Instructive Case

Superior sagittal sinus thrombosis in a child with Down syndrome

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CASE REPORT

A 15-year-old girl with trisomy 21 and hypothyroidism was hospitalized with a 2-day history of headache and vomiting. Examination showed no abnormalities. The symptoms resolved and she was discharged home. Nine days later she presented to the Emergency Department at Mackay Base Hospital, Queensland, Australia, with a history of a generalized tonic-clonic seizure lasting 15 min. She had been quiet with vomiting and headaches for the previous 6 days. On the day prior to the seizure she had had a 30-min episode of being vague during which she could not recognize her mother.

She had hypothyroidism, diagnosed at age 6 years, managed with thyroxine 150 µg per day (1.5 µg/kg). She had developed hidradenitis suppurativa 5 months previously, associated with a pre-existing seborrhoeic dermatitis, for which she was receiving erythromycin and isotretinoin. She was also taking Norimin (Pharmacia, Sydney, NSW, Australia) (norethisterone 500 µg, ethinyloestradiol 35 µg) for menstrual regulation. Her mother had a history of thromboembolism occurring on three occasions, the first with a pulmonary embolus during her pregnancy with this child. Eight months after the 15-year-old girl presented to the Emergency Department, her mother suddenly and unexpectedly collapsed and died, possibly due to a massive pulmonary embolus. The patient was able to communicate well, although intellectually impaired. She attended a special unit at a high school. An elder sibling had died from B-cell lymphoma at aged 11 years.

On examination the 15-year-old patient had Down syndrome features, weighed 102 kg and had hidradenitis suppurativa on her chest and axillae with no other abnormality. Fundoscopy did not show papilloedema. She had no evidence of middle ear infection. She did not appear dehydrated and had normal urea and electrolytes. Investigations showed mildly elevated platelets (411 × 10⁹/L), white blood cell count 7.7 × 10⁹/L, haemoglobin 134 gm/L, thyroid-stimulating hormone (TSH) 7.2 mU/L (normal range 0.3–5.0 mU/L), free T₄ 16 pmol/L (normal range 9.0–23 pmol/L), gamma glutamyl transpeptidase 162 U/L (normal range <50 U/L), alanine aminotransferase 94 U/L (normal range <40 U/L), and aspartate aminotransferase 37 U/L (normal range <35 U/L); other tests were normal. Subsequent TSH was 0.4 mU/L and free T₄ 21 pmol/L.

By the day after admission the girl was asymptomatic. A computed tomography (CT) scan of her head revealed a filling defect in the superior sagittal sinus (Fig. 1). Mastoid air cells and facial sinuses showed no abnormality on CT scan. A magnetic resonance (MR) venogram confirmed the presence of a large superior sagittal sinus thrombosis extending into the right transverse and sigmoid sinuses (Figs 2,3). There was no cerebral infarction, with only a small area of oedema and ischaemic change. A thrombophilia screen showed an elevated factor VIII, at 2.54 U/mL (normal range <1.50 U/mL) when her erythrocyte sedimentation rate (ESR) was 32 mm/hr, 2 months after presentation. Eight months after the thrombosis her factor VIII was 1.62 U/mL with a C-reactive protein of 14 mg/L and ESR of 39 mm/hr. Proteins C and S, antithrombin 3, homocysteine levels and activated protein C resistance were normal; factor V Leiden and prothrombin 20210G > A were absent; lupus anticoagulant screen and anticardiolipin were negative.

The Norimin was ceased. Subcutaneous low-molecular-weight heparin (enoxaparin sodium) was given for 3 days with oral warfarin commenced at the same time and continued for 8 months. She tolerated the warfarin without adverse effect and has remained well with no residual neurological sequelae. On cessation of the warfarin she was commenced on low-dose aspirin. She received medroxyprogesterone acetate (Depo Provera, Pharmacia, Sydney, NSW, Australia) initially and then received an implant of etonogestrel (Implanon, Organon, Sydney, NSW, Australia) to be retained for 3 years for menstrual control. A follow-up MR venogram showed recanalization of...
Cerebral venous sinus thrombosis (CVST) is rare in children and adolescents, with its incidence estimated to be 0.67 per million children per year, 43% being neonates. The superior sagittal sinus is one of the most common sites. Beyond the neonatal period it may go unrecognized at initial and subsequent presentations, unless there is a high index of suspicion.

Failure to diagnose CVST can result in death or disability. The commonest signs and symptoms are those of raised intracranial pressure. The diagnosis should be considered where findings suggest intracranial pathology, especially seizures, headache, vomiting, reduced level of consciousness and focal neurological signs. Associated cough and shortness of breath might suggest pulmonary embolus.

A similar case, unassociated with sepsis, had not been seen in the Child and Adolescent Health Service of the Mackay Base Hospital previously. Lateral and sigmoid sinus thrombosis arising from associated mastoid infection, usually presenting with symptoms and signs of raised intracranial pressure, had been seen in the department. The patient in the present report presented with symptoms consistent with raised intracranial pressure, but no signs. Her intellectual disability contributed to difficulty in diagnosis.

