

Ergotamine-Induced Upper Extremity Ischemia: A Case Report

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Ergotamine-induced limb ischemia is an extremely rare case. We present a case of a 64-year-old man, who developed ischemia on the right upper extremity due to long-term use of Ergot for migraine headache. Angiography revealed dif-fused, smooth, and tapered narrowing of the brachial artery. The patient was suc-cessfully treated with intravenous nitroprusside.

Ergot alkaloids are widely used for the relief from migraine headache (1). Ergotamine can cause serious peripheral vascular ischemia and results in amputation (2–6). As Ergotamine-induced ischemia is a very rare case, the radiologists are not entirely familiar with its characteristic features. However, the clinical importance lies in the fact that, delayed diagnosis leads to serious irreversible complications. In the present study, a review of literature on presentation, diagnosis and treatment of the complications induced by Ergotamine has been reported.

Index terms:

Angiography
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CASE REPORT

A 64-year-old man with a 15-year long history of hypertension was presented to the emergency room with a 24-hour history with symptoms of cyanosis and pain on the right upper extremity, consistent with acute ischemia. The major physical findings revealed that the right upper extremity was pale, cold, and exhibited reduced sensation and power. Radial pulses were observed to be absent.

Blood pressure was 130/80 mmHg and heart rate was regular at 64 beats per minute. Laboratory values indicated an increase in white blood cell count of 11,400 /uL, normal hemoglobin value of 15.5 g/dL and elevated creatininc kinasl MB (CK-MB) value of 33.2 ng/mL (normal, 0–5 ng/mL). The increased levels of BUN (31.9 mg/dL) (Blood Urea Nitrogen) and serum creatinine (1.8 mg/dL) returned back to baseline value within three days. Levels of Aspartate aminotransferase (range, 68–266 IU/L) and alanine aminotransferase (range, 28–79) were increased.

A right transfemoral approach was performed with placement of a 6-F sheath.

A 5-F angiographic catheter (H1; Cook, Bloomington, IN) was advanced into the right axillary artery. Angiogram obtained after injection of contrast medium in right axillary artery revealed a smooth, tapered narrowing of the brachial artery without opacification of radial and ulnar artery (Figs. 1A, B). At the time of angiography, passing of guide wire across the narrowing and occlusive segment was attempted, but these efforts were unsuccessful. The diagnosis of unusual pattern of Raynaud's disease was initially made, eventually incorrect.

A fear of gangrenous changes in right upper extremity, he had undergone intra-arterial papaverine injection of 30 mg and a right axillary-radial bypass surgery.

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Over a period of approximately two hours, there was a dramatic improvement in the color of the patient's upper extremity and radial pulses became palpable, but cyanosis and pain persisted at phalangeal area.

In addition to intravenous infusion of prostaglandin E1 and heparin, two days later, the patient underwent ipsilateral sympathectomy with the subsequent disappearance of cyanosis and pain on phalangeal area. There was improvement in motor disability, though there was no complete recovery. Follow up angiography was performed to evaluate the patency of graft seven days later.

Arteriography examination demonstrated normal arterial anatomy of the right arm as well as the patent graft (Figs. 1C–E). The patient's postoperative recovery was uneventful, and he was discharged in a good condition. Anticoagulation and antiplatelet regimens were prescribed at the time of discharging. Eight days later, the patient returned for the same ischemic symptoms of the right

upper extremity. Repeated angiography revealed the similar findings which had been demonstrated during first angiography and also occlusion of graft was noticed. The diagnosis of ergotamine-induced vasospasm was made only after that and treatment was initiated by discontinuing the intake of offending drug and an intravenous infusion of nitroprusside was initiated at a rate of 4 μ g/kg/minute.

The drug infusion was continued over four days until there was relief from pain and cyanosis. We noticed that for over a period of 10 years the patient had been prescribed Ergotamine for the treatment of migraine.

