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Case Report

A rare case report on hypertrophic pachymeningitis: Serum IgG4-related disease ☆

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ABSTRACT

IgG4-related disease (IgG4-RD) is an immune-mediated inflammatory condition of unknown etiology characterized by invasion of tissue by IgG4-producing plasma cells. It can affect almost any organ system, but central nervous system involvement is a rare occurrence. A careful clinicopathological correlation is required to establish the diagnosis. The condition is highly treatable with glucocorticoids, but it is likely that it is underdiagnosed. Although IgG4-related disease responds quickly to glucocorticoids, if left untreated, can lead to end-stage organ failure and even death. We present a case of a 46-year-old female patient who presented with headache, tingling, numbness, flickering movement in her left lower limb gradually extending to torso and head, and loss of consciousness. After radiological and immunohistochemical studies, the diagnosis of IgG4-related hypertrophic pachymeningtis was confirmed. Corticosteroid therapy was administered, and the patient symptomatically improved. Clinicians should be aware of this rare condition, and the importance of early diagnosis and appropriate corticosteroid therapy should be emphasized.

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Introduction

Immunoglobulin G (IgG)-4-related disease (IgG4-RD) is recognized as a systemic immune-mediated polyclonal lymphoproliferative condition affecting multiple anatomical sites including the pancreas, salivary glands, retroperitoneum, and lymph nodes [1]. However, neurological involvement is extremely uncommon, with most cases presenting as hypertrophic pachymeningitis and hypophysitis [2]. In hypertrophic pachymeningitis, inflammatory lesions in the dura mater of the brain or spinal cord or both, thicken the pachymeninges as a result of IgG-related fibrosis [3]. This rare inflammatory disorder causes localized or diffuse thickening of intracranial dura mater [4]. Headache and cranial neuropathy are the most common clinical manifestation [5]. Diagnosis is challenging as its clinical picture simulates other conditions like malignancy, infections, or inflammatory disease [1]. Here, we report the clinical and MRI imaging features of a rare case of IgG4-related hypertrophic pachymeningitis.

Case report

A 46-year-old female presented at our emergency room complaining of tingling, numbness, and flickering movement in her left lower limb (mostly dorsal aspect of the foot), which had over the course of the preceding week gradually extended to her torso and head. She also complained of severe, intermittent, and generalized headache. Additionally, she experienced 2 instances of 5- to 10-minute loss of consciousness, one each 14 and 10 days earlier. The patient has been diagnosed with type II diabetes mellitus and hypertension, and has a father who has tested positive for tuberculosis. Clinical examination revealed: power 5/5 in all 4 limbs with Grade I deep tendon reflex and negative Babinski test.

Subsequent CSF analysis showed protein 100 mg/dl, glucose 122 mg/dl, lymphocyte 70%, and neutrophil 30%, Negative gram stain, and no growth of microorganisms in CSF. She had an MRI of her brain, which revealed focal T2 Flair hyperintensity in the right high parietal lobe without diffusion restriction or blood products or post-contrast enhancement and diffuse pachymeningeal enhancement in the interhemispheric fissure and left cerebral convexity (Figs. 1A and B), which are signs of hypertrophic pachymeningitis. There was also partial sella tursica.

On further workup, she had a raised erythrocyte sedimentation rate (ESR) level (54 mm/hr), C-reactive protein (CRP) 122.28 and RA factor level to be <10. She underwent a Mantoux test and was found to be 10 mm. The remaining lab parameters were normal. Serum ACE level (normal range 12-68 U/L) was found to be in the normal range (37 U/L). The serum ANA was positive with speckled pattern of ANA staining seen throughout the nucleus. However, the dsDNA antibody was negative.

To see the systemic involvement contrast CT chest abdomen pelvis was done, which showed mild hepatomegaly, tiny lung nodule in anterior segments of the right lower lobe, and few atelectatic bands in the right middle lobe that might be due to the previous infection. Few subscentric enlarged lymph nodes in periportal perigastric lesions, retroperitoneum as well as in mediastinum.

As serum IgG4 antibody level tests were not available in our country, we sent samples abroad. The level of IgG4 was 2.962 g/l (normal range 0.03-2.01 g/l), meeting the IgG4 organ-specific diagnostic requirements. The patient was managed with IV Methylprednisolone for 5 days and conservatively with antiepileptic (Levetiracetam-SR, 500mg twice a day for 1 month), antihypertensive (Losartan Potassium 50 mg + Hydrochlorothiazide 12.5 mg tablet once a day), and hypoglycemic medications (Linagliptin 2.5 mg + Metformin 1000 mg tablet twice a day) was continued. Other supportive measures (Lacosamide 500 mg once a day for a month and amitriptyline 12.5 mg once a day for 2 weeks) were also given. The patient's condition symptomatically improved and was discharged. Follow-up after 4 weeks showed significant symptomatic improvement.

