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## CASE REPORT

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# Hypertrophic Pachymeningitis as the First Manifestation of Systemic Lupus Erythematosus

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### ABSTRACT

*Hypertrophic pachymeningitis, characterised by focal or diffuse thickening of the dura mater, is an uncommon condition. An increasing number of cases have been reported for its association with underlying autoimmune and connective tissue diseases. We report the case of a Chinese woman with hypertrophic pachymeningitis as the first and only clinical manifestation for her underlying systemic lupus erythematosus, with histological confirmation of the diagnosis.*

*Key Words:* Cranial nerve diseases; Dura mater; Lupus erythematosus, systemic; Magnetic resonance imaging; Meningitis

## 中文摘要

### 肥厚性硬腦膜兒炎作為紅斑性狼瘡症的首發表現

余黃莉、Bhatia KSS、王琪

肥厚性硬腦膜兒炎是一種較為少見的情況，病人會出現硬腦膜的局部性或瀰漫性增厚。愈來愈多的病例顯示此病與潛在的自體性免疫及結締組織病有關。本文報告一名紅斑性狼瘡症女性患者，經組織學確認，她首發及唯一的症狀是肥厚性硬腦膜兒炎。

### INTRODUCTION

Hypertrophic pachymeningitis (HP) is an uncommon condition characterised by focal or diffuse thickening of the dura mater, with histology showing non-specific chronic inflammation. When the underlying cause is not identified, it is termed idiopathic HP. There is a wide spectrum of clinical presentations depending on the site of involvement — including chronic headache, cranial nerve palsies, ophthalmological involvement, ataxia, and seizure.<sup>1</sup> The underlying pathogenesis of HP is not

well-established, but an association with autoimmune conditions including Wegener's granulomatosis,<sup>2-5</sup> rheumatoid arthritis, undifferentiated connective tissue disease,<sup>6,7</sup> microscopic polyangiitis,<sup>8</sup> Sjogren's syndrome,<sup>9</sup> temporal arteritis and anti-neutrophil cytoplasmic antibody (ANCA)-positive vasculitis<sup>10-12</sup> has been noted.

We report a case of HP, as the first clinical manifestation associated with systemic lupus

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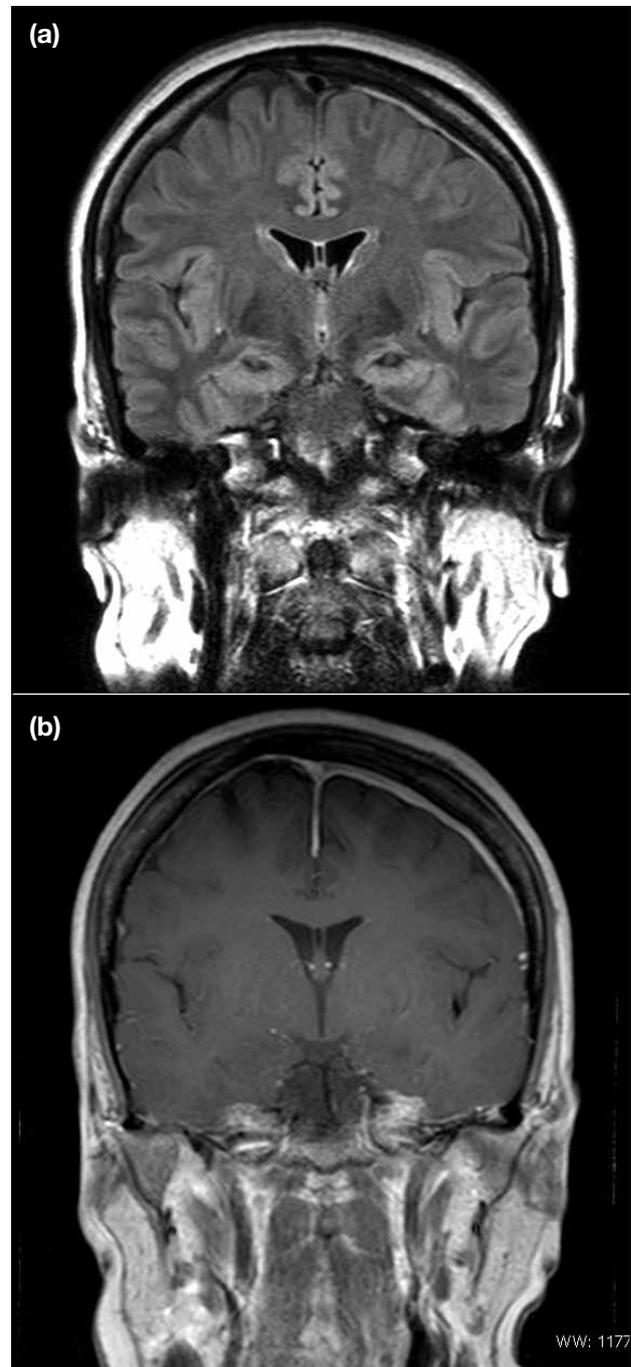
erythematosus (SLE), with histological confirmation of the diagnosis.

