Antiphospholipid syndrome manifesting as papilledema

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Abstract

• AIM: To report a rare case of antiphospholipid syndrome presenting as papilledema and sixth nerve palsy in right eye due to superior sagittal sinus thrombosis, and regression of papilledema following anticoagulation and acetazolamide therapy.

• METHODS: A 44-year-old Chinese gentleman presented with headache, diplopia and mild blurring of vision. Clinical examination revealed the presence of sixth nerve palsy in right eye and papilledema. There was enlargement of blind spot in the visual fields and red green deficiency in both eyes. Computed tomography and magnetic resonance imaging showed superior sagittal sinus thrombosis. Hematological investigation confirmed the presence of antiphospholipid syndrome as the underlying cause.

• RESULTS: The condition was treated successfully in three months with the adjunctive use of anticoagulation and acetazolamide. Reversal of papilledema changes in the optic disc to normal indicates the anatomical recovery, while reduction of enlargement of blind spot to normal size, recovery of red green deficiency to normal colour vision in both eyes and visual improvement after regression of papilledema in right eye indicate functional recovery in this patient.

• CONCLUSION: Antiphospholipid syndrome should be considered in the differential diagnosis of papilledema, and oral acetazolamide is an important adjunct therapy to anticoagulation in cases of refractory papilledema to protect the optic nerve from potential damage which results in blindness.

• KEYWORDS: antiphospholipid syndrome; superior sagittal sinus thrombosis; papilledema; acetazolamide; sixth nerve palsy

Few splintered hemorrhages were noted around the disc (Figure 1, A and B). Colour vision tested with Ishihara charts showed red-green deficiency. However, light brightness was equal in both eyes. Examination of other cranial nerves and central nervous system was normal. Contrast CT scan showed a positive empty delta sign suggesting the presence of superior sagittal sinus thrombosis (Figure 2). The diagnosis was confirmed by MRI which showed the thrombosis within the superior sagittal sinus (Figure 3) and magnetic resonance venography (MRV) study.

Lumbar puncture done on the next day morning showed opening pressure of 50 cm H₂O; 20 mL of cerebrospinal fluid was drained; closing pressure reduced to 27 cm H₂O. Cerebrospinal fluid examination showed no evidence of meningitis or demyelination. Visual field examination done two days later showed enlargement of the blind spot in both eyes with generalized reduction of light sensitivity.

Routine blood investigations (including full blood count, erythrocyte sedimentation rate (ESR), renal function tests, collagen tissue disease screening and liver function tests) were normal. He started taking oral warfarin 5 mg daily. He was discharged from neurology ward ten days after admission and advised further follow-up.

Two days later, he was readmitted to the neurology ward to rule out the possibility of intracranial hemorrhage since the headache was worsening. An urgent CT scan done did not show any evidence of intracranial bleeding. He was seen in the eye clinic next day morning. Visual acuity was 6/12 (with pin hole test 6/9) in the right eye, and 6/6 in the left eye. Both eyes were orthophoric and extraocular movements were full in all directions. There was no diplopia. The anterior segments in both eyes were normal; fundus findings remained the same as initial presentation. He was discharged from neurology ward on the same day on oral warfarin 5 mg daily, with a target international normalized ratio (INR) of 2.0. He was seen in the eye clinic two weeks after being discharged from the neurology ward. Visual acuity was same as before; no relative afferent pupillary defects were noted; anterior segments were normal in both eyes with intraocular pressure of 18 mm Hg. Fundus examination showed worsening of the papilledema—more hyperemia of the disc, more edema in the nerve fibre layer around the optic nerve, extensive flame shape hemorrhages around the optic disc (Figure 1, C and D). After consultation with neurologist, he was given oral acetazolamide 250 mg four times daily to reduce the production of cerebrospinal fluid in view of the worsening papilledema. He was readmitted to the neurology ward. Lumbar puncture was done; opening pressure was 40 cm H₂O. He was referred to neurosurgeon who offered lumbo-peritoneal shunt, but the patient refused operation.

Hematological investigations done in the ward showed normal levels of antithrombin III and protein C, indicating absence of hypercoagulation disorders. Protein S was mildly reduced, and Lupus anticoagulant screening was positive indicating the presence of antiphospholipid syndrome. He was discharged from the ward the next day morning on oral warfarin 5 mg daily, oral acetazolamide 250 mg three times daily and potassium bicarbonate 25 mEq daily; and he was referred to the hematology team for further assessment and management. Follow-up was continued as outpatient in hematology and neurology and eye clinics.