Discussion

Hypertrophic pachymeningitis is an uncommon condition characterized by localized or diffuse dura mater thickening [4]. Numerous clinicopathological diseases induce thickening of the pachymeninges; hence, idiopathic hypertrophic pachymeningitis is diagnosed by exclusion; a dural biopsy is generally required for a definitive diagnosis [4,5]. Pathological findings include thick fibrous dura frequently accompanied by chronic inflammatory cell infiltrate composed of lymphocytes and plasma cells; compression of neural structures by the thickening fibrous dura resulting in neurological abnormalities.

This condition can occur in autoimmune and inflammatory diseases that affect the CNS, such as multiple sclerosis, neuromyelitis optica, sjögren syndrome, systemic lupus erythematosus, and sarcoidosis—or in infectious diseases that affect the CNS. Patients with IgG4-RD are frequently misdiagnosed as having cancer because the lesions can mimic tumors, infections, or immune-mediated diseases [4,6]. Symptoms are typically associated with the morphology of the lesions and are not disease-specific. Hypertrophic cerebral pachymeningitis is typically characterized by headaches and cranial neuropathies [5]. Hypoacusis, tinnitus, vertigo, trigeminal neuralgia, and dysphagia are other symptoms.

Initially, IgG4-related sclerosing illness was identified to be a type of autoimmune pancreatitis. It is now known, however, that this disease can affect the bile duct, gallbladder, salivary glands, retroperitoneum, kidneys, lungs, and even the prostate. This disease is characterized pathologically by a widespread infiltration of IgG4-positive cells in multiple organs [1]. Clinically, it frequently manifests as mass-like lesions. Involvement of the central nervous system is limited; however, recent evidence suggests that IgG4-related sclerosing illness constitutes a subset of cases initially diagnosed as idiopathic hypertrophic pachymeningitis [7–9]. In addition, igG4-associated sclerosing pachymeningitis may exhibit a diffuse infiltrative pattern with or without the development of masses [7–9].

