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Short communication

Malignant meningitis presenting as pseudotumor cerebri

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ABSTRACT

Malignant leptomeningitis can present as the clinical syndrome of pseudotumor cerebri due to infiltration of arachnoid villi in the superior sagittal sinus. We show that malignant pachymeningitis can also present with pseudotumor cerebri, likely due to cerebral venous hypertension from transverse sinus compression. We present 3 cases of pseudotumor cerebri due to pachymeningeal or leptomeningeal metastases and discuss the mechanism of intracranial hypertension in such cases, its diagnosis and treatment.

1. Introduction

Pseudotumor cerebri (PTC) is a clinical syndrome of isolated intracranial hypertension (ICH)—measured usually by lumbar puncture [1]. It is defined by 3 negatives [2]: (a) the absence of any neurological symptoms or signs not attributable to ICH; (b) the absence of an intracranial mass lesion; and (c) the absence of hydrocephalus. Typically the patient will present with headache and will be found to have papilledema as the sole clinical abnormality and have a normal CT or MRI scan, although some patients will not even have papilledema, at least in the beginning [3]. The most common form of PTC occurs in obese young women in whom it can be caused by, and cause, stenosis of both or only of the dominant transverse venous sinus [4]. Such cases used to be called *benign intracranial hypertension* (BIH)—benign in the sense that these patients do not have a (malignant) brain tumor, but since they can nonetheless go blind it is now called *idiopathic intracranial hypertension* (IIH) [5]. PTC can occur in infective, fungal [6] or rickettsial [7] meningitis. In patients with primary or secondary malignant leptomeningitis ICH is usually due to, or at least attributed to, communicating hydrocephalus [8,9]. However we have found single case reports of patients with malignant leptomeningitis [10,11] or pachymeningitis (dural metastases) [12,13] who have ICH with papilledema but without hydrocephalus, but are not recognized as having the clinical syndrome of PTC. Here we report 3 cases with PTC due to metastatic malignant meningitis, 2 with leptomeningitis and one with pachymeningitis, in order to show that PTC as well as communicating hydrocephalus can be the presentation of ICH in patients with malignant meningitis.

2. Case histories

2.1. Case 1: PTC due to secondary malignant pachymeningitis from prostate cancer

A 66 year old male was diagnosed with prostate cancer following detection of a PSA of 264 μg/L (N < 5.5). On initial scanning he was found to have metastases in multiple bones including the skull, and right ureteric obstruction. Despite hormonal therapy and radiotherapy his PSA continued to rise (to 1700). Sixteen months following diagnosis he was referred by his family doctor to an ophthalmologist for a complaint of blurred vision and headache for one month. At that time right VA was 6/9, left VA was 6/36 (the eye had been amblyopic since childhood). Visual fields showed marked peripheral constriction and the fundi showed marked papilledema. Lumbar puncture showed an opening CSF pressure of >350 mm H_20 (N < 200), a protein level of 0.32 g/L (N < 0.45), glucose level of 3.6 mmol/L (N > 3.5), 3 white cells (N < 5) and no malignant cells.

Brain MRI showed no parenchymal lesions and no hydrocephalus but multiple metastases in the base, and vault of the skull and in the dura (Fig. 1a). MR venogram showed stenoses of both transverse sinuses but no thrombosis. Catheter venogram showed these as intrinsic lesions within the right transverse sinus (Fig. 1b) as well as extrinsic compression; the left transverse sinus was atretic. Pressure was 58 mm Hg in the superior sagittal sinus, 8 mm Hg in the right sigmoid sinus and 16 mm Hg in the left sigmoid sinus. The patient underwent a left optic nerve sheath fenestration followed the next day by right transverse sinus stent placement, in order to preserve

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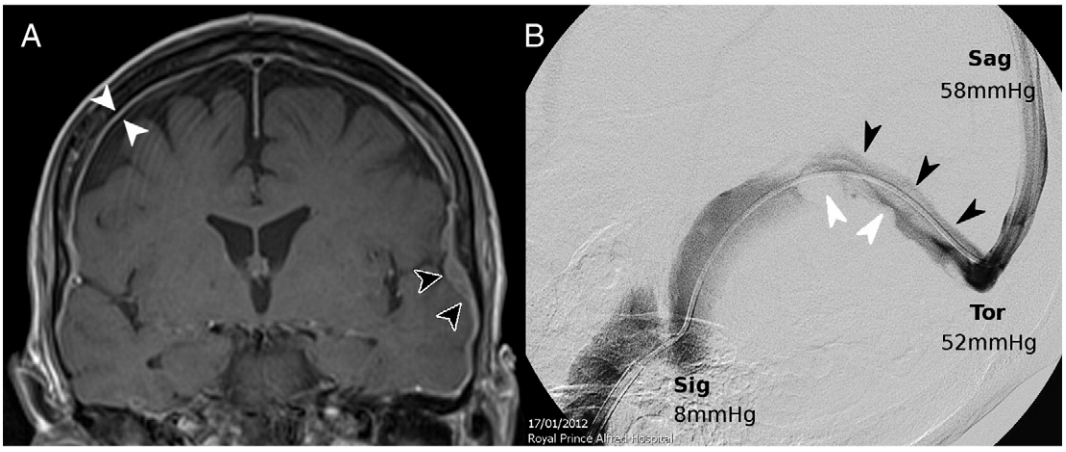

Fig. 1. (A) Contrast enhanced coronal T1 MRI of patient [1] with malignant pachymeningitis (dural metastases) showing a metastatic mass in the dura over the left temporal lobe (black arrowheads) as well as diffuse pachymeningeal enhancement (white arrowheads). (B) Catheter venogram of patient [1] showing multiple intrinsic lesions in the dominant right transverse sinus (white arrowheads) as well as extrinsic compression (black arrowheads) producing a pressure of 58 mm Hg (=760 mm H_2O) in the superior sagittal sinus (Sag) with a gradient of 46 mm Hg from the torcula (Tor) to the sigmoid sinus (Sig).

vision. His vision remained stable until his death 6 weeks later from presumed pulmonary embolism.

