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C A S E
R E P O R T

Idiopathic intracranial pachymeningitis in a patient on CAPD

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ABSTRACT

We report a very rare condition of idiopathic intracranial pachymeningitis (IIP) in a 66-year-old lady who had been on continuous ambulatory peritoneal dialysis (CAPD) for 3 years. Of the less than 20 reported cases of IIP in literature, this is a second case of IIP occurring in uremic patients. The presentation in this lady was drowsiness, hallucination and an abnormal afferent pupillary reflex. The diagnosis was made by magnetic resonance (MR) imaging which showed diffusely thickened meninges, and meningeal biopsy showed chronic fibrotic change, with scattered mononuclear cells without significant inflammatory element. There was transient symptomatic improvement with steroid therapy but she deteriorated 6 months later and finally died 15 months after steroid therapy.

Key words: Intracranial pachymeningitis, Continuous ambulatory peritoneal dialysis

中文摘要

我們這裡報道一位進行連續活動性腹膜透析 3 年的 66 歲女士併發原發性顱內硬腦膜炎(IIP)的罕見情況。在近20例有關原發性顱內硬腦膜炎的文獻報道中，這是第二例發生於尿毒症患者。患者臨床表現為倦感、有幻覺及異常的傳入瞳孔反射。根據磁力共振顯示硬腦膜彌漫性增厚及腦膜活檢顯示慢性纖維化改變，單核細胞浸潤但無炎症表現，而確定診斷。經激素治療有短暫的症狀好轉，但6個月之後病情惡化，於激素治療後 15 個月死亡。

CASE HISTORY

Continuous ambulatory peritoneal dialysis (CAPD) was commenced in a 66-year-old lady with history of old minor stroke in 1994 for end-stage renal failure from chronic glomerulonephritis. Immune markers were unremarkable. From 1994 to 1996, Kt/V was kept above 1.8. She developed diabetes mellitus with fatty liver changes requiring low dose insulin in 1995. In 1996, she had postural dizziness from postural hypotension. Autonomic neuropathy was diagnosed clinically. She also has an episode of right hemiparesis in April 1996; computerized tomographic (CT) scan of brain showed left internal capsule infarct.

In January 1997, she developed headache, vomiting and hallucination. Noncontrast CT brain was unremarkable. Lumbar puncture showed an elevated cerebrospinal fluid (CSF) protein of 1.83 g/L, slight pleocytosis (WCC 12 x 10^6/L) and normal glucose level. CSF cultures for bacteria and mycobacterium were negative. She was treated as bacterial meningitis with high dose penicillin G and cefotaxime with some apparent improvement. Three months later, she was found to have early "Parkinsonism" features with cogwheel rigidity and right upper limb tremor, benzhexol was given. Cisapride was also prescribed for her recurrent epigastric discomfort.

In June 1997, she was noticed to have memory deterioration and decreased mobility resulting in chair-bound. In August 1997, she developed *flavobacteria spp* peritonitis. Intraperitoneal vancomycin and tobramycin were given and peritonitis responded. However she was found to be confused with paranoid ideas 1 week after treatment. There was no abnormality in serum sodium,

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potassium and calcium levels. Mental state deteriorated gradually and she became semicomatose. A transient right afferent pupillary defect was noticed. CSF from lumbar puncture showed a markedly elevated protein level of 4.43 g/L, white cell count 18 x 10^6/L (N 77%, L 13%, M 8%) and normal glucose level. CSF cultures for acid fast bacilli, fungus and virus were negative. There was no evidence of malignancies, autoimmune diseases or syphilis. Anti-PR3, anti-HIV1 and 2, and anti-HTLV1 were negative. Electroencephalogram (EEG) showed nonspecific background slow waves. CT scan of thorax and abdomen were unremarkable. CT scan of brain was also unremarkable apart from the old lacunar infarct and decreased prominence of cerebral sulci. Subsequently magnetic resonance (MR) imaging of brain revealed diffuse grossly thickened meninges with prominent enhancement by gadolinium (Gd) (Fig. 1). There were also evidences of previous hematoma at the left basal ganglion and sub-insular white matter, and scattered multiple tiny hypointense spots compatible with hemosiderin deposits at the subcortical region in bilateral cerebral hemispheres and the left side of cerebellum

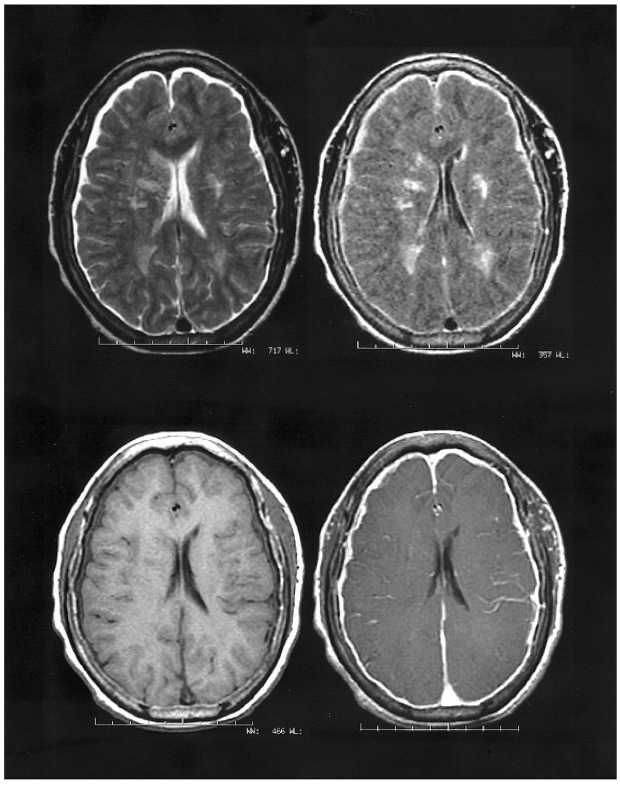

Figure 1. Images of MR imaging of brain showing diffuse thickening of meninges. The upper panel was an axial cut T2 weighted image (left) and fluid attennation inversion recovery (FLAIR) image (right) which showed the thickened meninges and some subcortical ischemic changes. The lower panel was an axial T1 weighted images, before (left) and after (right) contrast enhancement.

