Acute Intermittent Porphyria: An Unusual Cause of Malignant Hypertension

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Abstract

Hypertension is a rare complication of acute intermittent porphyria (AIP) and is related to the sympathetic over-activity seen in this condition. We report a patient with AIP with malignant hypertension that recurred with a subsequent episode. Mechanisms of hypertension and renal damage are discussed.

INTRODUCTION

Acute intermittent porphyria (AIP) is a rare inherited disorder of heme biosynthesis with highly variable clinical expression. Although most affected individuals remain asymptomatic, porphyrigenic drugs, exogenous or endogenous steroid hormones, alcohol ingestion and low calorie diets can precipitate an acute attack. As the neurovisceral symptoms rarely occur before puberty and are usually non-specific, a high index of suspicion is required to make this diagnosis. Abdominal pain is the commonest presenting symptom and is usually associated with manifestations of sympathetic over-activity. Hypertension is an uncommonly reported manifestation of sympathetic over-activity in AIP. We report a patient with AIP who presented with abdominal pain and malignant hypertension in whom malignant hypertension recurred with subsequent episode of AIP.

CASE REPORT

A 13 years male presented to a private clinic with severe abdominal pain. He was suspected to have intestinal intussusception and was subjected to an exploratory laparotomy under general anesthesia. At surgery no pathology was found and the abdomen was closed. Post-operatively he had an alteration in sensorium and generalized tonic clonic convulsions. He was found to have hypertension and was referred to this institute. He had a history of seizures since four years of age, which were controlled on carbamazepine prior to this illness.

At admission he was comatose with a blood pressure of 160/120 mm Hg, pulse rate of 110/min and had signs of moderate dehydration. Fundus examination revealed grade IV hypertensive retinopathy, with bilateral papilloedema, soft exudates and hemorrhages. Investigations revealed serum sodium of 116 mEq/L and serum potassium of 2.3 mEq/L with serum bicarbonate of 42 mEq/L. Rest of the biochemical and hematological investigations were normal. Urine for porphobilinogen was negative and urinary VMA was normal. Ultrasound scan of the kidneys, contrast enhanced CT scans of the head and abdomen were normal. After controlling blood pressure with sodium nitroprusside drip, his sensorium gradually improved and he was discharged on amlodipine and prazosin. On follow-up as an out-patient, his blood pressure recordings were low requiring gradual reduction in the anti-hypertensive drug dosages and subsequent stoppage of the drugs with normal blood pressure recordings.

Ten months later he again presented with pain abdomen, constipation, vomiting and passage of urine that darkened on storage. His blood pressure was 170/118 mm Hg and fundus again showed grade IV hypertensive changes. Urine for porphobilinogen repeated this time was positive. He was managed with IV dextrose 200-300 gm/day and atenolol and discharged. He was again admitted twice over the next six months with abdominal pain and hypertension and was advised to avoid factors precipitating episodes of AIP. The blood pressure continues to be under control with atenolol 25 mg/day.

DISCUSSION

This boy represents the classic story of a patient with AIP with recurrent episodes of abdominal pain and having been operated upon once for an acute abdomen. A prominent feature during his presentation to this hospital was malignant hypertension and hypertensive encephalopathy. The diagnosis could not be confirmed at first admission as urine for porphobilinogens was negative on two occasions. Hence other causes of hypertension like pheochromocytoma and Conn’s syndrome were considered and excluded by appropriate investigations. The diagnosis of AIP was confirmed during the second admission when urine tested positive for porphobilinogens.
Although occurrence of hypertension during the acute attack is not uncommon, this hypertension is often labile.\textsuperscript{1,3} Malignant hypertension, papilloedema, hypertensive encephalopathy and congestive cardiac failure have been reported but are rare. This acutely oncoming hypertension is usually associated with tachycardia with or without other features of autonomic dysfunction and occurs secondary to renal ischemia due to arterial vasospasm as a result of sympathetic over-activity during the acute episode.\textsuperscript{4} \(\beta\) blockers are the drugs of choice and other safe anti-hypertensive drugs include labetalol and diazoxide. Angiotensin converting enzyme inhibitors, hydralazine, methyldopa, thiazide diuretics, spironolactone and clonidine are considered unsafe and use of calcium channel blockers and prazosin/doxazosin is contentious.\textsuperscript{1,2}

Electrolyte abnormalities and acid base disorders are well recognized in patients with AIP with hyponatremia occurring as a result of SIADH. A less emphasized fact about hypertension in AIP is that 50-60\% patients suffer the more insidious but no less important complications of persistent chronic hypertension including occurrence of chronic renal insufficiency in approximately 50\% patients.\textsuperscript{2,5} Further, up to 30\% of first degree relatives of these patients are hypertensive, but do not have overt porphyria.\textsuperscript{2,5} Therefore first degree relatives of patients with AIP should be carefully screened. In a study on Indian patients with symptomatic or asymptomatic porphyria, 53.3\% patients had hypertension. Six of seven patients evaluated during an acute attack, five of 12 during remission and five of 11 asymptomatic patients had hypertension.\textsuperscript{6} The exact mechanism of chronic hypertension and renal damage is not clear.

Hypertension is attributed to various mechanisms including vasospasm, neuropathy and involvement of medullary inhibitory centres controlling vasomotor tone.\textsuperscript{2,4} There is some evidence from autopsy data that renal changes are non-specific and consistent with end stage hypertension and ischaemic damage. In some patients renal damage may also result from analgesic abuse or as a result of concomitant illness such as SLE.\textsuperscript{3}

**References**