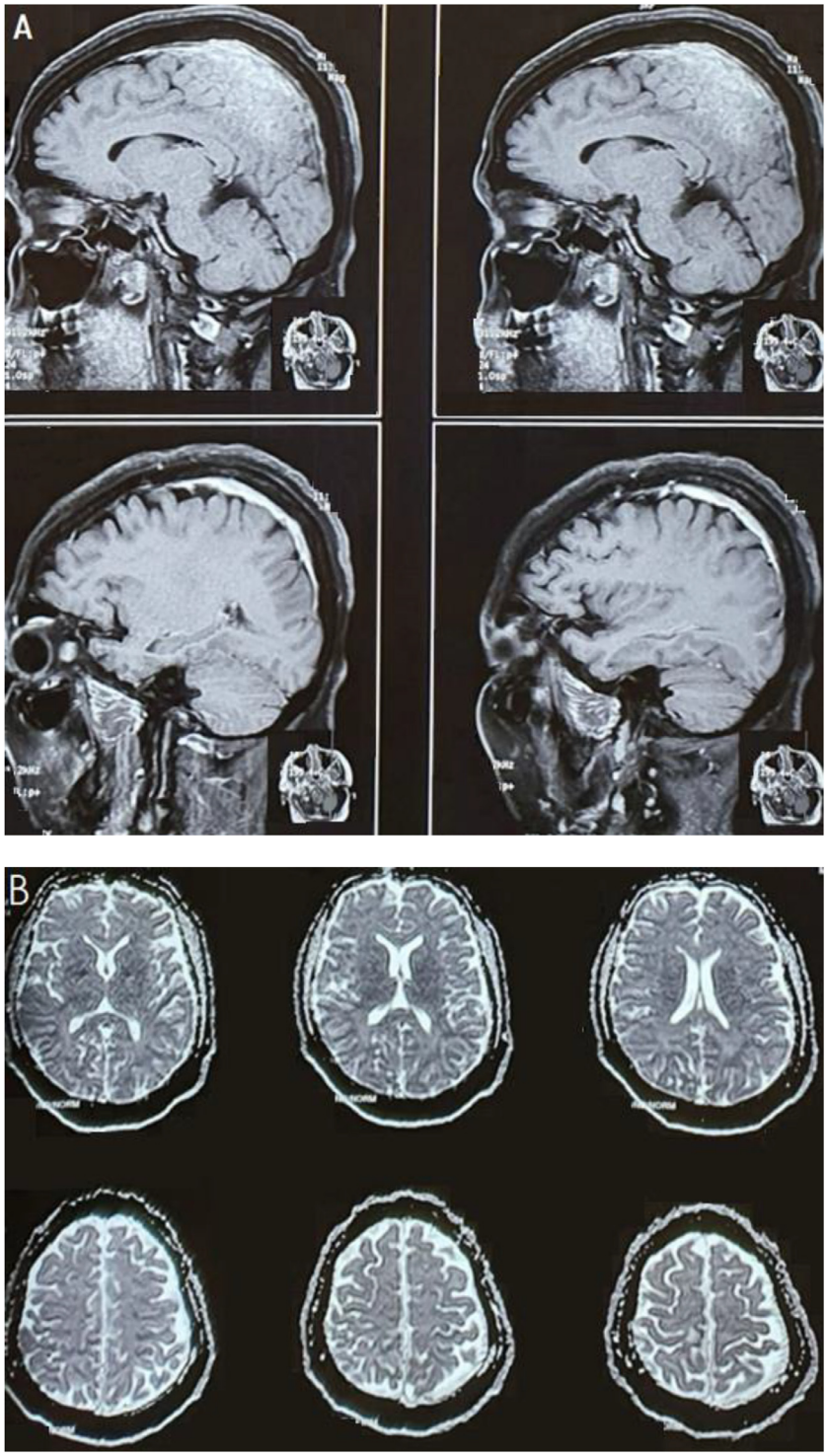

Fig. 1 – Focal T2 flair hyperintensity in the right high parietal lobe and diffuse pachymeningeal enhancement in the interhemispheric fissure and left cerebral convexity (A, B).

MRI is the most reliable radiographic technique for evaluating patients with suspected meningeal thickening. On T1-weighted slices, the MRI reveals a hypointense meningeal lesion that enhances with paramagnetic contrast injection. Depending on the degree of fibrosis and the ongoing inflammatory process, T2-weighted imaging exhibits hypo- and hyperintense images. In the early stages of the disease, peripheral enhancement and T2 hyperintensity are common and correspond to inflammatory activity, while hypointensity is related to fibrosis. Gadolinium is essential for evaluating the

pattern of meningeal enhancement, which can distinguish between pachymenigitis and leptomeningitis [10,11]. Pachymeningitis is observed in the interhemispheric fissure, tentorium, and basal dura [11]. In our case, focal T2 flair hyperintensity in the right high parietal lobe and diffuse pachymeningeal enhancement in the interhemispheric fissure and left cerebral convexity was seen. IgG4-related pachymeningitis is characterized by mild CSF pleocytosis, with occasionally more than 200 nucleated cells per mm. However, completely normal CSF examinations have also been observed [12]. The patient we are presenting also had normal CSF findings.

IgG4 elevation greater than twice the upper limit of normal (normal 140 mg/dL) has 99 % specificity for IgG4-RD [13]. Elevated IgG4 levels are nonspecific, and normal levels do not rule out the disease. Elevated levels can be found in 5% of healthy people and 10% of patients with pancreaticbiliary cancer, infectious diseases, and inflammatory disorders. Higher IgG4 concentrations indicate multiorgan involvement. Elevated total IgG and IgE, peripheral eosinophilia, ESR, and CRP have been reported, but these are nonspecific findings. Serum antinuclear antibody (ANA) titers are positive in nearly half of the cases, and RF (rheumatoid factor) levels are elevated in 20% of patients. Hypocomplementemia has also been reported, and it is linked to immune complexes found in the kidneys and pancreas of patients with the disease [14]. The patient we are presenting here also had raised CRP, ESR, and positive ANA.

Although radiological images cannot distinguish between malignancy and benign disease in the affected organs, a computed tomography (CT) and magnetic resonance imaging (MRI) combination can identify the affected organs and monitor disease activity, remission, or relapse. For example, a diffusely enlarged pancreas with delayed enhancement and borders, No features in the presence or absence of a capsule-like rim in CT with contrast or MRI with more than twice the upper limit of IgG4 levels usually indicates a high likelihood of autoimmune pancreatitis [15]. Similarly in our patient a CT scan of the chest, abdomen, and pelvis revealed mild hepatomegaly, a tiny lung nodule in the anterior segments of the right lower lobe, and a few atelectatic bands in the right middle lobe, as well as a few subscentric enlarged lymph nodes in the periportal perigastric lesions, retroperitoneum, and mediastinum, indicating multiorgan involvement.

A global consensus statement from more than forty researchers from Europe, North America, and Asia (based on the best available evidence) suggests glucocorticoids as first-line therapy for systemic diseases IgG4-RD was initially used as a monotherapy [16]. The patient was given IV Methylprednisolone as well as antiepileptic, antihypertensive, and hypoglycemic medications. The patient's condition improved with glucocorticoid monotherapy, supporting the evidence, but his serum IgG4 antibody levels were extremely high.

