

# Mixed Connective Tissue Disorder Associated Rare Case of Hypertrophic Pachymeningitis

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**Abstract:** *Hypertrophic pachymeningitis is a inflammatory disease of the dura matter characterized by localized or diffuse thickening of the dura mater with fibrosis. It is rare disorder of diverse etiology like secondary to infections, carcinomatosis , or inflammatory diseases or part of mixed connective tissue disorder. It may also be idiopathic. We report a case of pachymeningitis which was a 45 year-old female presented with left-extremity focal seizure and paraesthesia of both lower limbs and blurring of vision. Magnetic resonance imaging (MRI) revealed a diffuse thickening and enhancement of the right convexity dura matter and falx with focal nodularity. She was diagnosed to have mixed connective tissue disorder. The disease may have a remitting and relapsing course. She responded to steroids. She had relapse of disease after one month and recovered with immunosuppressants.*

**Keywords:** Hypertrophic pachymeningitis , Mixed connective tissue disorder, focal seizure

## 1. Case Report

A 45-year-old, previously healthy female presented with focal seizure of left extremities with paraesthesia of both lower limbs and blurring of vision since 4-5 years. She also had history of headache since 5-6 years , diffuse , lasting for 1-2 hrs , 4-5 times per week , relieved on taking medications , without associated vomiting, photophobia or phonophobia . On admission, her neurological examination was normal. MRI revealed irregular Dural thickening. The differential diagnoses included meningioma en plaque, lymphoma, tuberculosis, sarcoidosis, collagen vascular disorders, lymphoma, meningeal carcinomatosis diseases and IgG4-related disease.

Lumbar puncture revealed a clear cerebrospinal fluid (CSF). There were 4 cells/ mm<sup>3</sup> (95% lymphocytes). Total protein was 76 mg/dL and glucose were 59 mg/dL. Systemic investigation was negative for infections, metabolic dysfunction, inflammatory diseases (including rheumatoid disease) or any other medical condition. She was tested for an extensive panel of autoantibodies like ANA , PM-Scl , PCNA, Mi-2 , KU were positive and anti-dsDNA, RF, anti-RO, anti-LA, anti-SCL70, anti-mitochondrial, p-ANCA, c-ANCA, anti-RNP, Anti-Jo-1 were negative and the blood level of angiotensin converting enzyme (ACE) was normal. EEG shows mild degree of non specific , electrophysiological dysfunction over left temporal and right posterior head regions. She responds oral steroid therapy and seizure was subsided.

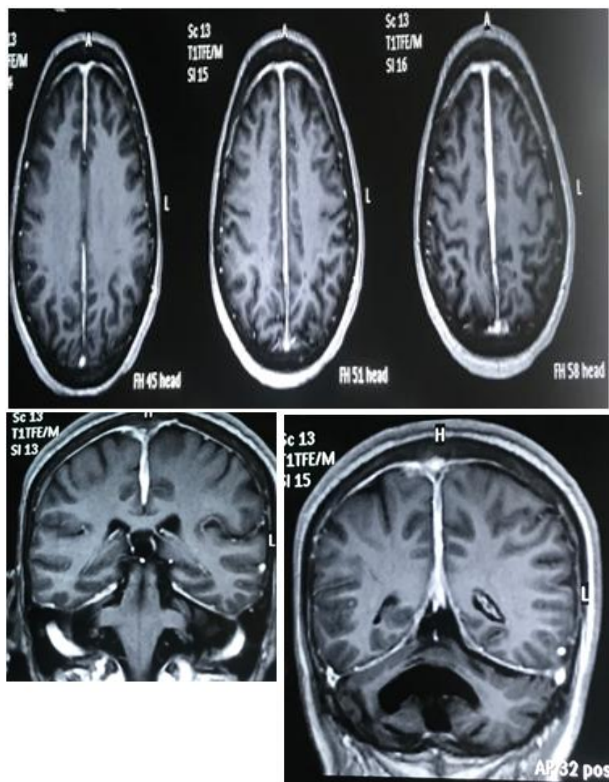
After one month, she was re-admitted again with history of lower motor right facial palsy. On admission, her neurological examination was normal except right lower motor facial nerve palsy. MRI revealed diffuse pachymeningeal thickening showing intense post contrast enhancement involving falx cerebri and along bilateral fronto-parietal convexities. She was given pulse therapy

of immunosuppressant cyclophosphamide for the relapse. She recovered and was discharged on steroids.

