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Clinical Records

Genetically-induced deep venous thrombosis presenting as acute mastoiditis

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Abstract
Sigmoid sinus thrombosis (SST) usually follows acute as well as chronic otitis media with coalescent mastoiditis. A singular case of noncoalescent mastoiditis complicated with thrombosis of deep cerebral sinuses occurring in a young child is presented. A genetic thrombophilic disorder (prothrombin G20210A allele mutation) was identified as the predisposing factor for this unusual complication. Particular emphasis is placed on the course of the disease, which showed regression only after surgical exploration and additional anticoagulant therapy. We conclude that a thorough and early assessment of coagulation factors should always be performed, especially in the population at risk, in order to rule out unusual aetiologies of these rare but still life-threatening pathological processes.

Key words: Mastoiditis; Cranial Sinuses; Thrombosis; Lateral Sinus Thrombosis; Prothrombin; Mutation

Introduction

Sigmoid sinus thrombosis (SST) is considered a possible complication during acute or chronic suppurative otitis media.[1] Similarly to other complications, such as meningitis, intracranial abscesses and otitic hydrocephalus, its incidence has dramatically dropped since the start of the antibiotic era. In fact, early, wide-spectrum antibiotic therapy has proven in most cases to control mucosal and bone inflammatory involvement within the mastoid and middle-ear cleft.[2] A retrograde involvement of the ipsilateral deep sinuses, i.e. transverse and sagittal sinuses, is even rarer, although its incidence in the presence of SST has never been precisely reported.

In this paper, we describe a case of extensive involvement of the venous cerebral sinuses (sigmoid, transverse and superior sagittal) with concomitant acute, noncoalescent mastoiditis in a child affected by a congenital defect of a coagulation factor (prothrombin G20210A allele mutation).

Case report

An 11-year-old boy was referred from a primary care centre with left-sided acute mastoiditis associated with cerebral sinuses thrombosis. He had complained of fever, otalgia, otorrhoea, headache and vomiting for four days, all symptoms which wide-spectrum antibiotic and steroid administration failed to control.

The patient was fully conscious but signs of prostration were present. Inspection of the external ear showed disappearance of the retroauricular fold, while otomicroscopy showed dehiscence of the posterior canal wall and reddish bulging of the eardrum. Blood tests showed a normal white cell count and a slight decrease in red blood cell haematocrit, mean globular volume and mean cell haemoglobin levels, while coagulation tests (prothrombin time, international normalized ratio (INR) and adjusted partial thromboplastin time) were normal.

A computed tomography (CT) scan of the temporal bone showed diffuse infiltration of the mastoid by hypodense material, with neither bony erosion nor intracranial involvement. Venous magnetic resonance angiography (MRA) of the brain revealed thrombosis of the left sigmoid, transverse and lower side of the sagittal sinuses, along with involvement of the jugular bulb and reversal of blood flow in the left superior sagittal sinus (Figure 1). Ophthalmological examination revealed bilateral papilloedema, with no signs of cerebral focal lesions.

Anticoagulant therapy with heparin was immediately started, followed four days later by an extended mastoidectomy which included exenteration of the sino-dural angle and retrosinusal and mastoid tip cells. During the surgical exploration, the walls of the sigmoid sinus were found to be completely involved, and the opening of the sinus revealed the lumen to be filled down to the level of the jugular bulb. Antibiotic treatment was implemented with amikacin and piperacillin, together with

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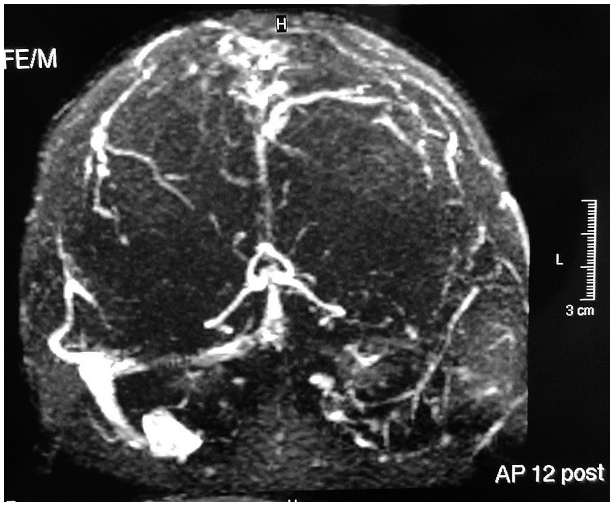

FIG. 1

Magnetic resonance angiography (MRA) of the brain. Complete occlusion of the left sigmoid and transverse sinuses, as well as of the ipsilateral jugular bulb, can be seen.

anticoagulants (low-molecular-weight heparin) and oedema-reducing therapy (intravenous mannitol 18 per cent). The child was monitored every four days by MRA, ophthalmologic examination and assessment of haemopoietic, renal and liver functions. Seven days after surgery, amikacin was suspended and antibiotic therapy was continued by administration of piperacillin.

