SIDE EFFECTS OF DRUGS

Thrombocytopenic purpura during treatment with Librax

There have been no reports relating thrombocytopenia to the consumption of Librax—a combination of chlordiazepoxide (5 mg/tablet) and clidinium bromide (2·5 mg/tablet). We have observed a case of thrombocytopenic purpura apparently induced by this medication.

Case report

A 32-year-old White woman teacher, weighing 56 kg, consulted her doctor complaining of fatigue, nervousness, non-specific gastrointestinal disturbances, and family problems. A gastrointestinal transit test and routine blood tests showed no abnormalities. The patient had no other metabolic disease or a family history of adverse drug effects. Her doctor prescribed Librax (Roche) orally three tablets a day and a diet without acid fruits. After seven days on only this treatment she presented at hospital with generalised petechiae. Her platelet count was 12×10^9/l (12 000/mm^3), the total white cell count 9×10^9/l (9000/mm^3), and the haemoglobin 15·4 g/dl. The leucocyte differential count and the morphology of thrombocytes in peripheral films were normal. Fibrinogen concentration, prothrombin time, and partial thromboplastin time were also normal. A bone-marrow aspirate showed an increased number of megakaryocytes. Librax was withdrawn, and, without any other treatment, the number of thrombocytes returned to normal within five days. Virological tests for *Mycoplasma*, adenovirus, Q fever virus, influenza A and B viruses, parainfluenza 3 virus, rubella virus, *Toxoplasma*, cytomegalovirus, mononucleosis, hepatitis B surface antigen, and respiratory syncytial virus were all negative. Tests for antinuclear factor, anti-DNA antibodies, cold agglutinins, and antiplatelet antibodies were also negative. She was not exposed again to Librax.

Comment

This case seems to represent an example of drug-induced platelet destruction, although we do not know which of the two compounds in Librax induced the damage. We considered thrombocytopenia secondary to a viral disease, but virological tests proved negative, and, on the other hand, the thrombocytopenia disappeared when Librax was withdrawn. We did not re-expose the patient to Librax for ethical reasons. Only one case of purpura without thrombocytopenia after treatment with chlordiazepoxide has been reported.[1] Nevertheless, because Librax is widely used it seems likely that cases similar to the one we have reported may appear.

[1] Copperman, I J, *British Medical Journal*, 1967, **4**, 485.

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Pneumatosis coli: complication of practolol

Several adverse side effects have been associated with practolol, including skin and ocular manifestations, a systemic lupus erythematosus-like syndrome, fibrinous peritonitis, and nephrotic syndrome.[1] We report here another complication.

Case report

In February a 61-year-old man developed loose stools. A barium meal enema examination showed nothing abnormal and he was treated with Lomotil (diphenoxylate hydrochloride and atropine sulphate). The symptoms settled within four weeks. After he developed angina in April 1971 he was started on practolol 300 mg/day, the dose being gradually increased to 1000 mg/day by September 1972. In July 1973 he presented with severe diarrhoea—15 stools daily—with blood, mucus, and recurrent attacks of severe abdominal pain. A repeat barium enema examination showed classical subtotal left-sided pneumatosis coli, a diagnosis which was confirmed by sigmoidoscopy and biopsy. A chest *x*-ray examination and barium meal and follow-through examination showed nothing abnormal. He never had symptoms of obstructive airways disease. Serological investigations for immunoglobulins and C3 and C4 complement showed normal levels, while tests for rheumatoid factor and antinuclear factor (ANF) antibodies were negative. Symptomatic treatment, Lomotil or codeine phosphate and Isogel, was then started with moderate success. In 1974 repeat investigations showed no significant changes, and his symptoms persisted. After reports of its other side effects practolol was stopped in April 1975 and sotalol substituted. Within one week his stool count fell to three a day. Although he had a further attack of abdominal pain three months after stopping practolol, this subsided spontaneously. Barium enema examination, sigmoidoscopy, and biopsy in September 1975 and 1976 were normal.

Comment

The pathogenesis of pneumatosis coli (intestinalis) is uncertain. Although it has been reported in association with other gastrointestinal lesions[2] and pulmonary diseases,[3] there remains a group of so-called "primary" cases. The known disease associations have suggested two possible mechanisms for its development. Firstly, as a result of changed gastrointestinal motility, increased intraluminal pressure might force gas through the mucosa to produce cysts. Secondly, air might track down through the mediastinum and retroperitoneum after alveolar rupture.[4] This patient had no respiratory symptoms, and investigations (repeated chest *x*-ray examinations and subsequent lung function tests) were normal. Apart from an isolated episode of diarrhoea in 1970 he had no evidence of other gastrointestinal disease.

We believe that the pneumatosis coli was induced by practolol. A previous barium enema examination had shown nothing abnormal, and he was asymptomatic before starting practolol. After taking practolol for two years he developed severe gastrointestinal symptoms and was shown to have pneumatosis coli, which persisted while he was on this drug. After stopping practolol and while on another beta-blocker his symptoms rapidly cleared; repeat gastrointestinal investigations were then normal.

The possible mechanisms by which practolol (in this case in relatively high doses) could induce pneumatosis coli can only be speculative. Patients with other side effects of practolol have shown changed immunological reactivity, with ANF antibodies, LE cells, etc.[5] In this case these indices were negative. Possibly the patient developed fibrinous peritonitis; gastrointestinal motility may have been disturbed, which in turn might have led to increased intraluminal pressure, mucosal damage, and gas cysts, changes that were reversed when practolol was stopped.

[1] *British Medical Journal*, 1975, **2**, 577.
[2] Koss, L G, *Archives of Pathology*, 1952, **53**, 523.
[3] Doub, H D, and Shea, J J, *Journal of the American Medical Association*, 1960, **172**, 1238.
[4] Culver, G J, *Journal of the American Medical Association*, 1962, **186**, 160.
[5] Wright, P, *British Medical Journal*, 1975, **1**, 595.

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