

References

Sternal perforation with verapamil

Sir,

Constipation is the commonest and most troublesome non-cardiac side effect of verapamil use.1,2 We would like to report a case of sternal perforation in a woman taking verapamil. A 78 year old woman was admitted with sudden onset of lower abdominal pain associated with signs of generalized peritonitis. She had developed chronic constipation after commencement of verapamil for recurrent supraventricular tachycardia 9 months previously and prior to this time she had had a normal bowel habit. Two months prior to admission she had been found to be biochemically hypothyroid and was treated with thyroxine. On admission she was clinically and biochemically euthyroid.

After resuscitation, laparotomy revealed a perforation in an otherwise normal sigmoid colon. The proximal and distal colon was loaded with scybalous stools. The peritoneum was lavaged and the perforated colon exteriorized. Postoperatively the patient suffered from recurrent supraventricular tachycardias until verapamil was recommenced on the third day. This was followed by a prolonged (13 day) ileus which rapidly resolved on substituting atenolol for verapamil.

Previous reports of gut immotility secondary to verapamil describe patients susceptible to constipation because of underlying medical conditions.3 Our patient had been diagnosed as being hypothyroid in the recent past, although she was clinically and biochemically euthyroid on admission. Serpell and Nichols' review of colonic stercoral perforation notes that scybala formation may occur months prior to perforation, as it takes time to traumatize and breach the intestine.4 It is possible that hypothyroidism was a contributing factor to this patient's sternal perforation but it is unlikely to be the sole cause. There are virtually no reports of hypothyroidism causing intestinal perforation or immotility other than a case of fatal intestinal atony attributed to myxoedema in 1969.5

It is therefore most likely that verapamil was the major cause of this patient's perforation, with hypothyroidism as a possible exacerbating factor. Verapamil significantly reduces motor activity of the intestine; this returns to normal on cessation of the drug.2

Severe constipation is frequently described as one of the most troublesome side effects of verapamil use. We suggest that verapamil should be used with caution in patients with pre-existing tendency to constipation and that its use should be reviewed if other factors which exacerbate constipation develop during treatment.

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Cerebral infarction after cisplatin-based chemotherapy

Sir,

Oncological patients may suffer acute cerebrovascular accidents but a relationship to chemotherapy toxicity is rare. We report the case of a patient who developed cerebral infarction directly related to cisplatin treatment.

A 50 year old woman, with no known risk factors, was diagnosed as having ovarian adenocarcinoma, FIGO IIIc stage. Post-surgical masses measuring more than 2 cm in diameter were present and CAP chemotherapy (cyclophosphamide 500 mg/m², i.v. day 1, doxorubicin 40 mg/m², i.v. day 1, and cisplatin 80 mg/m², i.v. day 1) was started. Twenty-four hours after the first cycle, she developed motor aphasia and agaphria. The haematological laboratory tests (haematocrit, white cells, differential count, platelets, prothrombin time and partial thromboplastin time) were normal as were blood chemistry tests (cholesterol, HDL-cholesterol, triglycerides, magnesium and lactate dehydrogenase). VDRL was negative, and echocardiogram and electrocardiogram were normal. A computed tomographic (CT) brain scan was also normal.

Given the sequential relation between previous chemotherapy and the neurological disorders, we changed the treatment to cyclophosphamide 500 mg/m², i.v. day 1 and carboplatin 350 mg/m², i.v. day 1. She received two cycles without neurological problems, but the abdominal disease progressed. We therefore changed the treatment back to cisplatin 90 mg/m², i.v. days 1–3, doxorubicin 30 mg/m², i.v. day 3, cyclophosphamide 300 mg/m², i.v. day 3, and hexamethylmelamine 200 mg/m², orally days 4–14. Six hours after cisplatin administration, the patient experienced dysarthria and a left homonymous hemianopia, and a CT brain scan revealed an acute infarction on the right occipital lobe. Again, the same laboratory tests that had been performed previously were normal. The anti-emetic treatment was always metoclopramide and diphenhydramine.

The neurotoxicity of cisplatin is well known. The most common disorders are distal neuropathy (mainly sensory), ototoxicity and encephalopathy. However, cerebrovascular accidents very rarely follow its administration, and there is generally evidence of associated risk factors, or synergic toxicities of the chemotherapy in these cases.1–3

The pathogenesis is unknown. Increase in the von Willebrand factor antigen, arterio-occlusive disorder, platelet alterations, thromboxane prostacyclin homeostatic disturbances and variations in magnesium levels are
possible causes.\textsuperscript{2,4} In our patient, there were no known risk factors and the relation to cisplatin treatment was direct.

We suggest that cisplatin should be included among the agents capable of producing acute cerebral infarction, regardless of the accumulated dose and the form of administration.

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Cerebral infarction after cisplatin-based chemotherapy.
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