2.2. Case 2: PTC due to malignant leptomenigitis secondary to gastric cancer

A 52 year old Chinese male presented with 12 months of dyspepsia and was diagnosed on gastroscopy and laparoscopy to have a poorly differentiated signet-ring adenocarcinoma involving the serosa and local lymphnodes with perineural invasion. He had a radical gastrectomy, local radiotherapy and adjuvant chemotherapy. At a routine visit 6 months later he complained of headache and a visual disturbance. His oncologist found "no neurological abnormality". His tumor markers had risen markedly: CEA to180 ng/ml (N < 2.5) and CA19.9 to 2000 U/ml (N < 37). His brain MRI with contrast showed no abnormality and a CT of the chest and abdomen showed no tumor recurrence. A month later he was referred by his family doctor to an ophthalmologist for the continuing visual disturbance and headache; the ophthalmologist found normal visual acuity 6/9 in each eye but also marked bilateral papilledema with enlarged blinds spots and peripheral constriction of visual fields (Fig. 2). Repeat MR with contrast of brain and spine still showed no abnormality. Lumbar puncture showed a pressure of 320 mm H_2O, 21 white cells (14 lymphocytes and 7 neutrophils), a protein of 0.63 g/L, a glucose of 1.7 mmol/L. Cytology was positive for adenocarcinoma. A diagnosis of PTC secondary to malignant leptomeningitis was then made. Due to progressive visual field constriction (Fig. 2) he underwent bilateral sequential optic nerve sheath fenestrations in order to preserve his visual fields. He then had 30 Gy radiation in 10 fractions covering the whole brain and the optic nerves. Two months later his vision was 6/6, 6/12 and his visual field loss had stabilized after a slight deterioration in the right eye following surgery. (Fig. 2). He died 10 weeks later from biliary obstruction.

2.3. Case 3. PTC due to malignant leptomeningitis secondary to systemic lymphoma

A 62 year old male presented with a mass in his right flank. Biopsy showed diffuse large B-cell lymphoma. He was treated with chemotherapy and local radiotherapy, but despite this his PET scan showed extension of disease. He had an autologous stem cell transplant 8 months later. Six weeks after this he presented with headache, nausea, vomiting and diarrhea. Stool had *Clostridium difficile* and with pentamidine treatment the diarrhea settled, but not the headache and vomiting and he became less responsive. On neurological examination 2 weeks later he had marked bilateral papilledema, but was not responsive enough for a visual examination. MRI showed normal size ventricles but widespread leptomeningeal enhancement (Fig. 3). At lumbar puncture the CSF pressure was >300 mm H_20 and contained 8.82 g/L protein, 0.4 mmol/L glucose, 2320 white cells, mostly lymphoma cells. In the four days following he became progressively less responsive and died.

3. Discussion

Rare primary malignancies of the cranial or spinal leptomeninges, such as glioma [8], melanoma [14,15] or lymphoma [16–18] and also the more common secondary leptomeningeal malignancies [9,19,20] can all produce ICH. While it is well recognized that these patients can have hydrocephalus without papilledema, only a few have been noted to have papilledema without hydrocephalus—i.e. the clinical syndrome of PTC [11,17,21]. Here we show that secondary malignant invasion not only of the leptomeninges, but also of the pachymeninges, can cause PTC.

Malignant leptomeningitis can produce a variety of focal or multifocal neurological syndromes as well as symptomatic or asymptomatic, sometimes isolated, ICH [22,23]. The diagnosis of malignant leptomeningitis can be suspected from brain or spine MRI, showing leptomeningeal enhancement (Case 3). However MRI can be normal [24], as in our case 2. The definitive diagnosis of malignant leptomeningitis is made by finding malignant cells in the CSF, as in Cases 2 and 3; this might need more than one attempt [25].

The diagnosis of malignant pachymenigitis (i.e. dural metastases) can be suspected from the appearance of nodular dural enhancement on MRI but with normal CSF contents [13]. About 20% of dural metastases are from prostate and about 20% produce ICH. The definitive diagnosis of malignant pachymeningitis is made by dural biopsy. In our case 1 the presence of widespread and increasing bony metastases from prostate cancer, including the skull base, made it highly likely that the progressively increasing nodular dural enhancement on MRI represented dural metastases.

ICH in general can have 4 different basic pathophysiological mechanisms [2]: 1. intracranial mass lesion (e.g. brain tumor); 2. diffuse cerebral edema (e.g. severe head injury, hepatic encephalopathy); 3. block of CSF circulation (i.e. hydrocephalus—obstructive or communicating) or 4. failure of CSF reabsorption (i.e. PTC). Mechanism 4 of ICH—failure of CSF absorption, at the level of the arachnoid villi in the superior saggital sinus [1], can also occur in patients with meningitis [6,7,26] and the result will be PTC. The most frequent cause of the clinical