responsible for poorly controlled asthma. Even though PEF monitoring is not popular in India ,its recording will be helpful in establishing a proper diagnosis of brittle asthma[3].

Management:

Patients with brittle asthma are extremely difficult to manage. The standard guidelines for asthma are not applicable, because the brittle asthmatic patients are on high doses of inhaled steroids and bronchodilators. So when there is worsening, they have to take oral steroids.

Type 1 brittle asthma:

Patients with type 1 brittle asthma already receive treatment with the high doses of inhaled and / or oral steroids & inhaled bronchodilators. Non-pharmacological treatment includes the control of allergens, identification and avoidance of allergic food, good dietary support etc[13].

1. The treatment begins with a control of allergen exposure and avoidance of food products to which the patients are intolerant .
2. Immunomodulators: Cyclosporine, Methotrexate and intravenous immunoglobulins have been tried to reduce high dose of steroids.
3. Long term continuous subcutaneous infusion of beta 2 agonist - terbutaline 3-12mg/day[14].
4. Long acting beta 2 agonists: Salmeterol & formoterol are effective in view of the wide variation in PEF in selected cases. Clinically formoterol is better than salmeterol in managing brittle asthma[15].

Type 2 brittle asthma:

Managing type 2 brittle asthma is less complex. The treatment of patients with type 2 brittle asthma, who are relatively symptom free, includes control of allergen exposure, identification of triggers, self management and management of acute attacks[16]. Every patient should be supplied with a card providing relevant information and if possible a preloaded adrenalin syringe (Epi-pen) also because of sudden, severe, unexpected attacks that require emergency interventions[17]. Once adrenalin has been injected the patient should be advised to use a dose of nebulised salbutamol or terbutaline and proceed to the emergency department. In the case of acute respiratory insufficiency, mechanical lung ventilation is required.

Other agents :

Leukotriene antagonists, type IV phosphodiesterase inhibitors, cytokine inhibitors and tachykinin antagonists have been tried with limited success in selected patients[18].

Conclusion :

Type I and type II brittle asthma should be regarded as separate clinical phenotypes of asthma. These patients are rare and pose difficult and complex management problems. The patients affected with type 1 brittle asthma have to be closely monitored and treated. Patients affected with type 2 brittle asthma, are mostly free of symptoms, but they have severe attacks that lead them to emergency treatment. Brittle asthma is a rare form of severe asthma, that clinicians have to recognize and treat very strictly, because of high morbidity and mortality.

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