## CASE REPORT

A 37-year-old Chinese woman presented to the Emergency Department in April 2010 with severe headache for one week. Her past health was unremarkable. There were no clinical signs of cranial nerve palsy, increased intracranial pressure or neurological deficits. Initial non-contrast computed tomography of the brain was unremarkable. Conservative treatment failed and her symptoms persisted. Magnetic resonance imaging (MRI) of the brain then showed a localised thickening of the pachymeninges of the left frontoparietal region with hyperintense signal on fluid-attenuated inversion recovery (FLAIR) sequence and avid gadolinium contrast enhancement (Figure 1). The dural sinuses were patent and of normal calibre on MRI venogram. Further investigations were performed for possible causes of pachymeningeal thickening, including infective, neoplastic and granulomatous aetiologies. Lumbar puncture revealed a high opening pressure of 280 mm H<sub>2</sub>O. Cerebrospinal fluid (CSF) biochemistry (protein, glucose, white cell count) was within normal limits. The CSF was negative for bacterial, fungal and tuberculous cultures, and CSF viral studies were negative for herpes virus and enterovirus. Cytology of the CSF was negative for malignant cells. Dural biopsy was performed to obtain a histological diagnosis. This showed thickened dura with foci of dystrophic calcification and a small number of chronic inflammatory cells. There was no evidence of granuloma or tumour. Microbiological cultures were negative.

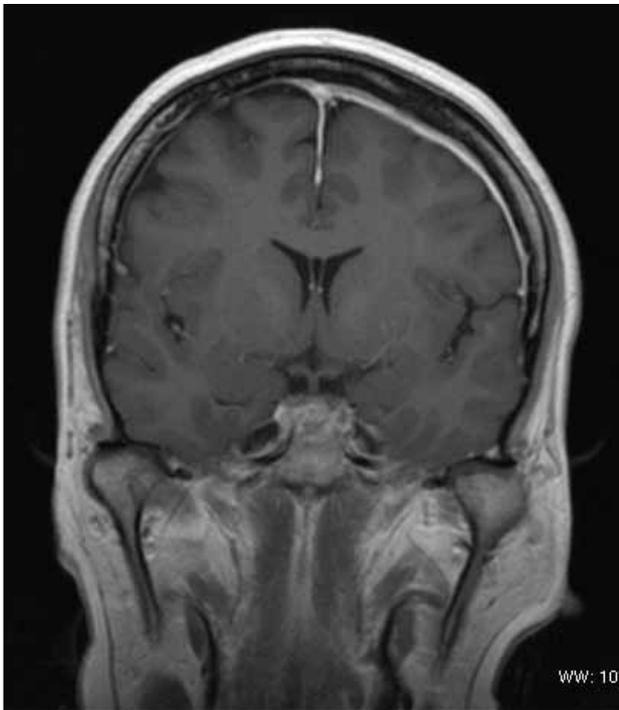
Blood tests on admission showed normal blood count, liver function, and renal function. The erythrocyte sedimentation rate was raised to 40 mm/hour. Immunological profile revealed positive antinuclear antibodies (ANA), elevated anti-double stranded DNA (anti-dsDNA) of >1000 IU/ml (normal level, <70 IU/ml), positive anti-extractable nuclear antigen and anti-Smith antigen (anti-Sm). Rheumatoid factor (RF) and ANCA testing were negative. There were two documented episodes of lymphopenia ( $<1.5 \times 10^9$  /L), one episode of leukopenia ( $3.9 \times 10^9$  /L), and one episode of low complement 4 level. Although there was no other clinical manifestation of SLE, the autoimmune profile was highly suggestive of the diagnosis.

