

## Varicella may cause asthma

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**Key words:** asthma; chickenpox; exacerbation; varicella; virus.

• VARICELLA, more commonly known as chickenpox, is an extremely contagious infectious disease characterized by generalized exanthematous rash (1). Varicella has recently become a concern in patients with asthma because of the potential for pulmonary and/or systemic infection with high-dose inhaled corticosteroids. Although no link has yet been established, a potential association is theoretically possible (2, 3). Two cases of varicella associated with asthma exacerbations are described.

### Two cases of chickenpox-induced asthma exacerbation.

Patient 1 was a 6-year-old girl with a 4-year history of asthma who presented to our outpatient clinic with cough and maculopapular eruption mainly localized on her body. She was taking 200 µg beclomethasone daily and had been found to be allergic to house-dust mites. In December 1997, 2 weeks after the outbreak of chickenpox in her classmates, she developed a mild fever and pruritic maculopapular exanthema consistent with varicella. On day 2 of her illness, she developed a mild,

nonproductive cough with a nighttime and early morning predominance, which responded poorly to salbutamol. On chest auscultation, few rhonchi were audible. Spirometry revealed mild airway obstruction (Table 1), and the chest radiograph was clear. On day 5 of her illness, the cough worsened although no change in the severity of obstruction was found by spirometry. A repeat chest radiograph was clear with no infiltration. Over the next 5 days, the cough lost its dry character and subsided. The pulmonary function studies returned to baseline 1 week after the onset of the illness. Methacholine challenges (4) performed on days 10 and 24 after the onset of the illness revealed PC<sub>20</sub> of 0.11 and 1.13 mg/ml, respectively.

Patient 2 was an 11-year-old boy who presented to our outpatient clinic with a dry cough, reduced exercise capacity, and skin eruptions. The patient had a history of nonatopic asthma diagnosed at 5 years of age. He was well controlled with formoterol and 400 µg budesonide daily. Exacerbations mainly occurred with viral infections. A week before presentation, there was an outbreak of chickenpox among his classmates. A cough was noted on the day that the first varicella skin lesions appeared. Physical examination revealed active varicella with end-expiratory wheezing and mild intercostal retractions. Spirometry showed a severely obstructive pattern (Table 1), and the chest radiograph was

clear with no infiltrates. Since he had several attacks which required systemic corticosteroids within the last year, the dose of inhaled budesonide was increased to 1200 µg daily in three divided doses. Daily controls revealed that symptoms and airway obstruction subsided gradually to baseline levels within a week.

This is the first report of an association between chickenpox and asthma exacerbation. Since chickenpox is a disease of childhood, 90% of cases occur in children less than 3 years of age (1), and this may partly explain its escape from medical attention as a provoking agent of asthma. The impracticality of pulmonary function tests, as well as the fact that cough is a common symptom of most respiratory infections in this age group, may result in an underestimation of the true incidence of airway obstruction. Additionally, the mild and self-restricted nature of varicella-associated asthma exacerbations may lead to the impression that the symptoms are not related to asthma. Furthermore, varicella does not seem to cause exacerbation in all patients with asthma. A similar situation occurs with many other respiratory viruses that may cause either upper or lower respiratory tract infection. The factors that determine which children develop upper respiratory tract symptoms, wheezing, or pneumonia after infection are currently not well defined but seem to involve both host-specific contributions and environmental exposures