About eight days after the commencement of warfarin administration, an increased INR level forced us to suspend the anticoagulant therapy. The INR level remained altered for five days, even after suspension of the therapy, making it necessary to administer intravenous vitamin K. After two days of vitamin K administration, INR levels returned to normal and warfarin and heparin therapy was restarted. Five weeks later, antibiotic therapy was suspended and after about seven days of oedema-reducing therapy, neurological symptoms regressed and headache almost disappeared.

- **This is a case report of widespread sinus thrombosis which occurred in a child with coalescent mastoiditis. The child had a congenital defect of a coagulation factor (prothrombin 20210A allele)**
- **The aetiology of the condition and the management are discussed**

The abnormal feedback to the anticoagulant therapy and the presence of a deep thrombotic event prompted us to perform a thorough haematologic investigation, including autoimmune tests (antinucleus Hep2, anti-native DNA, anticardiolipin and anti-beta2-glicoprotein) and genetic tests (factor V Leiden, MTHFR C677T and prothrombin G20210A allele mutation). The patient was found to be heterozygous for the prothrombin G20210A allele. Venous MRA one month after discharge from hospital revealed a partial visualization of the lower part of the left longitudinal sinus, whilst the left transverse and sigmoid sinuses remained unperfused.

After one year of longitudinal follow up, the general condition of the young patient was satisfactory.

Discussion

Deep sinus thrombophlebitis is an uncommon but still serious otological complication, although data regarding its incidence are scanty.[1] Its more common isolated form, SST, usually follows a coalescent acute mastoiditis, presenting in 20 to 40 per cent of cases as a complication of chronic otitis media.[1] More rarely, it occurs after minor head trauma or mild middle ear infection. Hypercoagulability conditions are also involved in its pathogenesis. Thrombotic occlusion of the sigmoid sinus may grow in a retrograde fashion and involve the ipsilateral transverse sinus and/or the superior and inferior sagittal sinuses.[3] In such a case, estimated overall mortality is nowadays still high (8.3 per cent).[4]

Sigmoid sinus thrombosis without an associated coalescent mastoiditis is uncommon. Pregnancy or estroprogestinic treatments are reported to be predisposing factors.[5] Similarly, generalized hypercoagulation conditions, either inherited (antithrombin, protein C or protein S deficiency, factor V Leiden mutation and prothrombin gene 20210A mutation) or acquired (antiphospholipid syndrome, myeloproliferative disease and paroxysmal nocturnal haemoglobinuria) may play a crucial role.[6] Congenital thrombophilia has been detected in six of 40 patients with cerebral venous thrombosis:[7] protein S deficiency in one patient, protein C deficiency in another and factor V Leiden mutation in the other four; additionally, five of the patients also had other associated risk factors for thrombosis.

The young patient in the presented case also displayed a congenital form of thrombophilia (heterozygosity for prothrombin G20210A allele). The prothrombin G20210A allele mutation is a genetic variation of the prothrombin gene, with a G–A transition at nucleotide 20210, which is associated with elevated plasma levels of prothrombin and increased prothrombin activity. The mechanisms by which increased prothrombin levels may promote thrombosis are not yet fully understood. It is unclear whether the ongoing thrombin generation is a direct consequence of elevated prothrombin activity; alternatively, the thrombotic tendency may be linked to the larger amounts of thrombin that are formed once thrombin generation is triggered.

The present case illustrates an important point. Young patients with deep dural vein thrombosis should always be investigated for congenital thrombophilia even when other plausible clinical presentations, such as acute mastoiditis, are present (potentially distracting from the deeper pathogenesis).

Sigmoid sinus thrombosis always needs to be confirmed by imaging studies. In the present case, the CT scan did not clearly demonstrate the involvement of the sigmoid sinus, since the empty 'delta sign' may be absent in cases of incomplete occlusion of the sigmoid sinus.[8] Magnetic resonance angiography plays a crucial role in this regard – it allows confirmation of the diagnosis of SST and also definition of the eventual extension of the pathological process to the other deep sinuses; it also enables thorough follow up, as was the case with our patient.

Gold-standard treatment of SST involves both antibiotic therapy and surgical debridement. Great controversy exists about the usefulness of anticoagulant therapy in the form of intravenous heparin, since this drug could predispose to the detachment of septic emboli from the main thrombus and also spontaneous brain haemorrhage, especially when intracranial hypertension coexists.[9] The early administration of heparin in our young patient was prompted by the involvement of the transverse and superior sagittal sinuses, reflecting unanimous current recommendations.[10]

General agreement exists on the surgical treatment of

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SST – a complete or extended mastoidectomy is always performed, with sinus puncture and opening for possible recanalization.[11] In our patient, full-thickness involvement of the sigmoid sinus walls and complete obliteration of the venous course down to the jugular bulb was discovered, so recanalization was not feasible.

Conclusion

From this case, we conclude that once deep venous thrombosis is diagnosed a prompt investigation of congenital prothrombin status is mandatory, even in the presence of acute or chronic involvement of the mastoid. In fact, the surgical exploration of the mastoid cavity should always be accompanied by anticoagulant therapy, which will reduce the risk of thromboembolism relapses and, most importantly, prevent further thrombi propagation within the cranial venous system.

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