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Case Report

Hypertrophic pachymeningitis: a rare manifestation of IgG4 related disease

Kumar Sandeepan[1]*, Monika Jha[2], Shiv Purari[1], Pallav K. Sharma[1], Shreyash[1], Chandan Kumar[1]

[1]Department of Medicine, Patna Medical College and Hospital, Patna, Bihar, India
[2]Sadar Hospital, Madhepura, Bihar, India

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***Correspondence:**
Dr. Kumar Sandeepan,
E-mail: kumarsandeepana@gmail.com

ABSTRACT

Hypertrophic pachymeningitis (HP) is a rare form of diffuse inflammatory disease that causes thickening of the dura mater. It can involve the cranial or the spinal dura or both. An increasingly well-known symptom of IgG4-related illness, a fibroinflammatory syndrome that may affect almost any organ, is IgG4-related hypertrophic pachymeningitis (IgG4-RHP). It is estimated that IgG4-RHP may account for a high proportion of cases of hypertrophic pachymeningitis once considered idiopathic. Contrast magnetic resonance imaging (MRI) shows pachymeningeal enhancement. Serum IgG4 levels may be elevated but are normal in most patients. However, most patients have elevated cerebrospinal fluid (CSF) IgG4 index. Hence, CSF IgG4 index could serve as a less invasive diagnostic marker of IgG4-RHP. Confirmation of diagnosis is by meningeal biopsy that shows swirling "storiform" fibrosis with lymphocytic infiltrates, obliterate phlebitis and IgG4 positive plasma cells. This case highlights the diagnostic dilemma of IgG4-RHP as gold standard of diagnosis is meningeal biopsy which has many of its own limitations. CSF IgG4 index could be an alternate option for meningeal biopsy when the procedure is contraindicated or uninformative.

Keywords: Hypertrophic pachymeningitis, IgG4 related disease, CSF IgG4 index, Storiform fibrosis

INTRODUCTION

The dura mater thickens as a result of the uncommon diffuse inflammatory condition known as hypertrophic pachymeningitis (HP). The spinal dura or the cranial dura may be affected, or perhaps both. The disorder may currently be roughly split into two forms: "secondary" where recognised causes co-exist but may have a disputed role in the development of this illness, and "primary" or "idiopathic hypertrophic pachymeningitis," when no identified cause is detected.[1]

Vasculitic disorders, such as granulomatosis with polyangiitis (formerly Wegener granulomatosis; herein termed GPA), giant cell arteritis, and Behçet disease, as well as other immune-mediated conditions, such as rheumatoid arthritis and sarcoidosis, cancers, such as lymphoma, and infections, such as tuberculosis, are included in the differential diagnosis for HP.[2] A fibroinflammatory illness that may affect almost any organ, IgG4-related disease manifests as IgG4-related hypertrophic pachymeningitis (IgG4-RHP). According to estimates, a significant fraction of cases with hypertrophic pachymeningitis—once thought to be idiopathic—may be caused by IgG4-RHP.

Regarding the pathophysiology of IgG4-RHP, nothing is established. Inflammatory meningeal niches include oligoclonally limited IgG4-positive plasma cells, which clearly supports a targeted reaction against an unidentified antigen. The clinical picture of IgG4-RHP indicates mechanical compression of vascular or nerve systems,

which results in functional impairments, and cannot be distinguished from other types of hypertrophic pachymeningitis.[3]

Symptoms include of headache, seizures, and specific symptoms due to dural involvement in the brainstem, clivus, periorbital, vestibular, and spinal cord. Numerous tissues, including the pancreas, thyroid, lungs, retroperitoneum, lacrimal, parotid, and submandibular glands, orbits, kidney, aorta, and liver, may be affected by systemic IgG4-related illness.[4]

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often elevated in clinically suspicious individuals. Pachymeningeal enhancement is seen on contrast MRI. The majority of patients have normal serum IgG4 levels, which may be increased. But the majority of individuals have a high IgG4 index in their CSF. As a result, the CSF IgG4 index may be used as a less intrusive diagnostic indicator of IgG4-RHP.[5] Meningeal biopsy results confirm the diagnosis and reveal swirling "storiform" fibrosis with lymphocytic infiltrates, severe phlebitis, and IgG4 positive plasma cells.[6]

There isn't agreement on the best course of action for IHP patients right now. On diagnosis, glucocorticoids are preferred, with the inclusion of additional immunosuppressive medications in the case of a recurrence. Patients who did not respond to glucocorticoids or traditional steroid-sparing medications are given rituximab.[6]

CASE REPORT

A 65-year-old male patient presented to medical emergency, PMCH, with complaints of headache, dizziness and blurring of vision for last one and half years.

