Hypoxanthine guanine phosphoribosyl transferase deficiency

SUMMARY An 8 year old girl treated with carbamazepine developed eczema, wheeze, and evidence of pulmonary eosinophilia. Single dose challenge confirmed allergy to this drug. This reaction should be considered in patients being treated with carbamazepine who develop respiratory symptoms.

Case report

A Pakistani girl aged 8 years 11 months who had no past history of respiratory symptoms presented with cough and wheeze of two months' duration and a generalised eczematous rash that had been present for one month. She had been started on carbamazepine elixir 12 weeks previously for the treatment of temporal lobe seizures, and at the time of presentation was taking 300 mg daily. There was no other notable past history or relevant family disorders apart from a maternal history of recurrent cough and wheeze treated with cromoglycate.

On examination the child was afebrile with a generalised itchy, eczematous rash. Her chest was of normal shape and she had widespread expiratory wheeze. Peak expiratory flow rate was 120 l/min (expected 190 l/min). Chest radiographic examination showed collapse/consolidation of the right middle lobe accompanied by a diffuse increase in bronchovascular markings (Figure). Her blood count yielded an absolute eosinophilia of 11.07 x 10^9/l (11 070/mm^3) (54% of 20-5). Serum immunoglobulins including IgE were not raised, a complement screen was negative, and no immune complexes were detected in serum. Screening of urine, stool, and blood for fungal, parasitic, and bacterial infection was negative. Avian and fungal precipitin testing was negative and serum titres to mycoplasma and common respiratory viruses showed no evidence of recent infection. Prick tests to animal dander, pollen, and fungal allergens were negative.

Carbamazepine was stopped and she was given sodium valproate. The eosinophil count fell to 2-06 x 10^9/l (2060/mm^3) four days later. The wheeze and rash were treated with sodium cromoglycate, salbutamol, and chlorpheniramine. One month later there was no detectable wheeze or rash, her peak expiratory flow rate was 190 l/min, and no seizures were reported. All treatment except sodium valproate was stopped and she remained well except for one episode of wheeze associated with an upper respiratory infection.

Six months after presentation she was challenged with 20 mg of oral carbamazepine elixir. Peak expiratory flow rate fell from 200 l/min (100% expected) to 100 l/min, when measured 3½ hours after this dose and she also developed wheeze with pruritis. Over the next 24 hours her peak flow rate steadily improved to 155 l/min and she became asymptomatic.

Discussion

Of the four similar adult cases described in reports, two were complicated by tuberculosis and mycoplasma infection. A third patient presented with respiratory symptoms after the drug had been withdrawn, and in the fourth, recovery was delayed until 6 months after drug treatment was stopped: a subsequent clinical challenge did not show air flow obstruction, although there was a worsening of asthmatic control on reintroducing carbamazepine at a therapeutic dose. In the child we describe,

References


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Pulmonary eosinophilia associated with carbamazepine

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clinical signs and symptoms rapidly resolved on stopping carbamazepine and the subsequent in vivo challenge seemed to confirm sensitivity. It should be noted, however, that a family history of atopy and the recurrence of wheeze during an intercurrent respiratory infection make a diagnosis of asthma likely in our patient.

The marked peripheral eosinophilia, rash, and chest radiological changes suggest an immunological basis for this reaction. An eosinophilic marrow response and acute interstitial inflammation with plasma cells and eosinophils is also reported in this condition.\textsuperscript{1,2} There seem to be no reliable in vitro tests for drug hypersensitivity; lymphocyte transformation tests with carbamazepine may be negative during and shortly after hypersensitivity reactions to this drug,\textsuperscript{3} and tests for specific antibody and patch testing are also unhelpful.

It seems unlikely that other constituents of carbamazepine elixir (which include sorbitol, sorbic acid, sodium saccharine, methylhydroxybenzoate, propylhydroxybenzoate, and propylene glycol) are responsible for the allergic reaction since these additives are present in small quantity and they are not present in the tablet preparations used in those adults who developed allergy. This possibility cannot, however, be completely discounted.

Hypersensitivity to carbamazepine should be considered in children receiving this drug who develop respiratory symptoms, especially wheeze. Awareness of this potential hazard and investigations including peak expiratory flow rate, full blood count and differential count, and chest radiograph aid early diagnosis.

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