After six weeks, the retinal hemorrhage was completely resolved, and the disc swelling was minimal in both eyes. An optic disc cup of 0.3 was appreciable. Visual acuity and the rest of eye examination remained the same. Acetazolamide was stopped after he discussed with neurologist. Oral warfarin was continued and he was given appointment for follow-up after three months.

After three months, Fundus examination showed pink optic discs with clear margins and 0.3 cup to disc ratio. Macula was normal, papilledema was almost resolved (Figure 1, E and F). Refraction was +3.25 DS/-1.75 DC × 160 (6/9) in the right eye, and +0.75 DS (6/6) in the left eye, so spectacles were prescribed. Visual field test showed normal size of the blind spot in both eyes, and general reduction of light sensitivity. Ishihara colour vision test showed normal colour vision in both eyes. There was no recurrence of papilledema during the next 12 months of follow-up; vision remained same in both eyes. He is on maintenance dose of warfarin 4 mg daily, and on regular follow-up in hematlogy, neurology and eye clinics.

**DISCUSSION**

Papilledema can occur at any age, except during infancy before the fontanelles close. Headache is the most common presenting symptom[9]. Headaches are characteristically worse on awakening, and they are exacerbated by coughing and Valsalva maneuver. Nausea, vomiting and focal neurological signs are also known as presenting symptoms. Since these symptoms are common in daily general practice, papilledema is often overlooked during first presentation. In this case, fundus examination was not done when the patient first presented to the emergency unit, and hence papilledema was missed. Visual acuity is preserved except in very advanced disease. Visual symptoms often are absent; however, some patients experience transient blurring of vision, constriction of the visual field, and decreased color perception. Diplopia may be seen occasionally if a sixth nerve palsy is associated. In the first visit to the emergency unit, the patient did not have these features; but, by the time of second presentation, he had developed all the above mentioned ocular signs.
In this case, the cause of papilledema was found to be superior sagittal sinus thrombosis from CT scan, MRI and MRV studies. The radiological features of this disease were reported by Davies et al. Empty delta sign, though not pathognomonic, is the first sign to be seen on contrast CT scans. It comprises a filling defect at the region of the superior sagittal sinus next to the occipital cortex. Sagittal sections of MRI might help direct visualization of the clot within the sinus. If an empty delta sign or a possible clot was seen in CT scan or MRI, the next step should be MRV to confirm the diagnosis. This patient had typical findings of superior sagittal sinus thrombosis on the three imaging procedures.

Thrombosis of dural sinuses is more common in females than males due to pregnancy and contraception which increase the coagulability of blood. Unlike in females, the most common cause in males is hematological-related hypercoagulative status. A strong association between superior sagittal sinus thrombosis and antiphospholipid syndrome was reported previously. In this patient, a laboratory evidence of antiphospholipid syndrome was found, in terms of positive lupus anticoagulant antibodies and deficient protein S.

Antiphospholipid antibodies are a family of autoantibodies that exhibit a broad range of target specificities and affinities, all recognizing various combinations of phospholipids, phospholipid-binding proteins, or both. The term "antiphospholipid syndrome" or "Hughes' syndrome" was first coined in 1983 by Hughes to denote the clinical association between antiphospholipid antibodies and a

抗磷脂综合征表现为视乳头水肿 1 例
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目的：报告 1 例罕见抗磷脂综合征的患者，由于上矢状窦血栓形成而表现为双眼视乳头水肿及右眼第 6 颅神经麻痹，经抗凝和乙酰唑胺治疗后视乳头水肿恢复。

方法：病例报告：一 44 岁中国男性，主诉为头痛、复视及轻度的视物模糊。临床检查发现右眼第 6 神经麻痹和双眼视乳头水肿，双眼视野盲点扩大和红绿色觉缺失，计算机断层摄影及磁共振扫描显示上矢状窦血栓形成，血液学检查证实抗磷脂综合征是其潜在原因。

结果：在联合应用抗凝和口服乙酰唑胺治疗 3 个月后，视乳头水肿恢复正常至正常的解剖，扩大的视神经盲点降至正常水平，双眼红绿色觉恢复正常，伴随右眼视乳头水肿消退和视力改善表明这个患者视神经功能得以恢复。

结论：抗磷脂综合征应与视乳头水肿鉴别诊断；对于顽固性的视乳头水肿，口服乙酰唑胺是抗凝治疗的重要辅助治疗，它可以保护视神经避免有可能导致失明后果的视神经损害。

关键词：抗磷脂综合征；上矢状窦血栓形成；视乳头水肿；乙酰唑胺；第 6 颅神经麻痹