Ergotamine abuse and extra-hepatic portal hypertension.

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Summary: Arterial complications following ergotamine therapy have been well recognized since the beginning of this century. Venous complications, however, have only rarely been reported. A 48 year old Nigerian woman developed extra-hepatic portal hypertension coincident with a chronic overdosage of ergotamine. The literature elucidating the possible mechanisms involved is reviewed.

Introduction

It has long been recognized that toxicity due to ergotamine overdosage is directly related to its arterioplastic action (Yater & Cahill, 1936; Gould et al., 1936). This most commonly results in ischaemia of the extremities (Cranley et al., 1963; Sutton & Preston, 1970). Also documented are spasm of the coronary (Yater & Cahill, 1936), carotid (Greene et al., 1977), cranial and renal arteries (Fedotin & Hartman, 1970; Greene et al., 1977). Arteriographic studies have demonstrated spasm of the coeliac axis and superior mesenteric artery (Greene et al., 1977; Stillman et al., 1977) and even aorto-iliac spasm has been recorded (Glazer et al., 1966; Fedotin & Hartman, 1970).

Only very rarely has a specific venous complication, as a direct result of ergotamine poisoning, been reported. Included in the literature are cases of thrombophlebitis (Greene, 1959) and deep venous thrombosis of the leg (Mintz et al., 1974), following ergotamine administration.

The dearth of reported cases of venous complications following ergotamine abuse may, in part, be due to the more nebulous clinical presentation of venous occlusion, as opposed to the clear-cut clinical features of arterial insufficiency.

This report describes an association between the development of extra-hepatic portal hypertension and the chronic overdosage of ergotamine, an as yet unrecognized complication of ergotamine therapy.

Case report

A 48 year old Nigerian woman presented with an acute left-sided hemiparesis. She had suffered with severe classical migraine for 8 y, and her medication included oral ergotamine tartrate with caffeine (Cafergot, Wander Pharmaceuticals) for the acute migraine episode. She had however been taking 6 mg/day for at least the 3 months immediately previous to her admission. This constitutes a substantial chronic overdosage of ergotamine, which has a recommended maximum dose of 12 mg in any one week, and a recommended break of at least 4 days between courses for an acute migraine attack.

Her past medical history included a Caesarian section 25 y previously, and a laparotomy for secondary infertility 10 y previous to this presentation, both of which were uncomplicated. No abnormalities of the portal system were noted at either of these operations. She had otherwise, apart from her migraine, been perfectly well. Examination at presentation revealed a left-sided hemiparesis. She was normotensive and had no signs of cardiovascular disease. All investigations, including computerized tomography of the head, were normal.

It was thought unlikely that her hemiparesis represented a thromboembolic episode, and the diagnosis was made of cranial artery spasm resulting in an ischaemic episode, either due directly to a severe attack of migraine, or, more likely, due to systemic ergotamine toxicity, a well recognized complication of ergotamine abuse (Brazeau, 1970). Ergotamine was therefore withdrawn from her treatment regimen, and the hemiparesis completely resolved within one week.

One month later she re-presented with melaena and...
frank rectal bleeding, requiring resuscitation with 5 units of blood. She had been currently ingesting large quantities of aspirin to cope with a particularly severe migraine attack. Physical examination at this time revealed splenomegaly, a finding not noted previously. Otherwise examination was entirely normal.

Endoscopy revealed severe gastric erosions as expected, but an unexpected coincidental finding was the disclosure of grade 4 oesophageal varices. All blood tests, including liver function tests, were normal. Liver biopsy revealed a normal histology.

Splenoportograms and superior mesenteric angiograms did not reveal any recognizable splenic, superior mesenteric or portal veins. At laparotomy the angiographic findings were confirmed, with completely fibrosed splenic, superior mesenteric and portal veins. Splenomegaly was noted to three times normal size and there was a profusion of dilated, tortuous, variceal veins extending beyond the oesophago-gastric junction. No shunt procedure was possible, and injection sclerotherapy of her oesophageal varices was performed. She remains well at current follow-up.

Discussion

In up to 50% of patients presenting with extra-hepatic portal hypertension no cause is found (Webb & Sherlock, 1979). The present patient is of interest, because she had a well documented history of ergotamine abuse. This was thought to have been responsible for her episode of cerebral ischaemia, and the possibility exists that the ergotamine abuse could in addition have played an aetiological role in her extra-hepatic portal hypertension.

The pathogenesis of arterial disease induced by ergotamine and the clinical sequelae have been well documented. Ergotamine causes vasoconstriction, the production of mural thrombi and, microscopically, there is vascular smooth muscle hypertrophy and reduction of vessel lumen diameter (Yater & Cahill, 1936; Cranley et al., 1963). These effects, on both arteries and veins, are mediated by partial \( \alpha \)-adrenoceptor agonism (Boissier, 1978; Muller-Schweinitzer & Sturmer, 1974; Aellig, 1975), enhanced prostaglandin E production (Muller-Schweinitzer, 1974; Muller-Schweinitzer & Brundell, 1975) and a direct action on the vascular smooth muscle even more potent than noradrenaline (Mikkelsen et al., 1981).

Although, in general, veins are poor responders to vasoconstrictor stimulation, portal and superior mesenteric veins have been shown to be exceptional, contracting vigorously in response to a variety of catecholamines (Richardson & Withrington, 1978, 1979).

Animal studies involving perfusion of the portal vein with ergotamine (Richardson & Withrington, 1977), have shown classical dose-response contractions, with consequently markedly reduced portal blood flow. Chronic repeated dosage with ergotamine resulted in an increased number of \( \alpha \)-adrenoceptors with corresponding increased sensitivity to ergotamine. In vivo studies performed. She remain well at current follow-up.

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References


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