CASE REPORT

Malignant systemic hypertension, encephalopathy and bradycardia following splenectomy for hereditary spherocytosis

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SUMMARY

An 8-year-old girl suffering from hereditary spherocytosis underwent splenectomy for chronic severe anaemia. Surgery was uneventful and the patient had a good early postoperative recovery. On the third postoperative day, however, she developed severe headache with associated abnormal movements of upper limbs and nystagmus. She had a heart rate of 50 bpm and a blood pressure of 180/110 mm Hg. She was managed with triple antihypertensives, antiepileptics and sedatives. She recovered slowly over 2 weeks and is fine at 5 months follow-up.

BACKGROUND

Hereditary spherocytosis (HS) is a hereditary haemolytic disorder with an autosomal dominant pattern of inheritance usually presenting with chronic haemolytic anaemia, jaundice and splenomegaly. Splenectomy is the standard treatment for patients with clinically severe HS, reducing the severity of symptoms and requirement for blood transfusions. Though there are reports of pulmonary and portal hypertension postsplenectomy for HS, there have been no documented cases of malignant systemic hypertension following splenectomy.^{1–4} This case describes this rare and fatal complication associated with encephalopathy and bradycardia, a combination of complications probably hitherto unreported.

CASE PRESENTATION

An 8-year-old girl, a diagnosed case of HS, was referred to our department for splenectomy. She presented with symptoms of chronic anaemia with a haemoglobin of 2.8 gm/dL and a history of multiple transfusion requirements in the past 3 years. She first became symptomatic at the age of 3 years and had a family history of HS (two older sisters who previously underwent splenectomy at our centre and had uneventful postoperative recoveries). At presentation she had splenomegaly with the spleen palpable 10 cm below the left costal margin. Preoperative blood pressure was within normal limits and preoperative heart rate was 56 bpm (both values taken with the patient lying comfortably in bed). There was no previous history of hypertension, seizures or any other neurological abnormalities. She received preoperative blood transfusions to build up to a haemoglobin value of 11 gm/dL, and then underwent open splenectomy. The blood pressure remained normal

during surgery. Surgery was uneventful and the patient had a smooth postoperative recovery for the first 3 days. The nasogastric tube was removed on the second postoperative day and she was allowed oral sips of water. On the third postoperative day, however, she started reporting of severe headache with associated abnormal movements of upper limbs and nystagmus. She had a heart rate of 50 bpm and a blood pressure of 180/110 mm Hg. She was started on antihypertensives and a loading dose of phenytoin was given. The patient was sedated with benzodiazepines to tide over the acute crisis. Over the next few days, the child continued to have multiple episodes of severe headache accompanied by recordings of high-blood pressure (in the range of 200/120 mm Hg) and a low heart rate (40–50 bpm).

INVESTIGATIONS

She was thoroughly investigated for underlying causes of hypertension. Ultrasound Doppler revealed no evidence of renal artery stenosis or any mass lesions in the adrenal glands or elsewhere in the abdomen. Non-contrast CT of the head showed no focal abnormalities, urinary vinyl mandelic acid levels were within normal limits and fundus examination revealed hypertensive retinopathy but no evidence of papilloedema or raised intracranial tension. Serum cortisol and thyroid function test levels were normal. MRI of the brain revealed bilateral parieto-occipital hypodensities.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included acute gastric dilatation that may occur following splenectomy due to the ligation of short gastric vessels. The nasogastric tube was reinserted when the patient developed symptoms, keeping this diagnosis in mind, however, there was no relief.

TREATMENT

The patient was managed on sedatives (benzodiazepine), triple antihypertensives (amlodipine, enalapril, minipress XL and antiepileptics (phenytoin). As no underlying cause was identified for the hypertension, the antihypertensives were gradually tapered off to only amlodipine after postoperative day 10. The patient did not have further attacks of hypertension and was eventually discharged on postoperative day 18.

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OUTCOME AND FOLLOW-UP

At her follow-up visit after 6 weeks, the patient had a normal blood pressure and was asked to stop all antihypertensive medications after gradual tapering. She has been asymptomatic at 5-month follow-up.

DISCUSSION

HS is an inherited haemolytic disorder characterised by defects in the erythrocyte membrane proteins leading to formation of erythrocytes that are spherical, less deformable and prone to cause small vessel occlusion due to increased red blood cell aggregability.⁵ The cause for generalised seizures in this patient was probably due to encephalopathy caused by malignant systemic hypertension. This is known as posterior reversible encephalopathy syndrome (PRES), and is characterised by localised oedema or swelling of the neural tissue.⁶ Typical symptoms of PRES include headache, nausea, vomiting, altered mental status, seizures and visual disturbances. Focal neurological signs are uncommon in PRES. The treatment depends on the underlying cause. Many cases resolve within 1–2 weeks of controlling the blood pressure and eliminating the inciting factor. However, long-lasting or even permanent neurological dysfunction may remain.