**Table 1.** Pulmonary function (patient 1, height: 118 cm; patient 2, height: 133 cm)

| Day of eruption |                  | 3          |            | 5          |             | 7 (10 in patient 2) |            |
|-----------------|------------------|------------|------------|------------|-------------|---------------------|------------|
|                 |                  | pre        | post       | pre        | post        | pre                 | post       |
| Patient 1       | FVC              | 1.08 (78%) | 1.08 (78%) | 1.31 (95%) | 1.63 (118%) | 1.37 (99%)          | –          |
|                 | FEV <sub>1</sub> | 0.69 (56%) | 0.83 (67%) | 1.37 (99%) | 1.50 (120%) | 1.31 (105%)         | –          |
| Patient 2       | FVC              | 0.73 (33%) | 0.81 (36%) | 0.96 (43%) | 1.63 (69%)  | 1.09 (49%)          | 1.50 (64%) |
|                 | FEV <sub>1</sub> | 0.65 (32%) | 0.65 (32%) | 0.88 (43%) | 1.57 (73%)  | 1.09 (54%)          | 1.50 (70%) |

(5). In conclusion, varicella should be considered a potential cause of asthma exacerbations.

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## Acetaminophen-induced rhabdomyolysis

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**Key words:** acetaminophen; cytokines; drug reactions; oral challenge; rhabdomyolysis.

● AMONG the side-effects of acetaminophen, previous reports have included anaphylactic shock and various skin reactions (1–3). Thrombopenia and agranulocytosis have been also observed, as well as hepatitis. We

report the first case of hypersensitivity rhabdomyolysis.

A 17-year-old man was admitted for numerous iatrogenic accidents. When aged 3 months, he had presented hepatitis with agranulocytosis after acetaminophen administration. At 10 years of age, desquamative dermatitis occurred during treatment with cefaclor and acetaminophen. At 14 years of age, he developed a febrile eruption after receiving amoxicillin and acetaminophen, which intensified after paracetamol injection. Epicutaneous tests (ECT) and the intradermal test (IDT) on delayed reading with amoxicillin were distinctly positive. Delayed-type hypersensitivity to amoxicillin was considered. Prick test and ECT with acetaminophen were negative, as was the IDT with paracetamol on immediate and delayed reading and paracetamol-specific IgEs. However, the whole history led the patient's parents to incriminate acetaminophen, requesting further investigations. An oral challenge was carried out with paracetamol 400 mg. Within 5 h, he presented febrile exanthema, neutropenia, and a rise of CRP and CPK MM (Table 1) and an elevation of the seric levels of TNF- $\alpha$  (49 pg/ml; N=8–10), IL-6 (23 pg/ml; N=0–2), and IL-10 (6 pg/ml; N=nd). The lymphocytic subpopulations showed a decrease of CD4+ (16%) with an increase of CD8+ (37%). The eruption and fever lasted 36 h.

### The first report of a patient with rise of serum IL-6, TNF- $\alpha$ , and IL-10.

Hypersensitivity accidents have rarely been reported. One single case of toxic paracetamol-induced myocarditis is described (4). It can be postulated that until now rhabdomyolysis has been overlooked. The mechanisms of acetaminophen hypersensitivity have not yet been elucidated. Acetaminophen is probably involved per se when the onset of symptoms is fast, and immediate tests prove positive (1, 3). The occurrence of delayed reactions, and the negative skin tests, are more in favor of a drug metabolite. Specific IgEs might be involved in shocks, but no proof has been obtained by cutaneous tests or leukocyte histamine-release tests.

The increase of TNF- $\alpha$  and IL-6 may point to activated macrophages and lymphocytes. Among their effects, fever and muscular catabolism were reported. The severity of toxidermia after a single dose of 400 mg would have been potentially life-threatening, had the acetaminophen not been immediately stopped.

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**Table 1.** Evolution of CRP and muscular and hepatic enzymes

| Days | C-reactive protein<br><5 mg/l | ASAT<br>5–35 UI/l | Total CPK<br>25–220 UI/l | CPK MM<br>UI/l | ALAT<br>5–40 UI/l |
|------|-------------------------------|-------------------|--------------------------|----------------|-------------------|
| 1    | 7                             | 49                | 1747                     | –              | 24                |
| 2    | 34                            | 53                | 1268                     | 1236           | 35                |
| 13   | <5                            | 20                | 252                      | –              | 14                |