representing previous insult with associate bleeding. Meningeal biopsy revealed chronic fibrotic change of the dura and hemosiderin deposition in the arachnoid vascular connective tissue indicating old hemorrhage. There were scattered mononuclear cells and giant cells of non-specific reactive changes without significant inflammatory element or evidence of herpetic infection or granulomatous inflammation. Idiopathic intracranial pachymeningitis (IIP) was diagnosed and she was given a trial of prednisolone with 1 mg/kg/day. Her mental state gradually improved to her premorbid state with coherent speech and she was able to walk for short distances with some support. She was maintained on a low dose prednisolone 2.5 mg/day at 2 months.

Six months later, she developed drowsiness again and prednisolone was increased to 10 mg/day with some improvement. However, she still had some fluctuation in conscious state and hallucination. By November 1998, she became progressively unresponsive. MR imaging brain was repeated and did not reveal any significant changes. Prednisolone was increased to 20 mg/day without significant improvement. She finally succumbed on 7 January 1999, 2 years after the first presentation of IIP and 17 months after the diagnosis was made. Necropsy was suggested but was refused by her family members.

DISCUSSIONS

Altered conscious state in dialysis patients is quite common. The common causes include infective and metabolic encephalopathy (including uremia, drug induced, electrolyte disturbances and aluminum toxicity), cerebrovascular diseases, subdural hematoma and accelerated cerebral atrophy (1). The diagnosis in this lady is IIP which is based on the circumstantial evidences from MR imaging, lumbar puncture and meningeal biopsy. As the name implies, IIP has isolated meningeal thickening which may involve intracranial or extracranial areas. It is a very rare disorder and there were less than 20 reported cases from our Med Line literature search (2-4). There was no consistent association with other diseases. Its etiology and pathogenesis are unknown. Before making the diagnosis, one must actively exclude other conditions that cause meningeal thickening: syphilis, tuberculosis, chronic fungal infection, sarcoidosis and multifocal fibrosclerosis. There were two case reports of such similar pathological findings with HTLV-1 infection (5).

From the reported cases so far, the commonest presentation was headache. Other symptoms were related to the entrapment or compressive effect of the thickened meninges, namely ataxia, visual neuropathy and various

cranial nerve palsies. In our indexed patient, the main symptoms were drowsiness and hallucination. There was once an abnormal pupillary reflex which signified cranial nerve involvement. The most consistent investigation findings are raised erythrocyte sedimentation rate, increased CSF protein (varies from normal to 4.4 g/L) with variable pleocytosis (from 0 to 104 x 10^6/L). MR imaging shows widespread meningeal thickening with homogeneous Gd enhancement. Meningeal biopsy is mainly used to rule out other diseases and is nonspecific with fibrotic thickening of dura mater, infiltrated by lymphocytes, plasma cells and a few giant cells, together with scattered areas of necrosis.

The disease usually runs an indolent course from 1 to 10 years. In our patient, the disease should have preceded the diagnosis for more than a year. The so-called "bacterial meningitis" with symptoms of headache and hallucination was more likely an early presentation of IIP. The apparent improvement after antibiotic therapy was probably due to the fluctuation of symptoms of the disease. Up till now, there is no definite treatment for IIP. If hydrocephalus happens as a complication, surgery is the treatment of choice. Symptoms usually improve with steroid, but there is no consensus on the dose and duration of treatment. Other less effective treatments include azathioprine and radiotherapy. The meningeal thickening on imaging is not responsive to treatment and does not parallel with the clinical course.

The first case of IIP occurring in uremic patients was described in 1975 in a hemodialysis patient (2). This is a second case of IIP. The first case of IIP that occurred in uremic patients was a 50-year-old man with unknown cause for his renal failure and had received 1.5 years of hemodialysis before he presented with cranial nerves palsies which included vagus nerve palsy, blindness with loss of afferent pupillary reflex. He died 3 months after the onset of blindness. Necropsy showed a large recent intracerebral hematoma involving the surface and extended deeply into the right cerebral hemisphere and diffuse markedly thickened dura mater. This was probably the direct cause of death. There was thickened dura mater with infiltrates of chronic inflammatory cells including lymphocytes, plasma cells and scattered eosinophils. No microbiological cause was identified including mycobacterium, fungi, and pyogenic bacteria. The term *hypertrophic granulomatous cranial pachymeningitis* was given and this condition was renamed IIP as there are more cases of similar pathological findings with similar clinical presentation and the pathological condition described subsequently. Though by definition of an idiopathic condition, an underlying infective cause could not be identified, a response to an unidentified agent is still a possibility as HTLV-1 infection has been shown to be related to such a similar pathological condition in two patients (5). As uremia is a form of immunosuppressive state, it may predispose patients to such an unidentified agent. It is also interesting to note that in both cases, there was evidence of recent or previous intracerebral hematoma. It may just represent a coincidence or it may point to a pathological link between the two though meningeal thickening is not a feature of intracerebral hemorrhage.

It has to be pointed out that the diagnosis of IIP can be easily missed with CT scan. MR imaging is much more sensitive to pick up this condition (6). As dialysis patients are predisposed to various conditions affecting the central nervous system function, a MR imaging of brain should be considered as an essential neurological investigation when the picture cannot be adequately explained by CT scan or CSF findings.

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