DISCUSSION

Ergotamine is an alkaloid produced by a fungus, *Claviceps purpurea*. Epidemics would sometimes occur when food stuffs become contaminated with *Claviceps purpurea*. People who consumed the fungus contaminated

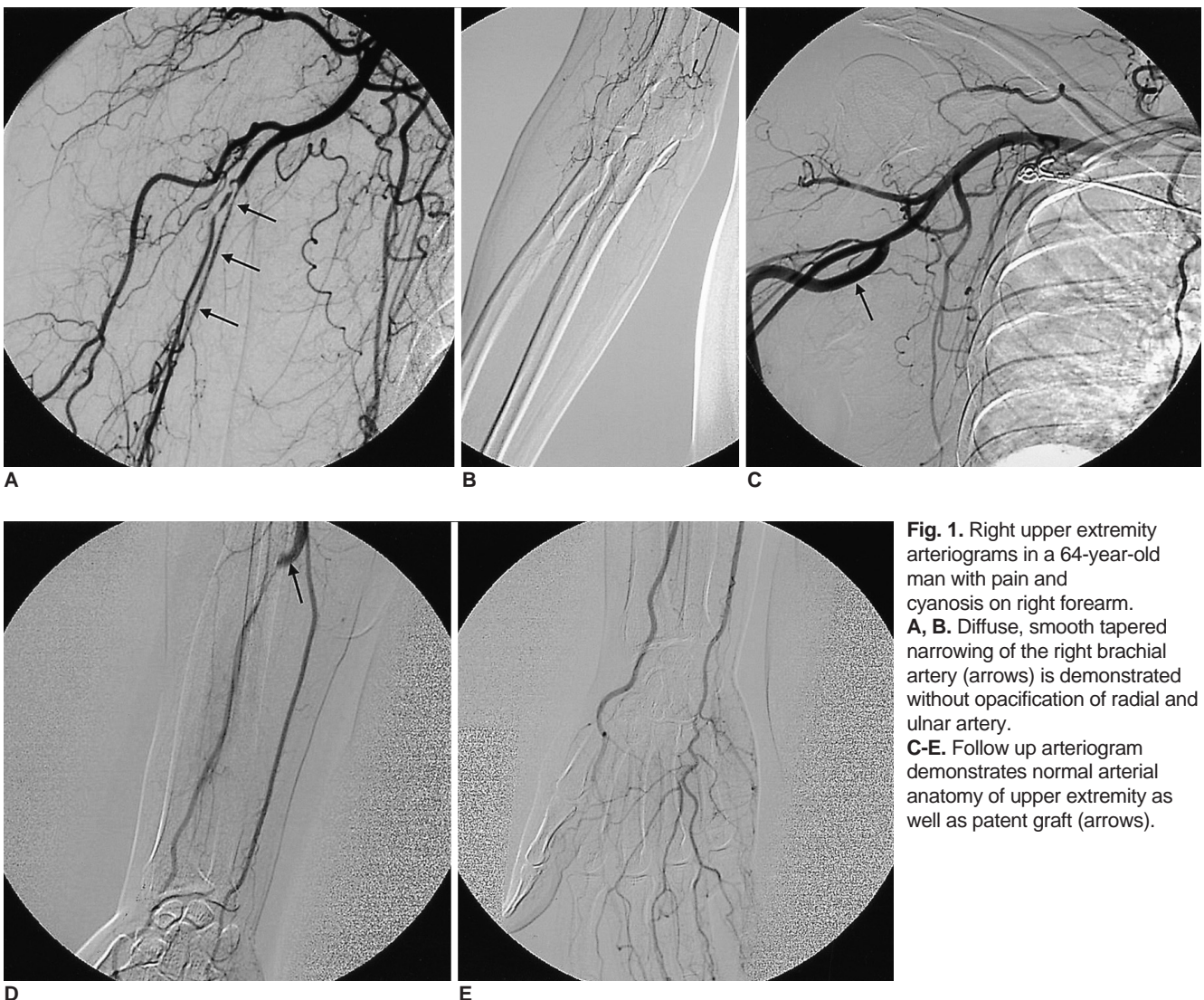


Fig. 1. Right upper extremity arteriograms in a 64-year-old man with pain and cyanosis on right forearm. **A, B.** Diffuse, smooth tapered narrowing of the right brachial artery (arrows) is demonstrated without opacification of radial and ulnar artery. **C-E.** Follow up arteriogram demonstrates normal arterial anatomy of upper extremity as well as patent graft (arrows).

grain suffered from limb ischemia and discoloration of extremities.