A diagnosis of HP with evolving SLE was established.



**Figure 1.** Magnetic resonance images of the brain performed on initial diagnosis in April 2010. (a) Coronal FLAIR image shows the hyperintense signal of the focal pachymeningeal thickening over the left side. (b) Coronal T1-weighted image with contrast shows avid enhancement of the pachymeningeal thickening.

The patient was treated with prednisolone 10 mg daily for control of headache, and drug treatment was further tapered to 10 mg on alternate days, with hydroxychloroquine 400 mg daily. Her symptoms were



**Figure 2.** Follow-up contrast magnetic resonance imaging of the brain in May 2011, one year after initial diagnosis. There is no significant interval change in the thickness and enhancement pattern.

under control, and the level of anti-dsDNA was on a decreasing trend.

A follow-up MRI brain scan was performed one year later (Figure 2). The pachymeningeal thickening of the left frontoparietal region had remained static, with similar contrast enhancement. No new area of involvement or other intracranial lesion was evident.

## DISCUSSION

Our patient presented with severe headache, which is the most common presentation of HP.<sup>1</sup> The diagnosis of HP is based on the imaging finding of enhancing pachymeningeal thickening, and confirmation by dural biopsy. The differential diagnoses of thickened pachymeninges include infective, granulomatous, and neoplastic causes, which should be excluded with appropriate investigations. There was an absence of other common neurological involvement in our case, such as cranial nerve palsies, papilloedema, diplopia or ataxia; only the left frontoparietal region was involved, without affecting the cranial nerves.

The exact mechanism of HP was unclear although there were increasing numbers of reports suggesting an association with autoimmune conditions, most commonly Wegener's granulomatosis<sup>2-5</sup> and ANCA-positive vasculitis.<sup>10-12</sup> An association with connective tissue diseases, such as undifferentiated connective tissue disease,<sup>6,7</sup> Sjogren's syndrome,<sup>9</sup> positive RF,<sup>13</sup> and positive ANA<sup>14</sup> had also been reported.

In our patient, although there was no other clinical manifestation of autoimmune disorder, the combination of positive ANA, anti-dsDNA, anti-Sm antibodies, with two occasions of lymphopenia, was highly suggestive of serologically active SLE. The presence of HP was the first and only manifestation. The level of anti-dsDNA, correlating with disease severity of SLE, was on a decreasing trend when she was treated with corticosteroids and hydroxychloroquine. To our knowledge, there was only one other case report suggesting the association of HP and SLE,<sup>15</sup> but no histological diagnosis was obtained in that patient. Furthermore, that patient developed HP after 20 years of SLE, whereas in our patient, HP preceded the diagnosis of SLE. Most of the reported cases suggesting an association of HP with connective tissue disorders were in patients with known connective tissue diseases. There was only one case report of a male patient presenting firstly with headache and diagnosed with HP, then subsequently developing clinical symptoms leading to a diagnosis of undifferentiated connective tissue disease.<sup>7</sup> To our knowledge, this was the first case report to suggest correlation of HP and SLE with histological confirmation. The presence of anti-Sm antibodies associated with SLE, and the occurrence of HP, being the first and only clinical manifestation, preceding the serological diagnosis of SLE, were also unique for our case. HP can partially resolve or persist after treatment.<sup>5</sup> Long-term follow-up of the patient is needed to monitor response to treatment and to identify any subsequent appearance of other clinical manifestations of the disease.

## CONCLUSION

An increasing number of case reports suggested an association of HP in patients with underlying autoimmune and connective tissue diseases. It typically presents in patients with previously diagnosed autoimmune diseases, whereas our case illustrated that HP might be the initial and sole clinical manifestation of underlying autoimmune disease. A thorough work-up, specifically for a possible autoimmune condition, should

be performed and long-term follow-up is required when HP is the only clinical manifestation.

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