The 3 classic features in histopathology of organs affected are lymphoplasmacytic inflammation, fibrosis with a storiform pattern, and obliterative venulitis [14]. Despite the fact that our case has not yet undergone biopsy testing and cannot be classified as a definitive instance of IgG4-RD, increased IgG4 blood levels and reactivity to glucocorticoids support our diagnosis. Additionally, a thorough workup has ruled out any additional factors that might be responsible for these findings.

Conclusion

In conclusion, hypertrophic pachymeningitis is a rare fibrosing inflammatory disorder characterized by localized or diffuse thickening of the cranial or spinal dura mater. Headache was the most frequent symptom. The most frequently altered laboratory finding was elevated ESR, followed by elevated CRP. MRI with contrast showed hyperintensity and diffuse pachymeningeal enhancement in the interhemispheric fissure and cerebral convexity. Serum IgG4 antibody levels were extremely high. Glucocorticoid was primarily used in the treatment of patient. Clinicians should be aware of this rare condition, and the importance of early diagnosis and appropriate corticosteroid therapy should be emphasized.

Patient consent

Written informed consent for the publication of this case report was obtained from the patient.

REFERENCES

[1] Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366:539–51. doi:10.1056/NEJMra1104650.
[2] Peng L, Zhang P, Zhang X, Li J, Zhao J, Liu J, et al. Clinical features of immunoglobulin G4-related disease with central nervous system involvement: an analysis of 15 cases. Clin Exp Rheumatol 2020;38(4):626–32.
[3] De Virgilio A, de Vincentiis M, Inghilleri M, Fabrini G, Conte M, Gallo A, et al. Idiopathic hypertrophic pachymeningitis: an autoimmune IgG4-related disease. Immunol Res 2017;65(1):386–94. doi:10.1007/s12026-016-8863-1.
[4] D'Andrea G, Trillò G, Celli P, Roperto R, Crispo F, Ferrante L. Idiopathic intracranial hypertrophic pachymeningitis: two case reports and review of the literature. Neurosurg Rev 2004;27:199–204. doi:10.1007/s10143-004-0321-1.
[5] Phanthumchinda K, Sinsawaiwong S, Hemachudha T, Yodnophaklao P. Idiopathic hypertrophic cranial pachymeningitis: an unusual cause of subacute and chronic headache. Headache 1997;37:249–52. doi:10.1046/j.1526-4610.1997.3704249.x.
[6] Mamelak AN, Kelly WM, Davis RL, Rosenblum ML. Idiopathic hypertrophic cranial pachymeningitis: report of three cases. J Neurosurg 1993;79:270–6. doi:10.3171/jns.1993.79.2.0270.
[7] Chan S-K, Cheuk W, Chan K-T, Chan JKC. IgG4-related sclerosing pachymeningitis. Am J Surg Pathol 2009;33:1249–52. doi:10.1097/PAS.0b013e3181abdfc2.
[8] Kim EH, Kim SH, Cho JM, Ahn JY, Chang JH. Immunoglobulin G4–related hypertrophic pachymeningitis involving cerebral parenchyma. J Neurosurg 2011;115:1242–7. doi:10.3171/2011.7.JNS1166.
[9] Shapiro KA, Bove RM, Volpicelli ER, Mallery RM, Stone JH. Relapsing course of immunoglobulin G4-related pachymeningitis. Neurology 2012;79:604–6. doi:10.1212/WNL.0b013e31826356fc.

[10] 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.
[11] Friedman DP, Flanders AE. Enhanced MR imaging of hypertrophic pachymeningitis. AJR 1997;169:1425–8.
[12] Lu LX, Della-Torre E, Stone JH. Clark SW IgG4-related hypertrophic pachymeningitis: clinical features, diagnostic criteria, and treatment. JAMA Neurol 2014;71:785–93.
[13] Ghazale A, Chari ST, Smyrk TC, Levy MJ, Topazian MD, Takahashi N, et al. Value of serum IgG4 in the diagnosis of autoimmune pancreatitis and in distinguishing it from pancreatic cancer. Am J Gastroenterol Aug 2007;102(8):1646–53. doi:10.1111/j.1572-0241.
[14] Nambiar S, Oliver TI IgG4 related disease In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Available from: https://www.ncbi.nlm.nih.gov/books/NBK499825/
[15] Kawa S, Ota M, Yoshizawa K, Horiuchi A, Hamano H, Ochi Y, et al. HLA DRB10405-DQB10401 haplotype is associated with autoimmune pancreatitis in the Japanese population. Gastroenterology 2002;122(5):1264–9. doi:10.1053/gast.2002.33022.
[16] Khosroshahi A, Wallace ZS, Crowe JL, Akamizu T, Azumi A, Carruthers MN, et al. International consensus guidance statement on the management and treatment of IgG4-related disease. Arthritis Rheumatol 2015;67:1688–99.