Headache was insidious in onset, dull in nature, mild in intensity, holocrania with neck stiffness and associated with photophobia but not triggered or relieved with any relevant factor and persisting despite intake of analgesic on daily basis.

Dizziness was mild in intensity, constant throughout the day, not associated with any postural change or gait imbalance and there was no any provoking or relieving factor as well as it had no synchronization with episode of headache.

Blurring of vision was more in bright light associated with photophobia and it was not associated with excessive tearing or eye pain.

History of cataract surgery of both eyes, surgery of right eye in February 2020 and surgery of left eye in August 2020. No history of diabetes, hypertension, thyroid illness, tuberculosis or any chronic illness in past. No history of similar complains to any relative.

Table 1: Examination findings.

Findings	Observation
General examination	
Pulse	78 beats/min
Blood pressure	120/78 mm of Hg
Temperature	98°F
Pallor	Present
Icterus, cyanosis, clubbing, lymphadenopathy, edema	Absent
Eye examination	
Vision	
Right eye	6/18
Left eye	6/24
IOP by NCT (mm of Hg)	
Right eye	18
Left eye	19
Fundus	
Right eye	Normal disc and macula
Left eye	Normal disc and macula
Biochemical investigation	
CBC	TLC- 6800 cell/dl, Hb-8.2 g/dl
LFT and KFT	Bilirubin 0.8 mg/dl, SGPT/SGOT 24/22, creatinine 0.7 mg/dl
ESR	70 mm/hour
Iron profile	Suggestive of anemia of chronic disease
Reticulocyte count	0.4%
PBS examination	Normal, no any immature cell
HIV/HBsAg/HCV	Non-reactive
CSF examination	Cell-5; sugar- 28 mg/dl; protein-40 mg/dl; ADA-5; M.TB- not detected
Other investigations	
Serum ACE	Normal
Serum IgG4	11 g/l (upper normal limit 135 mg/dl[7])
ANA by IFA	Negative
RA factor	14 IU/ml
p-ANCA and c-ANCA	Negative
CSF IgG4	6.8 mg/dl (CSF IgG4 levels higher than 2.27 mg/dl identified 100% of IgG4-RHP[8])
Meningeal biopsy	Could not be performed

MRI findings

MRI brain and orbit with and without contrast images were obtained which revealed diffuse smooth thickening of pachymeninges on post contrast T1 images of axial section (Figure 1).

Coronal T1 with post contrast images revealed diffuse thickening with post contrast enhancement of bilateral Tentorium cerebelli and Falx cerebelli showing "Eiffel tower sign" (Figure 2).

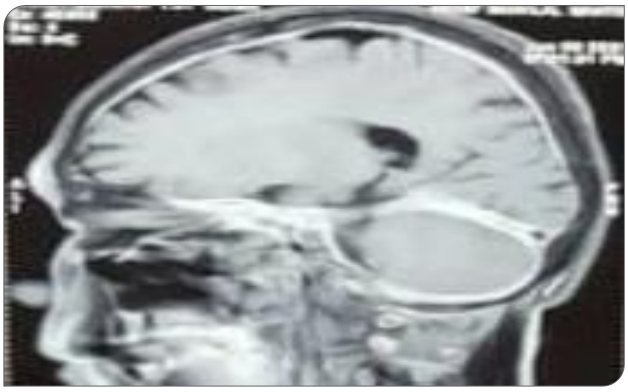

Figure 1: MRI brain and orbit with and without contrast images were obtained which revealed diffuse smooth thickening of pachymeninges on post contrast T1 images of axial section.