Most of the cases of Ergotamine toxicity are due to medication ingestion, either acutely or chronically (2). Ergotamine has been widely used for the treatment and prevention of migraine headaches. This particular alkaloid can cause intense peripheral vasoconstriction which can lead to gangrene and amputation. Ergotamine-induced vascular ischemia is rare, but potentially serious complication may be induced through two mechanisms: vasospasm and thrombus formation. The latter may be caused by stasis and a postulated direct endothelial damage may be caused by Ergotamine. Toxicity can occur from chronic use of therapeutic doses, acute ingestion of excessive amounts, and acute ingestion of normal doses in hypersensitive patients. A number of conditions are known to potentiate the vasospastic effects of Ergotamine like, fever, sepsis, malnutrition, thyrotoxicosis, pregnancy, liver and renal insufficiency, coronary artery disease, and peripheral vascular disease (3). The triggering factor for the development of Ergotamine toxicity in the present case is still uncertain, but a possible reason could be hepatitis (elevated liver enzyme) with transient renal dysfunction.

Drugs may also be responsible for an increase in the side effects of Ergotamine (4, 5): oral contraceptives, xanthine derivatives, antiviral agents, antibiotics interfering with the liver metabolism of Ergotamine (i.e. clarithromycin, ampicillin, erythromycin, and troleandomycin).

Recently, Baldwin et al. described a case of Ergotamine toxicity in an human immunodeficiency virus infected patient treated with antiviral protease inhibitor (6).

Ischemia caused by Ergotamine intoxication affects the lower extremities more commonly than the upper extremities. The external carotid arteries are often involved with a rare involvement of coronary, mesenteric, renal, and retinal arteries. The diagnosis of this rare condition requires a high index of suspicion in patients with migraine and a careful inquiry about their medication history. The angiographic findings of the affected vessels reveal thin, threadlike and smooth tapered narrowing of the arteries with or without collateral formation (7). Thrombus results from stasis distal to arterial spasm with either bilateral or symmetrical involvement, and the areas of stenosis may be diffused or localized. Many therapeutic modalities can be used to reverse the vasoconstriction (8, 9). The first step of the treatment is discontinuation from the offending drug.

When vascular thrombosis is suspected, heparin, a low molecular weight dextran and streptokinase has been suggested to reduce tissue loss. A number of pharmacologic agents have also been used to treat the vasospasm. Nitroprusside, a direct acting vasodilator, is effective but

can be used only for shorter periods of time and prompt recurrence of symptoms have been reported after discontinuation. Tolazoline, calcium channel blockers and prostaglandin E1 are able to produce vasodilatation. Nifedipine is the most potent peripheral vasodilator of the group and has been successfully used to treat Ergotamine toxicity. In severe forms of ischemia refractory to pharmacologic treatment, surgical sympathectomy or intraarterial balloon dilatation can be effective (10), and the management depends on early diagnosis of the symptoms.

In our case, Ergotamine-induced ischemia was not suspected during first angiography. Uninterrupted medication for migraine is thought to play a significant role in the development of recurrent symptoms.

The present case emphasizes the importance of acquiring a detailed medication history. Combination of heparin, prostaglandin E1, and sympathectomy did not prevent the progression of cyanosis in our case, but intravenous injections of nitroprusside could relieve the symptoms. An understanding of the clinical features and angiographic findings of Ergotamine-induced ischemia is essential in early diagnosis and treatment to prevent irreversible complications.

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