SHORT REPORT

Diffuse Vasospasm of All Four Extremities Resulting to Acute Arm and Legs’ Ischaemia Due to Cafergot Abuse

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Ergotism is a rare cause of vasospasm which occurs in 0.001–0.002% of patients receiving ergot derivatives primarily for treatment of migraine [Dagher FJ, Sidawy AN. Ergotism, current treatment in vascular surgery. 4th ed. Ernst-Stanley. p. 154–157]. Vasospasm though diffuse affects usually the lower limbs.

We present the case of a 38 year old woman with truly diffuse vasospasm, due to Cafergot suppositories abuse, of all four extremities causing severe ischaemia to her left arm and bilateral intermittent calf claudication.

The patient was treated successfully and recovered from vasospasm 72 h later.

Keywords: Ergotism; Vasospasm; Cafergot.

Case Report

A 38 year old woman was admitted for acute left arm ischaemia and bilateral intermittent calf claudication at 20 m. The patient was in severe arm pain, her left arm being cool and pale till over the elbow, with concurrent loss of sensation and digital mobility. Pain in the arm had started gradually 12 h before her admission and worsened during the last 6 h. On arrival, she was also complaining of chest pain radiating to the left shoulder and a persisting headache. She was a non smoker.

Physical examination revealed absent of brachial, ulnar and radial arteries’ pulses in both upper limbs and absent of femoral artery pulses on both sides.

With the hand held Doppler no audible flow signals were present over the left brachial artery. The right brachial artery pressure was 60 mmHg and both ankle pressures were 70 mmHg.

The patient suffered from chronic migraine and underwent treatment with ergotamine tartrate suppositories for more than 10 years. During the last 2 months, migraine deteriorated and she started drug overdosing. She was currently taking 600–800 mg ergotamine tartrate per day. At that same period she experienced episodes of digital numbness and typical intermittent calf claudication which she attributed to sciatica.

The ECG on admission showed a sinus tachycardia and no ischaemic disorders. An angiogram was performed immediately which showed diffuse vasospasms. In particular we found a smooth edged gradual narrowing and obstruction of a seemingly left brachial artery and threadlike flow to the right radial and ulnar arteries and subocclusion of both superficial femoral arteries (Figs. 1 and 2).

In combination to patient’s medical history, the angiographic picture was attributed to ergotism and the treatment started, including:

1 discontinuation of all ergot-alkaloid products
2 hydration with crystalloid i.v solutions
3 LMWH (enoxaparine)-100 IU/kg twice daily
4 250 mg nitroglycerine IV in 24 h, under cardiac monitoring
5 IM opioid analgesia
Within 24 h from treatment initiation, the right arm responded to therapy followed some hours later by the lower limbs, all showing a gradual clinical improvement and increase in blood pressure up to 120 mmHg. The left arm remained ischaemic with its brachial pressure at 80 mmHg. We preserved the same pharmacologic scheme for the next 2 days and 48 h later palpable pulses were restored all vessels, including the left arm. By the end of third day ankle/brachial indices were totally normalised. An angiogram a week later was normal (Figs. 1 and 2). The patient was referred to the neurologists for treatment of her migraine.

Fig. 1. Left and right arm angios-pre and after treatment.

Fig. 2. Legs’ angios-pre and after treatment.
Discussion

Excessive use of ergot alkaloids can result in ergotism. Compounds that can cause this condition include ergotamine tartrate, dihydroergotamine and lysergic acid diethylamide (LSD). It is rarely caused by ingestion of foods contaminated with the fungus Claviceps purpurea.1

Ergotamine is an α-adrenergic blocking agent. It directly stimulates smooth muscles of peripheral and cranial vessels and is also an agonist of 5-hydroxytryptamine (5-HT).

Ergot alkaloid agents exert their effect by direct vasoconstriction, central sympatholysis, and peripheral-adrenergic blockade. They are metabolized in the liver by a subgroup of the cytochrome P-450 isoenzymes CYP3A4.

Compounds also metabolized by this enzyme pathway, including erythromycin, theophylline, carbamazepine, and cyclosporine, can alter ergot metabolism, resulting in increased drug levels. Protease inhibitors such as ritonavir and indinivir, used for their antiviral properties in patients positive for human immunodeficiency virus (HIV), are also metabolized through the cytochrome P-450 pathway and are potent inhibitors of the CYP3A4 isoenzyme. Therefore, the HIV-positive population receiving antiviral therapy may be a group at risk for ergotism through decreased hepatic metabolism of ergot preparations.2,3

Cafergot, a widely prescribed drug for the treatment of migraine consists of ergotamine tartrate and caffeine. The latter is by itself a potent vasoconstrictor, and it enhances the vascular effects of ergotamine.

The disorders of iatrogenic ergotism include gastrointestinal complaints, neurologic symptoms and vascular symptoms of the extremities. The vascular symptoms appear in the form of ischaemia due to vasospasm to either the upper extremities or most commonly the lower extremities, bilaterally or unilaterally. Patients with symptomatic vasospasm present with symptoms of vascular insufficiency, most commonly in both lower extremities. Patients complain of relatively recent onset of numbness and intermittent claudication progressing to rest pain with coolness and pallor and if the condition is neither recognised nor treated properly, i.e. ischaemic ulcers and frank gangrene may develop. In the 17th century this presentation was called 'Saint Anthony’s fire’ to describe extremities with gangrene suffering from burning pain. Victims of the disease prayed at Saint Anthony’s shrine for relief.1 The gastrointestinal side effects are the most common and include cramping, abdominal pain, nausea, vomiting and diarrhea.

In pregnant women, uterine cramping and abortions can occur. Neurologic side effects consist of headaches, vertigo, impaired mental function, symptoms of psychosis, convulsions in the form of grand mal epilepsy and coma.

Management of iatrogenic ergotism begins with discontinuation of all agents containing ergotamine tartrate. Other vasoconstrictors such as those containing caffeine (coffee, tea) or nicotine should also be discontinued.

Ergot drug withdraw—-together with fluid therapy and systemic heparinization—usually improves patients’ symptoms.

However, additional aggressive therapy is required in patients who have more severe ischaemic symptoms or whose limbs are threatened by gangrene.

- Prazocin hydrochloride, 1 mg orally three times per day may be given.4 It is a direct acting vasodilator, reducing peripheral vascular resistance through its α-adrenergic blocking action.
- Nifedipine, given 20 mg orally twice daily has been reported to improve the symptoms and eliminate the vasospasm.
- Sodium Nitroprusside, a potent direct smooth muscle vasodilator, is recommended. Its infusion rate and duration should be titrated and monitored carefully.5
- Nitroglycerine and prostaglandins have been used successfully.

Ergotism has a sporadic nature and no specific therapy. No single agent, or procedure has been consistently successful, as evidenced by the large number of therapeutic measures and drugs that have been used.4,6

References

4 Cobourg DS. Prazocin treatment of ergotamine-induced peripheral ischaemia. JAMA 1980;244:1360.

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