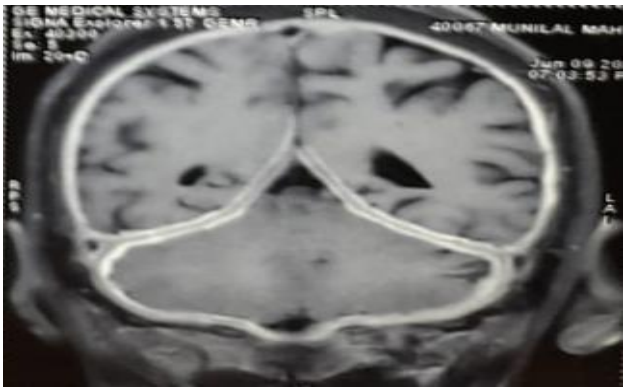

Figure 2: Coronal T1 with post contrast images revealed diffuse thickening with post contrast enhancement of bilateral Tentorium cerebelli and Falx cerebelli showing "Eiffel tower sign".

Axial T2 image of brain showed smooth thickened hypointense duramater (Figure 3).

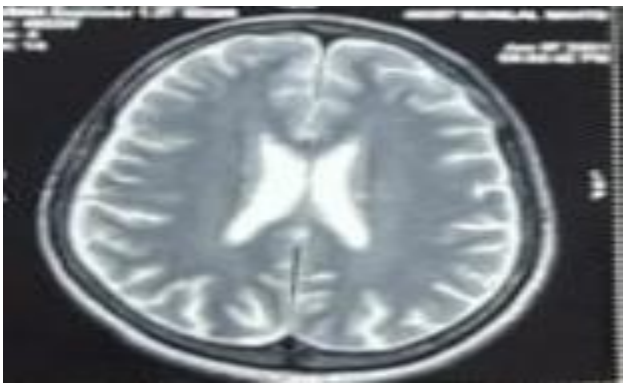

Figure 3: Axial T2 image of brain showed smooth thickened hypointense duramater.

Axial T2 fat suppressed image of both orbit was normal (Figure 4).

Based on the above mentioned findings, a diagnosis of IgG4-RHP was made and the patient was started on injection methylprednisolone (pulse therapy) i.e., 1 g/day was given for 5 continuous days following which patient showed improvement and was discharged with low dose steroid i.e. 0.5 mg/kg body weight/day for 8 weeks followed by tapering over next 4 weeks.

DISCUSSION

An uncommon condition with several etiological factors is hypertrophic pachymeningitis. Charcot was the first to describe it, followed by Naffziger and Stern. The first accounts included syphilis or TB. Although the precise etiopathogenesis of this condition is not yet established, it is assumed to be an autoimmune phenomena or the direct outcome of an infectious or infiltrative disease. Progressive cranial nerve palsies, headaches, and cerebellar dysfunction are some common symptoms of cranial pachymeningitis. Initial-presentation seizures are uncommon.

The best way to diagnose hypertrophic cerebral pachymeningitis is via MRI. By ruling out all other granulomatous and infectious disorders, the diagnosis is confirmed. However, in the majority of instances, the symptomatology and imaging features are sufficient to draw a valid judgement.[9]

MRIs showing hypertrophic pachymeningitis must be evaluated for the presence of IgG4-RHP if clinically suspected or other diseases have been ruled out.

Even if a meningeal biopsy is necessary for diagnosis confirmation, the CSF IgG4 index may be used as a diagnostic marker in the lack of resources. When a meningeal biopsy is unadvisable or ineffective, the CSF IgG4 index may be a better alternative.[8] Prompt recognitions of IgG4-RHP is helpful in limiting further disability and most patients respond to a course of steroid.

CONCLUSION

This case highlights the diagnostic dilemma of IgG4-RHP as gold standard of diagnosis is meningeal biopsy which has many of its own limitations. Easy recognition of the condition and initiation of steroids leads to resolution of the condition. All patients with hypertrophic pachymeningitis on MRI must be evaluated for IgG4 related disease. Although confirmation of diagnosis is by meningeal biopsy, whenever it is contraindicated or uninformative or cannot be done due to resource scarcity, CSF IgG4 index could serve as a diagnostic marker of the disease.

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Ethical approval: Not required

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