Patients with HS may have one of several membrane protein defects. Many of these result in instability of spectrin and ankyrin, the major skeletal membrane proteins responsible for erythrocyte stability.⁷ Membrane protein deficiency leads to structural changes including membrane instability, loss of surface area, abnormal membrane permeability and reduced red cell deformability.⁵ The cause of bradycardia in this patient can be explained by instability in the ankyrin protein, which is critical in maintaining membrane stability and also in the localisation of specific transmembrane ion channel proteins to specific membrane domains.^{8–10} Ankyrin B mutations have been linked to loss of cellular targeting of ankyrin-binding proteins Na/K ATPase, Na⁺/Ca²⁺ exchanger and InsP3 receptor to cardiomyocyte membrane domains.^{8–10} The calcium signalling is altered, and the functions of several channels and pumps that normally interact with wild-type ankyrin-B are impaired in the presence of mutant ankyrin-B. These lead to a cardiac arrhythmia syndrome termed ‘ankyrin-B syndrome’, a cardiac disease with a spectrum of clinical presentations that may include bradycardia with sinus node dysfunction, as seen in the patient described: ventricular tachycardia, idiopathic ventricular fibrillation, catecholaminergic polymorphic ventricular tachycardia and sudden cardiac death in response to catecholaminergic stimuli.

Splenectomy has been linked to multiple vascular complications postprocedure possibly because of the hypercoagulable state occurring after removal of the spleen. Possible mechanisms include persistence of abnormal erythrocytes and other pro-coagulant particles that normally get filtered by the spleen, reduced level of anticoagulant proteins C and S in the circulation, altered lipid profiles, endothelial activation and increased blood viscosity. No cause, however, was identified for the sudden development of malignant hypertension in this patient. Speculative mechanisms include micro emboli or ‘in situ’ thrombosis with medial hypertrophy and intimal fibrosis blocking small renal vessels or vessels supplying the vasomotor centre, hidden undiagnosed catecholamine secreting tumour, or

endothelial activation as a result of postsplenectomy hypercoagulability leading to peripheral vasospasm resulting in high-blood pressure. Surgeons operating on patients with HS should be cautious about postoperative complications arising due to predisposition to thromboembolism. Ensuring good hydration and monitoring for at least a week following splenectomy may help to decrease these complications.

Learning points

- ▶ Hereditary spherocytosis is associated with increased red blood cell aggregability. Malignant systemic hypertension can lead to posterior reversible encephalopathy syndrome, characterised by localised oedema of the neural tissue.
- ▶ Instability of the ankyrin protein in hereditary spherocytosis can cause bradycardia.
- ▶ Splenectomy has been linked to multiple vascular complications postprocedure, possibly because of the hypercoagulable state occurring after removal of the spleen, predisposing to thromboembolism.
- ▶ Ensuring good hydration and monitoring for at least a week following splenectomy may prevent fatal complications.

Contributors AV wrote the first draft and approved the final version. SS critically reviewed and revised the draft, operated and managed the case and approved the final version. SD reviewed the literature and approved the final version. DKG reviewed the draft, added intellectual content, managed the case and approved the final version.

Competing interests None declared.

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REFERENCES

- 1 Hoepfer MM, Niedermeyer J, Hoffmeyer F, *et al.* Pulmonary hypertension after splenectomy? *Ann Intern Med* 1999;130:506–9.
- 2 Jardine DL, Laing AD. Letters to the editor: delayed pulmonary hypertension following splenectomy for congenital spherocytosis. *Int Med J* 2004;34:214–16.
- 3 Yoshida M, Watanabe Y, Horiuchi A, *et al.* Portal and splenic venous thrombosis after splenectomy in patients with hypersplenism. *Hepatogastroenterology* 2009;56:538–41.
- 4 Soyer T, Ciftci AO, Tanyel FC, *et al.* Portal vein thrombosis after splenectomy in pediatric hematologic disease: risk factors, clinical features, and outcome. *J Pediatr Surg* 2006;41:1899–902.
- 5 Croom RD III, McMillan CW, Orringer EP, *et al.* Hereditary spherocytosis. Recent experience and current concepts of pathophysiology. *Ann Surg* 1986;203:34–9.
- 6 Grossbach AJ, Abel TJ, Hodis B, *et al.* Hypertensive posterior reversible encephalopathy syndrome causing posterior fossa edema and hydrocephalus. *J Clin Neurosci* 2014;21:207–11.
- 7 Hanspal M, Yoon SH, Yu H, *et al.* Molecular basis of spectrin and ankyrin deficiencies in severe ankyrin hereditary spherocytosis: evidence implicating a primary defect of ankyrin. *Blood* 1991;77:165–73.
- 8 Kline CF, Mohler PJ. Defective interactions of protein partner with ion channels and transporters as alternative mechanisms of membrane channelopathies. *Biochim Biophys Acta* 2014;1838:723–30.
- 9 Mohler PJ, Healy JA, Xue H, *et al.* Ankyrin-B syndrome: enhanced cardiac function balanced by risk of cardiac death and premature senescence. *PLoS ONE* 2007;2:e1051.
- 10 Wolf RM, Glynn P, Hashemi S, *et al.* Atrial fibrillation and sinus node dysfunction in human ankyrin-B syndrome: a computational analysis. *Am J Physiol Heart Circ Physiol* 2013;30:H1253–66.

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