SHORT REPORTS

Idiosyncratic reactions to carbamazepine mimicking viral infection in children

Adverse reactions to carbamazepine include rashes, lymphadenopathy, hepatosplenomegaly, and bone marrow depression ranging from mild leukopenia to aplastic anaemia. Such reactions are rare in children. Mild leucopenia does not indicate withdrawal of the drug, but more serious bone marrow and systemic effects do. We report two cases in which the initial presentation mimicked viral infection and was associated with profound neutropenia.

Case reports

Case 1—A 1 year old girl with poorly controlled myoclonic and complex partial epilepsy developed fever and cervical lymphadenopathy eight weeks after carbamazepine had been added to her treatment. Five days later her neutrophil count had fallen from 1·72 x 10⁹/l to 0·25 x 10⁹/l and the carbamazepine was stopped. After three further days the neutrophil count had returned to 1·8 x 10⁹/l and her clinical illness resolved. She was subsequently challenged with carbamazepine; after six days her neutrophil count had fallen to 0·85 x 10⁹/l, increasing to 3 x 10⁹/l five days after the drug was stopped.

Case 2—A 6 year old girl with myoclonic and complex partial epilepsy developed an ichy maculopapular rash on her trunk, scalp, palms, and soles two weeks after her treatment was changed from phenytoin to carbamazepine. Palatal petechiae, cervical and inguinal lymphadenopathy, and subsequently hepatosplenomegaly were also found. A blood film showed “atypical lymphocytes,” but there was no neutropenia (neutrophils 5·78 x 10⁹/l). Monospot and viral titres were negative, as were other indices of infection. A week later she became anorectic and lethargic. The rash had faded and become pigmented, but the lymphadenopathy and hepatosplenomegaly persisted. The neutrophil count fell to 0·07 x 10⁹/l. Carbamazepine was stopped, and over the following week her clinical condition and neutropenia resolved.

In both patients the haemoglobin concentration and platelet count remained normal, and because of this and the rapid response to withdrawal of the drug bone marrow examinations were not performed.

Comment

Both children’s neutropenia was thought to have been caused by a viral illness, but their problems resolved when carbamazepine was stopped. The table summarizes these and four other reported cases. In those children taking other anticonvulsant treatment the neutrophil count increased when only the carbamazepine was stopped. Challenge with carbamazepine produced recurrence of the leucopenia in our first case and of the clinical features in the case reported by Bertrand et al (case 6 in the table). In all patients the symptoms were initially thought to be infective (streptococcal or viral) in origin, and malignancy was also suspected in one patient.

These reactions to carbamazepine are thought to be idiosyncratic and may be due to hypersensitivity and formation of immune complexes. The exact prevalence of such reactions is not known; fewer than 20 cases of rash, lymphadenopathy, and fever have been reported in adults and children, and only two other cases of hepatosplenomegaly, both in adults.

It has been suggested that haematological reactions occur more commonly in adults, but Silverstein found an incidence of leucopenia of 17% in a group aged 0–12 years and 8% in a group aged 12–17. This does not appreciably differ from the generally accepted incidence of 10% in all ages. He recommended undertaking blood counts monthly for six months and then every three months. An idiosyncratic reaction to carbamazepine causing a potentially serious haematological abnormality should be considered in patients with clinical symptoms of viral or streptococcal infection or of lymphoma. In these cases haematological examination is essential, but routine blood counts are unlikely to be worth while.

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Doses of aminophylline given intravenously in casualty department and resulting serum theophylline concentrations

Aminophylline is commonly given intravenously as emergency treatment for asthma and acute bronchitis, even to patients already receiving theophylline treatment who have appreciable serum theophylline concentrations. We noted doses of aminophylline used in a hospital casualty department, and measured the effect on serum theophylline concentrations.

Patients, methods, and results

We studied 33 consecutive adults, 22 (16 women, 6 men) with asthma and 11 (all men) with chronic obstructive Airways disease, who received aminophylline intravenously in the casualty department. Prior treatment with theophylline orally, rectally, or parenterally was recorded. The dose of aminophylline, given over at least 10 minutes, was at the discretion of the administering doctor. Blood was taken before and one to two hours after the completed injection for assay of theophylline by the enzyme multiplied immunossay technique (Technicon).

The 22 patients with asthma and 11 with chronic obstructive Airways disease had mean (SD) ages of 45·1 (15) and 65·8 (5·3) years respectively and weighed 65·5 (15·8) kg and 65·2 (19·3) kg. Fifteen with asthma and seven with...