CSF Report	Result
Sugar	59 mg/dl
Protein	76 mg/dl
ADA	7 U/L
LDH	104 U/L
Total count	4 cells/cumm
Lymphocytes	95%
Polymorphs	0
Ependymal cells	5%
Appearance	Clear /colourless
CSF TB PCR	Negative

Blood Investigations	RESULT
Haemoglobin	11 gm%
Total WBC count	5300 cell/cumm
Total RBC count	4.72 Mil/ $\mu$ L
Total platelet count	3.08 lacs/cumm
HIV	Negative
HBsAg	Negative
HCV	Negative
CRP	55.75mg/l
TSH	4.53 $\mu$ U/ml
SGPT	53 U/L
S.Creatinine	0.6 mg%
RBS	122 mg%
ESR	81 mm/hr
IgG4	0.572gm/l (0.03-2.0gm/l)
Chest Xray	Normal
ACE level	Negative
ANA	Positive
PM-Scl	Positive
PCNA	Positive
Mi-2	Positive
KU	Positive
dsDNA	Negative
SS-A /Ro-60	Negative
SS-A/ Ro-52	Negative
SS-B/La	Negative

Scl-70	Negative
Jo-1	Negative
Nucleosome	Negative
Histones	Negative
Ribosomal P- protein	Negative
AMA M2	Negative
SmD1	Negative
nRNP-Sm	Negative
U1-snRNP	Negative



## 2. Discussion

Hypertrophic pachymeningitis (HP) refers to inflammation leading to a localized or diffuse thickening and fibrosis of the cranial or spinal cord dura mater. Hypertrophic thickening of the meninges can be caused by a variety of pathological processes. Some diseases selectively involve the dura mater whereas others affect predominantly the leptomeninges. When limited to the dura mater it is called pachymeningitis. When only arachnoid or pia mater is involved, the term is leptomeningitis. This subdivision is important when investigating the patient for a specific cause.

Neurologic manifestations of hypertrophic pachymeningitis are determined by the anatomic location of the inflammation and its consequences. Persistent headache with or without a stiff neck, hydrocephalus, cranial neuropathies, radiculopathies, and cognitive or personality changes are the cardinal features. The differential diagnosis for HP is broad, including vasculitis disorders (for example, granulomatosis with polyangiitis, giant cell arteritis, and Behcet disease); other immune mediated conditions (for example, rheumatoid arthritis, sarcoidosis); malignancies (for example, lymphoma); and infections (such as, tuberculosis) and rarely IgG4 related disease<sup>1</sup>.

The evaluation of HP cases involves laboratory investigations of both bloods including autoimmune profile, cerebrospinal fluid (CSF) examination, imaging studies, and meningeal biopsies.

MRI is the most useful radiological method in evaluating a patient with suspected thickening of meninges. The MRI aspect is a hypointense meningeal lesion on T1-weighted slices that enhances with paramagnetic contrast injection. In T2-weighted imaging hypo- and hyperintense images can be seen dependent on the degree of fibrosis and active inflammatory process. Peripheral enhancement and T2 hyperintensity are common in the early stages of the disease and correspond to inflammatory activity while hypo intensity is attributed to fibrosis. The use of gadolinium is important for evaluation of the pattern of meningeal enhancement, that may differentiate between pachy- and leptomeningitis. When the enhancement following contrast injection, accompanies the sulci and gyri of the brain the diagnosis is leptomeningitis because the pia mater is closely attached to the brain surface. Pachymeningitis is observed in the interhemispheric fissure, tentorium and basal dura. MRI also demonstrates areas suitable for biopsy and secondary lesions that may accompany the disease<sup>2,3,4</sup>.

Differential diagnoses are extensive. Syphilis and tuberculosis have been described as the main causes of classic secondary pachymeningitis<sup>5</sup>.

Neoplasms such as lymphoma, adenocarcinoma, melanoma, meningioma, especially "meningioma en plaque", should be considered whenever there is thickening of the meninges. Meningeal carcinomatosis can cause pachymeningitis but most cases have a progressive course, the CSF may show neoplastic cells and patients usually present symptoms of the primary neoplasm<sup>2</sup>.