A filling defect due to the thrombosis needs to be looked for carefully on a CT scan, which would usually be requested as it is the most readily available investigation, as in the present case. Magnetic resonance venogram is more able to show cerebral venous sinus thrombosis. It should be undertaken if there is any doubt, and where symptoms and signs suggest the diagnosis of thrombosis despite a negative CT scan.

The term thrombophilia describes the condition of increased tendency to thrombosis, often due to inherited factors. It is important that prothrombotic factors are sought following thromboembolism that is spontaneous, in an unusual site and at an early age. Prothrombotic factors found to increase the risk of thrombosis include protein C, protein S and antithrombin deficiencies, factor V Leiden, raised prothrombin or factor VIII, abnormal fibrinogen and hyperhomocysteinaemia. Pregnancy, some disease states or drugs, including oral contraceptives, increase the risk of thrombosis.

The oral contraceptive, associated with a high relative risk of CVST, is most likely to have been a contributing factor to the development of the thrombosis in the present case. Although the absolute risk of CVST in oral contraceptive users is very small, consideration of other means of menstrual control might be appropriate in patients with intellectual disability. The options with lower thrombosis risk include medroxyprogesterone acetate injections 3-monthly, etonogestrel subdermal implant to last for 3 years, levonorgestrel intrauterine device lasting 5 years (Mirena. Schering P/L, Sydney, NSW, Australia) or endometrial ablation.

Cyproterone acetate and ethinyloestradiol have been shown to be effective in the management of hidradenitis suppurativa (HS) but was contraindicated in the present case because of the increased risk of thrombosis. Finasteride, a type two 5-alpha-reductase inhibitor of testosterone to dihydrotestosterone, might be a suitable alternative for the management of HS in the present case. High levels of factor VIII are felt to be a cause of thrombosis rather than a consequence. It appears that the raised factor VIII level does not act synergistically with the oral contraceptives.

The origin of elevated levels of factor VIII is uncertain, but the purulent skin infection in this case might have contributed as factor VIII is an acute phase reactant. The maternal history of thromboembolism raises the possibility of a familial coagulopathy despite our inability to document this.

Only a minority of patients with CVST will show an underlying prothrombotic disorder (32% in a recent study), the most common factor being anticardiolipin antibody. Almost all, however, will have risk factors, especially acute or chronic systemic illness. The association of superior sagittal sinus thrombosis with trisomy 21 has been reported in one case.

DISCUSSION

Cerebral venous sinus thrombosis (CVST) is rare in children and adolescents, with its incidence estimated to be 0.67 per million children per year, 43% being neonates. The superior sagittal sinus is one of the most common sites. Beyond the sagittal right transverse and sigmoid sinuses, but with reduced diameter and attenuation in the sagittal sinus in the occipital region. She was advised to take preventive measures for prolonged travel and to avoid oestrogen-containing oral contraceptives.
previously.\textsuperscript{11} Despite this second reported case, there seems to be no recognized association of Down syndrome and CVST. Similarly, the hypothyroidism in this case seems to be incidental to the thrombosis.

Anticoagulation using low-molecular-weight heparin followed by warfarin is the most preferred method of managing children with CVST, based on its efficacy and safety in adults.\textsuperscript{1,2,12,13} Local thrombolysis or thrombectomy could be indicated if the clinical condition worsens.\textsuperscript{1,14}

We described the present case to encourage clinicians to think of CVST where symptoms or signs might suggest this, and to encourage the close examination of CT scans for signs of sinus thrombosis. Following diagnosis of CVST, patients should be screened for a prothrombotic disorder and should receive anticoagulation.

**SUMMARY**
- Most non-neonatal CVST is secondary to systemic illness, such as mastoid infection.
- Cerebral venous sinus thrombosis should be considered where findings suggest raised intracranial pressure, especially seizures, headaches, vomiting and altered consciousness.
- A cranial CT scan needs to be carefully examined for a sinus filling defect due to thrombosis.
- Magnetic resonance venogram is the best means of demonstrating CVST and should be undertaken if there is clinical suspicion or doubt.
- Thrombophilia investigation, including factor V Leiden mutation, prothrombin gene mutation, antithrombin III, proteins C and S, antiphospholipid antibody, lupus anticoagulant, factor VIII and homocysteine levels, should be undertaken in all cases of CVST.
- Although the risk of thrombosis when using oral contraceptives is small, alternative means of menstrual control in disabled young people such as the subdermal etonorgestrel implant might be more appropriate, especially where there is a family history of thrombotic disease.
- Anticoagulation with low-molecular-weight heparin followed by warfarin is the preferred therapy for CVST, largely based on extrapolation from adult trials.

**REFERENCES**