CASE REPORT

Acrocyanosis in a young adult: a rare presentation of extra-adrenal pheochromocytoma

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SUMMARY

Extra-adrenal pheochromocytomas (EAPs) are rare catecholamine-secreting tumours. The patient commonly present with headache, palpitation, anxiety, diaphoresis, raised blood pressure and heart rate which can be sustained or episodic and less commonly Raynaud's phenomenon. We present a case of an adult woman who presented with unilateral upper limb acrocyanosis and hypertension which was secondary to EAP and resolved completely after surgical removal of the tumour.

BACKGROUND

Raynaud's phenomenon is known in pheochromocytoma and extra-adrenal pheochromocytoma (EAP) but the association of acrocyanosis in pheochromocytoma is unknown.

There are no case reports of acrocyanosis in adult due to EAP in current medical literature until now.

CASE PRESENTATION

A 28-year-old unmarried woman presented with bluish discolouration of fingers of left hand since 15 days, which she noticed after waking up in the morning from sleep, it was persistent and gradually progressive since then. Initially, it started from distal part of middle finger only but later progressed to involve proximal part of four fingers of same hand. It was not associated with any swelling, weakness, paleness, pain, numbness, burning or tingling sensation in the involved site. There was no history of any trauma to the hand, bluish discolouration on any other part of the body or Raynaud's phenomenon. She had no significant medical history, was not on any medication and never had a similar episode before. There was no family history of similar symptoms, hypertension or diabetes.

On examination, her pulse rate was 100/min which was regular, good volume, normal in character, there was no radio-radial or radio-femoral delay and all peripheral pulses were palpable. Her blood pressure was 190/100 mm Hg in supine position and was recorded in all four limbs without any significant variation. There was fall in systolic blood pressure of 24 mm Hg on standing which was suggestive of orthostatic hypotension.

There was bluish discolouration of the left hand which involved the distal and middle phalanges (figure 1). Discolouration was more severe in middle and ring fingers and involved the nails also but the thumb was spared. Discolouration was blanchable and returned to baseline colour after few seconds. Her left hand was colder as compared

with the right and was moist. Radial and ulnar arterial pulses were palpable. The discolouration did not change on raising the hand or on warming, there was no demarcation line and there were no sensory or motor deficits. There was no thyromegaly or signs of thyrotoxicosis or renal bruits and other systemic examinations were normal. Her fundus was also normal.

INVESTIGATIONS

Her baseline investigations such as haemogram, blood sugar, lipid profile, serum electrolytes, cardiac enzymes, renal and liver function tests were normal. Thyroid profile, cytoplasmic-antineutrophil cytoplasmic autoantibody, perinuclear-antineutrophil cytoplasmic autoantibody, antinuclear antibody, antiphospholipid antibody and C reactive protein levels were also normal. However, there was three-fold rise in 24 h urinary free metanephrines levels.

Chest X-ray was normal, ECG had features of left ventricular hypertrophy. Two-dimensional echocardiography showed moderate concentric left ventricular hypertrophy with ejection fraction of 65%. Colour arterial Doppler of left upper limb and both renal arteries were normal. CT angiography of the left upper limb showed normal flow with no evidence of any obstruction. Ultrasound of the abdomen showed a well-defined lesion of size 3.5×3.6 cm in right paravertebral region, anterolateral to inferior vena cava (IVC) which was suggestive of paraganglioma. On contrast-enhanced CT of the abdomen (figures 2 and 3) there was a well-defined, rounded, hypodense, soft tissue attenuation of size 4.3×4.1 cm in precaval region

Figure 1 Bluish discolouration of fingers of the left hand of the patient.

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Figure 2 Coronal section of contrast-enhanced CT of the abdomen showing a well-defined, rounded, hypodense, soft tissue mass in the right paravertebral region.

posterior to second part of duodenum and abutting the head of pancreas and IVC which showed contrast washout on delayed scan with adjacent fat stranding, which was suggestive of EAP. Meta-iodobenzylguanidine scan was performed which revealed a mass of size 4.9×4.8 cm with heterogeneously increased tracer uptake in the right side of the upper abdomen, paravertebral region, abutting the pancreatic head (figure 4).

Figure 3 Transverse section of contrast-enhanced CT of the abdomen showing the same lesion in the precaval region posterior to second part of the duodenum and abutting head of pancreas with contrast washout on delayed scan and adjacent fat stranding, suggestive of extra-adrenal pheochromocytoma.

