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Association of nephrotic syndrome with bronchial asthma: two case reports

Sir,

Little is known about the relationship between Nephrotic syndrome (NS) and bronchial asthma. However, an association between NS and other allergic phenomena has long been described with case reports describing NS triggered by bee stings, poison ivy and pollen hypersensitivity **[1,2]**. Several other studies **[3-7]** have also confirmed that there is an increased incidence of atopy and family history of atopy in patients with NS. Overt atopic disease at the time of nephrosis is uncommon with only one case report of 2 children with infantile nephrotic syndrome (one had bronchial asthma, the other infantile eczema) **(8)**. We therefore report 2 cases of NS occurring in older children, one developed an acute attack of bronchial asthma before and during a relapse of NS and the other developed her acute attacks of bronchial asthma while clinically stable from NS.

Case 1. A 6-year-old male patient presented with 5 day history of facial swelling and cough and a day history of difficulty in breathing. He was discharged from the hospital 10 days earlier after receiving treatment for acute bronchial asthma. He had no preceding history of sore throat or skin rash. Cough started around the same time the facial swelling was noticed. It was worse in the night and was followed by difficulty in breathing a day to presentation. There was no paroxysmal nocturnal dyspnea or orthopnea. He had recurrent facial swelling on 3 differrent occasions within the 2 year period preceding the current presentation. He is the 5th of 8 children of a monogamous marriage with no family history of bronchial asthma, allergic rhinitis or infantile eczema.

Major findings at physical examination included a conscious and restless child who was wheezing, in obvious respiratory distress and had widespread bilateral rhonchi. There was facial puffiness but no pedal edema. The blood pressure was 160/120 mmHg and no gallop rhythm.

Urinalysis showed nephrotic range proteinuria (3+ and 3g/24hours) and hematuria -2+. Electrolyte and urea result showed urea of 7.9 mmol/l, potassium of 6.4 mmol/l and sodium of 134 mmol/l. An assessment of NS with acute pulmonary edema to exclude bronchial asthma was made. He received anti-hypertensives (hydralazine and reserpine) to control the blood pressure. He also received frusemide which was changed to oral hydrochlorothiazide when the facial puffiness, cough and respiratory distress subsided on the 4th day. At this period the rhonchi had also diminished remarkably. However, on the 8th hospital day, 4 days after this observed clinical improvement, cough started again with difficulty in breathing and increased rhonchi bilaterally. Salbutamol inhaler was administered to the patient first, every 15 minutes for 4 hours then every hour for 4 hours then every 2 hours. Marked improvement occurred within 24 hours and he was discharged from the hospital 2 days later.

The patient has been attending both the nephrology and respiratory clinic since discharge and did not develop a relapse of NS until 9 months after discharge. He also developed another acute episode of bronchial asthma 7 months after discharge to which he responded promptly to nebulised salbutamol and was discharged home after observation for 2 hours. At last follow up, his NS was in relapse. His urinalysis showed proteinuria of 3+ and hematuria of 3+. He is currently on oral hydrochlorothiazide, spirinolactone and lisinopril daily.

Case 2. A 12 year old girl who presented with NS at 5 years of age and was in remission for 6 years until she relapsed and was admitted because of severe hypertension and acute renal failure. A year after this admission, she presented with cough and difficulty in breathing of a day duration. There was no preceding runny nose. There is no history of bronchial asthma, allergic rhinitis or infantile eczema in her siblings or both parents.

Physical examination revealed that she was dyspneic and tachypneic with widespread rhonchi and no crepitations. A clinical impression of bronchial asthma was made. Chest radiograph revealed no abnormality. She was given intravenous aminophylline 250 mg stat and thereafter salbutamol inhaler 2 puffs two hourly and improved shortly after the administration of aminophylline. The patient was discharged from the hospital one day later. She remained free of attack until 7 months later when she presented again with one day history of cough, dispend and presence of rhonchi bilaterally in the chest. She responded promptly to salbutamol inhaler and did not require hospitalization. She has been attending the respiratory and nephrology clinic regularly. She is currently on thiazide and spironolactone only. She still develops relapse of NS occasionally.

Discussion

In the 2 patients under review, only patient 1 had an attack of bronchial asthma during a relapse of NS. That episode was initially suspected to be due to pulmonary oedema despite the obvious wheezing and presence of rhonchi and diuretics was given. Although this patient's symptoms seemed to have subsided, they recurred a few days later. The resurgence completely subsided after the administration of bronchodilators, which may imply that an acute episode of bronchial asthma occurred in that patient. Furthermore, this same patient developed a similar episode 10 days earlier. In patient 2, her 2 attacks of bronchial asthma occurred independently of relapses of NS. None of the routine drugs she was receiving was known to trigger bronchial asthma. She also has no family history of asthma, allergic rhinitis or infantile eczema.

Our report is unique because the association between NS and bronchial asthma was specifically observed in older children (5 years and 12 years). Furthermore, a simultaneous occurrence of NS and bronchial asthma occurred in one of them during a relapse of NS. However, none of our patients had a family history of atomic diseases.

NS and bronchial asthma bear similarity in their hyper-responsiveness to foreign antigens through immune mediated mechanism. This results in immune complex glomerular injury **[9]** in the nephrotic syndrome and airway constriction in the case of bronchial asthma. The comparison or similarity stops at the immune mediated responses but the pattern and mediator for responses differ markedly. In bronchial asthma, there are several mediators involved in causing bronchoconstriction which include major basic protein (MBP), histamine, leukotrienes, prostaglandins, thromboxanes and platelet activating factors (PAF) **[10]**. Most of these are not involved in glomerular injuries. However it has been found that atopic individuals presenting with NS especially if the nephrosis is frequently relapsing may

have increased level of serum IgE [11] and interleukin-4 with the IgE correlating with IL-4 levels and the degree of proteinuria correlating with IL-4 concentration [12].

In conclusion NS and bronchial asthma can occur in the same patient either simultaneously during a relapse of NS as seen in patient 1 or in a stable state as seen in patient 2. The fact that one of our patients presented simulataneously with a relapse of NS and acute bronchial asthma suggest that there may be some association between NS and bronchial asthma. Further research into the immunological pathways activated in the 2 diseases is suggested.

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