Non-infectious inflammatory diseases can cause meningeal thickening and must be considered in the differential diagnosis of pachymeningitis. Wegener's granulomatosis is a necrotizing granulomatous vasculitis that predominantly affects the upper and lower respiratory tract and the kidneys<sup>2</sup>. It has a higher incidence in the fourth and fifth decade of life, but it can occur at any age. Neurological involvement occurs in 22% to 54% of cases, predominantly manifested as mononeuritis multiplex. Brain and meninges are affected in approximately 10% of patients and are manifested by facial weakness, diplopia, hearing and visual loss and sometimes diabetes insipidus due to involvement of hypothalamus-hypophysis axis. The presence of cANCA, an antineutrophil cytoplasmic antibody, is highly suggestive of Wegener's granulomatosis, but its absence does not exclude this diagnosis<sup>6</sup>. Biopsy of affected tissues is important when the diagnosis is not clarified by non-invasive investigation. Other systemic vasculitis or connective-tissue disorders, such as rheumatoid disease, can cause pachymeningitis, although less frequently.

Hypertrophic cranial pachymeningitis is rare form of granulomatous pachymeningitis that is mostly a diagnosis of exclusion. It presents in a nonspecific pattern mimicking any disease that cause pachymeningitis. It sometimes is accompanied by fibrosclerosis of other organs, including

orbital pseudotumor, mediastinal and retroperitoneal fibrosis, Riedel's thyroiditis, sclerosing cholangitis, Dupuytren's contracture, Peyronie's disease, testicular and subcutaneous tissue fibrosis<sup>7</sup>. Tolosa-Hunt syndrome may be a focal manifestation of hypertrophic pachymeningitis since they share common pathological features.

Spontaneous intracranial hypotension (SIH) is a rare syndrome of low intracranial pressure and postural headache with CSF opening pressure of 60 mm H<sub>2</sub>O or lower. MRI in SIH also shows diffuse or focal thickening and gadolinium enhancement of the pachymeninges. But other conditions that predispose to low intracranial pressure such as lumbar puncture, back trauma, neurosurgical procedure or medical illness must be ruled out first. Histopathological features are lymphomononuclear infiltration and fibrosis of the dura and cannot be differentiated from other idiopathic causes of pachymeningitis. The meningeal lesion in SIH may be caused by disruption of the architectural relation between dural and arachnoidal border cells, which regulates the homeostatic fluid environment<sup>2</sup>.

IHP is diagnosed if no cause can be identified. Contrast-enhanced MRI is vital when investigating IHP. The gold standard for diagnosing IHP is a dural matter biopsy. Microscopic findings of IHP include the following: densely dispersed mixed inflammatory infiltrates, abundant lymphoplasmacytic cells, exuberant fibroplasia, and focal hyaline degeneration<sup>8,9</sup>. Dural matter biopsy should be considered if the symptoms are progressing.

### 3. Conclusion

Hypertrophic pachymeningitis is an important cause of recurrent cranial neuropathies and headaches. Many infectious, inflammatory, non-infectious and malignant conditions can produce a similar picture, although the patterns of imaging characteristics and laboratory investigations help in differentiating between them. Idiopathic variety is usually responsive to steroids and specific therapy for secondary causes needs to be instituted. Aim of the therapy is to prevent permanent damage to neural structures.

### References

- [1] Idiopathic hypertrophic pachymeningitis. Kupersmith MJ, Martin V, Heller G, Shah A, Mitnick HJ. *Neurology*. 2004 Mar 9; 62(5):686-94.
- [2] Case Records of the Massachusetts General Hospital. Case 2—1998. *N Engl J Med* 1998;338:180-188.
- [3] Bang OY, Kim DI, Yoon SR, Choi IS. Idiopathic hypertrophic pachymeningeal lesions: correlation between clinical patterns and neuroimaging characteristics. *Eur Neurol* 1998;39:49-56.
- [4] Friedman DP, Flanders AE. Enhanced MR imaging of hypertrophic pachymeningitis. *AJR* 1997;169:1425-1428.
- [5] Adams JH, Graham DI. *An Introduction to Neuropathology*. 2<sup>nd</sup> edition. Edinburgh: Churchill Livingstone, 1994;97-98.
- [6] Siva A. Vasculitis of the nervous system. *J Neurol* 2001;248:451-468.
- [7] Lam BL, Barret DA, Glaser JS, Schatz NJ, Brown HH. Visual loss from idiopathic intracranial pachymeningitis. *Neurology* 1994;44:694-98.
- [8] Bang JH, Cho KT, Kim EJ. Idiopathic hypertrophic pachymeningitis in the craniocervical junction. *Korean J Spine* 2015;12:169–72.
- [9] Shi CH, Niu ST, Zhang ZQ. Clinical image and pathology of hypertrophic cranial pachymeningitis. *Genet Mol Res* 2014;13:10501–9.