Figure 4 ¹³¹I meta-iodobenzylguanidine scan of the whole body showing 4.9×4.8 cm right paravertebral upper abdominal mass with heterogeneously increased uptake of the radioactive tracer, abutting the pancreatic head, compatible with extra-adrenal pheochromocytoma.

TREATMENT

After diagnosis, the patient was started on tablet prazosin 1 mg twice daily, tablet amlodipine 5 mg once daily for 3 weeks prior to surgery. The dose of prazosin and amlodipine was doubled sequentially to achieve the target blood pressure. Tablet metoprolol 50 mg twice daily was added 1 week before surgical resection of the mass to control tachycardia.

Subsequently, she underwent exploratory laparotomy and excision of paraganglioma. A mass of size 5×5 cm was found in the right pararenal area, which was removed along with its capsule with few adjacent para-aortic lymph nodes and samplings from hepatic tissue, during the procedure.

OUTCOME AND FOLLOW-UP

The patient's blood pressure became normal after the surgical removal of EAP and all antihypertensive medications were stopped. Acrocyanosis of her left hand started resolving immediately after the procedure and resolved completely within a week (figure 5).

Histopathological examination of the resected mass reported as round to oval cells compartmentalised into small nests depicting Zellballen pattern with tumour cells being uniform and have

Figure 5 Resolution of acrocyanosis of the affected hand postoperatively.

Figure 6 Histopathological examination of the resected mass confirming benign pheochromocytoma.

moderate amount of finely granular cytoplasm and visible nucleoli, suggestive of benign pheochromocytoma (figure 6).

DISCUSSION

Pheochromocytomas (adrenal and extra-adrenal) are rare catecholamine-producing tumours with an annual incidence of 2–8 patients per million population. Only 0.2–0.4% of patients with hypertension have pheochromocytoma as the underlying cause.^{1 2} Ninety per cent of pheochromocytomas are located in the adrenal gland in adults and the rest are EAPs. EAPs are more common in the paediatric age group, 30% of paediatric pheochromocytomas are EAPs.³ EAPs are located in the abdomen regions in 95% of cases and can also rarely occur in the head, neck and thoracic regions.

Skin changes that can occur in pheochromocytoma are pallor, Raynaud's phenomenon and very rarely acrocyanosis. Acrocyanosis is painless bluish discolouration of the extremities which is generally symmetrical, persistent and aggravated by cold exposure.⁴ Acrocyanosis can be primary and secondary. Primary acrocyanosis is a benign idiopathic condition which is commonly seen in young women and does not require any treatment. Secondary acrocyanosis is due to underlying pathological conditions and sometimes it may be the first manifestation of a disease.⁵

There are several proposed mechanisms for acrocyanosis but the exact pathophysiology is elusive. The most accepted hypothesis for primary acrocyanosis is peripheral cutaneous vasospasm of arteries and arterioles along with secondary vasodilation of capillaries and venules leading to cyanosis.⁶ The common mediators of vasospasm in acrocyanosis are epinephrine, norepinephrine and serotonin.⁷

In pheochromocytoma, raised epinephrine and norepinephrine levels can possibly explain acrocyanosis in this patient although the exact pathophysiology is still not known and documented.

Acrocyanosis has been reported in paediatric adrenal and EAP. Stackpole *et al* had reviewed 100 cases of pheochromocytoma and found acrocyanosis in 22% of patients with pheochromocytoma in the paediatric age group, all of whom had bilateral involvement.⁸ Although pheochromocytoma is a catecholamine producing tumour having systemic manifestations, the cause of unilateral presentation of acrocyanosis is still unexplained to us. To the best of our knowledge we could not find any case report of acrocyanosis in adult adrenal or EAP, with unilateral affection, in medical literature so far.

Learning points

- ▶ Acrocyanosis is a rare arteriospastic disorder, which may be a manifestation of a pathological condition.
- ▶ Acrocyanosis needs to be differentiated from other common causes of bluish discolouration of extremities such as peripheral cyanosis, Raynaud's phenomenon, livedo reticularis and erythromelalgia.
- ▶ A complete workup should be performed to rule out secondary causes in all patients with acrocyanosis.
- ▶ Extra-adrenal pheochromocytoma (EAP) is a rare cause of secondary hypertension in adults. EAP is a completely curable disease, if diagnosed early and treated adequately.

Contributors PK diagnosed the case and arranged for the radionuclide scan. SG prepared the manuscript. HST investigated and managed the case. AKG clinched the tissue diagnosis.

Competing interests None.

Patient consent Obtained.

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