Superior sagittal sinus and inferior vena cava thrombosis with acute Budd-Chiari syndrome

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A 20-year-old man presented in May 1996 with complaints of severe frontal headache, vomiting and diplopia of 2 weeks duration. On examination there was bilateral papilloedema and 6th cranial nerve involvement. Magnetic resonance imaging (MRI) was suggestive of superior sagittal sinus thrombosis (figure 1). The patient was started on daltaparin, antibiotics and steroids.

In March 1997, he developed oral ulcers with painful swellings all over the body. The skin biopsy of these nodules was suggestive of erythema nodosum; the lesions disappeared spontaneously over the next few days. Collagen markers were negative. In August 1997, patient was re-admitted with gradual onset distension of the abdomen and swelling of his feet. On examination, he had oral ulcers, icterus, pedal oedema, prominent dilated veins over the anterior abdominal wall and back, with upward flow and tense ascites. Serum bilirubin was 111.15 $\mu\text{mol/l}$ (total), 68.8 $\mu\text{mol/l}$ (direct), aspartate transaminase 1280 IU/l, alanine transaminase 32 IU/l, alkaline phosphatase 90 IU/l, serum proteins 6.1 g/l, albumin 3.3 g/l, with transudate ascitic fluid. Prothrombin and activated partial thromboplastin time (APTT) were normal. MR venography showed inferior vena cava thrombosis with multiple dilated collateral channels along the abdominal wall, perihepatic, perisplenic and intersplenic region (figure 2). The patient was started on diuretics, the daltaparin was continued, and paracentesis was done under cover of plasma. His blood was tested for hypercoagulable state and was negative for all possible conditions. Bone marrow examination was normal.

Four weeks later, the patient had a sudden increase in abdominal girth, decreased urine output, progressively increasing jaundice and abnormal behaviour. He was diagnosed to have hepatic encephalopathy. Large volume paracentesis was done and the patient showed marginal improvement. Repeat ultrasound showed occluded hepatic veins and extension of thrombosis to portal vein radicals. Hepatic transplant was suggested to the patient, as his acute liver failure did not respond to conservative management. In October 97, the patient died of hepatic encephalopathy with possibly pulmonary embolism. Family history did not reveal any consanguineous marriages or thrombotic episodes.

Figure 1 MRI brain sagittal view, showing superior sagittal sinus thrombosis

Figure 2 MR venography, showing inferior vena cava thrombosis

Questions

- 1 What condition is the patient suffering from?
- 2 Which laboratory test should be done for screening?
- 3 Which individuals should be screened for such conditions?

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Answers

QUESTION 1

Two separate major episodes of life-threatening thrombosis suggest a diagnosis of thrombophilia. The term thrombophilia includes all familial or acquired disorders of haemostasis regulation which predispose to thrombosis. All acquired causes were ruled out by detailed history and examination.

QUESTION 2

The screening tests for familial thrombosis includes complete blood counts, prothrombin time (PT), APTT, thrombin time, factor V Leiden defect, protein C, protein S, and antithrombin deficiency, fibrinogen levels, and testing for antiphospholipid antibodies syndrome.

QUESTION 3

Patients with venous thrombosis under the age of 45 years, patients with deep vein thrombosis, and pulmonary embolism, thrombosis at unusual sites (retinal, portal, hepatic, mesenteric, cerebral), recurrent superficial thrombophlebitis, patients with a family history of thrombosis.

Discussion

In a recent review, the cause of familial thrombosis could be found only in 33% of cases.¹ Currently available plasma-based assays do not identify deficiencies or defects in the vasculature that may lead to thrombosis.² Moreover the levels of these natural anticoagulants in the blood may be quantitatively normal but qualitatively abnormal.³ Among the known causes of familial thrombosis (box 1), factor V Leiden mutation (a point mutation at position 506 in which arginine is replaced by glutamine) accounts for 20% of cases.¹ About 5% of the population have this mutation and those heterozygous may not have thrombotic events in life. In individuals homozygous for this defect, the risk of venous thrombosis is increased several-fold. Arterial thrombosis is not common due to this mutation.⁴ It is presently not known whether patients with factor V Leiden mutation should be treated with more prolonged or intense anticoagulation after a thrombotic episode or whether they require more aggressive prophylactic regimes in high-risk clinical situations.⁴ Protein S and protein C account for 6% and 4% patients of familial thrombosis, respectively.¹ Both protein C and protein S act by inactivating factors V and VIII. Homozygous protein C deficiency causes severe skin necrosis, and often fatal neonatal thrombotic complications. Milder symptoms have been reported for adults with very low or undetectable levels of protein C.³ Factor V Leiden defect can also reduce protein S levels.⁵ Antithrombin is the most important natural anticoagulant and its deficiency accounts for 3% of cases of inherited thrombophilia.¹ Other variables which have been implicated but not proved to confer a thrombotic risk include factor XII, plasminogen, and tissue plasminogen activator inhibitor deficiencies.⁵

Familial thrombophilic states

- factor V Leiden defect
- protein C deficiency
- protein S deficiency
- antithrombin III deficiency
- dysfibrinogenaemia

Box 1

Acquired risk factors for thrombosis

- previous thrombosis
- immobilisation
- major surgery
- malignancy
- oral contraceptives
- hormonal replacement therapy
- antiphospholipid syndrome
- myeloproliferative diseases
- polycythemia vera
- nephrotic syndrome

Box 2

Management of acute venous thrombosis in a patient with familial thrombosis

- immediately: 5000 units heparin intravenously followed by 1400 units/h
- monitor APTT, after 6 hours and then daily
- maintain APTT 1.8–3 times the mean normal
- start warfarin within 24 hours of heparin
- continue heparin for at least 5 days or until PT is in therapeutic range or INR 2–3
- continue warfarin until 6 months after acute thrombosis

Box 3

Screening for thrombophilia should be done after at least 1 month of discontinuation of anticoagulation and investigations should be repeated prior to reaching a definite diagnosis.⁵ Management of such patients includes family screening, counselling, and avoiding other risk factors like oral contraceptives and immobilisation. Treatment with low molecular weight heparin is preferred due to a more predictive response and greater bioavailability. Newer thrombin inhibitors, such as Hirudin and Hirulog, are useful in conditions that are resistant to heparin therapy.

Final diagnosis

Superior sagittal sinus thrombosis and inferior vena cava thrombosis with acute Budd-Chiari syndrome due to familial thrombophilia of unknown aetiology.

Keywords: thrombophilia; superior sagittal sinus thrombosis; inferior vena cava thrombosis; Budd-Chiari syndrome

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Progressive proptosis in a neonate

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A female infant, born at 34 weeks gestation, developed a right orbital proptosis at 14 days of age. Coagulation studies including platelet count were normal. Non-contrast computed tomography (CT) (figure 1) showed gross proptosis of the right eye and a retrobulbar high-density lesion consistent with fresh blood. Magnetic resonance imaging (MRI) was performed within 2 days of the onset of the proptosis. This demonstrated a large retro-orbital lesion, low in signal intensity on T2-weighted images with a bright margin, consistent with haematoma.

In spite of decompression, the eye remained proptosed and became progressively more so. The patient developed an ipsilateral swelling on the cheek which continued to increase in size. A further CT scan was performed 3 weeks after the initial scan (figure 2).

Figure 1 CT of the orbits (non-contrast). There is a homogenous high density intraconal lesion in the right orbit consistent with fresh blood

Figure 2 CT of the orbits (with contrast)

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Questions

- 1 List six possible causes of proptosis in a neonate.
- 2 Describe the findings in the second CT scan (figure 2).