IgG4-related hypertrophic pachymeningitis

IgG4-related hypertrophic pachymeningitis is a rare fibroinflammatory disorder that may cause localized or diffused thickening of the dura mater.

Clinical features

Patients may be asymptomatic, but if symptomatic, they commonly present with headaches.

Clinical manifestations depend on the location of the inflammatory lesion and on the compression of neural structures leading to functional deficits.

Patients often present with systemic manifestations of the disease.

Diagnosis

Elevated serum IgG4 levels and imaging examination help in the diagnosis of IgG4-RHP [1].

A high index of suspicion for this condition is suggested when a male patient with a history of autoimmune disease and compatible radiological findings, experiences a subacute headache that is disproportionate to the degree of dural involvement. Neurosurgeons should consider early meningeal biopsy to establish a definitive histological diagnosis in order for early effective immunosuppressive therapy to be initiated and to avoid unnecessary morbidity [2]

The diagnosis of IgG4-related hypertrophic pachymeningitis is challenging but is of great relevance as treatment differs significantly from other forms of pachymeningitis and a specific therapeutic approach may avoid long-term neurological complications [3].

Diagnosis is histologic and shows lymphoplasmocytic infiltration with IgG4+ plasma cell proliferation, storiform fibrosis, and obliterative phlebitis [4].

Radiographic features

In addition to radiographic features of IgG4-related hypertophic pachymeningitis, which are detailed below, other associated head and neck manifestations of IgG4-related disease, such as IgG4-related-hypophysitis, lacrimal and salivary gland enlargement and inflammation, orbital pseudotumor, and perineural spread along trigeminal and other cranial nerves, may also be seen.

CT Findings on CT can be very subtle. Plaque-like dural thickening may or may not be evident. Focal nodular thickening may mimic a meningioma.

MRI The following signal characteristics are seen:

T1: isointense dural thickening

T1 C+ (Gd): homogeneous enhancement

T2/FLAIR: markedly hypointense due to underlying fibrosis (a reasonably specific imaging finding)

GRE/SWI: hypointense due to underlying fibrosis

FDG-PET

FDG-PET has limited utility for detecting pachymeningitis due to avid brain uptake of FDG and inferior spatial resolution of PET compared to MRI. FDG-PET can detect systemic/multiorgan manifestations of IgG4-related disease and can be utilized to assess for treatment response [5].

Markers

Elevated serum IgG4 level and CSF IgG4 oligoclonal bands.

Differential diagnosis

Misinterpretations of the clinical and imaging findings are common.

The association of lymphocytic hypophysitis and hypertrophic pachymeningitis with IgG4-related pathologies have been reported. Although the diagnosis has not been confirmed in a patient, this relationship must be taken into account in these idiopathic cases and, above all, if they are associated with other systemic manifestations [6].

en plaque meningioma

infectious hypertrophic pachymeningitis

histiocytoses including Erdheim-Chester disease and Rosai-Dorfman disease

neurosarcoidosis

granulomatosis with polyangiitis

other granulomatous diseases including tuberculosis

Treatment

IgG4-related hypertrophic pachymeningitis treatment

Outcome

Generally there is a favorable prognosis.

Case series

Four patients with IgG4-related hypertrophic pachymeningitis were identified over a 5-year period. Patient-related characteristics including age, preoperative workup, signs, and symptoms of patients, and diagnostic procedures were evaluated. Furthermore, the surgical treatment and 5-year follow-up outcomes were analyzed.

There were two adults and two adolescents (mean age 32 years; range 15 to 67 years). Two patients were male, and two were female. No history of the disease was known in any of the patients. Clinical symptoms were epilepsy (n = 2), ataxia and nausea (n = 1), and facial nerve palsy (n = 1). MR imaging studies showed contrast-enhancing lesions in the temporal region in two patients, and in the cerebellar region in the other two patients. Subtotal resection was performed in two instances and a biopsy via a suboccipital retrosigmoid approach was obtained in the other two patients. Histochemical and immunohistochemical investigations revealed an IgG 4 disease in all of these patients. Immunomodulatory therapy led to clinical stability during follow-up of 5 years in all four cases.

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21 reports published in the English medical literature since 2009. PubMed was searched with the following terms: IgG4, pachymeningitis, IgG4-related pachymeningitis, IgG4-related disease, IgG4-related, and IgG4 meningitis. Only cases with biopsy-proven IgG4-RHP were considered and included in this review.

Findings: Little is known with certainty regarding the pathogenesis of IgG4-RHP. The presence of oligoclonally restricted IgG4-positive plasma cells within inflammatory meningeal niches strongly suggests a specific response against a still unknown antigen. Clinical presentation of IgG4-RHP is not distinguishable from other forms of hypertrophic pachymeningitis and reflects mechanical compression of vascular or nerve structures, leading to functional deficits. Signs of systemic IgG4-related disease may concomitantly be present. Diagnostic process should rely primarily on magnetic resonance imaging, cerebrospinal fluid analysis, and meningeal biopsy. In particular, hallmark histopathological features of IgG4-RHP are a lymphoplasmacytic infiltration of IgG4-positive plasma cells, storiform fibrosis, and obliterative phlebitis. High-dose glucocorticoids are still the treatment of choice for IgG4-RHP because immunosuppressive agents have shown variable efficacy in reducing the meningeal hypertrophy. Rituximab is a promising therapeutic approach but experience with B-cell depletion strategies remains limited.

IgG4-related disease accounts for an increasing proportion of cases of idiopathic hypertrophic pachymeningitis. Clinicians should become familiar with this alternative differential diagnosis because a prompt, specific therapeutic approach may avoid long-term neurological complications [8]

Four cases (66.6%) that had been regarded previously as representing idiopathic HP were diagnosed as IgG4-RD; of all the reviewed cases, IgG4-RD represented 29% of cases. Of the remaining cases, 3 cases were associated with granulomatosis with polyangiitis (GPA), 2 with lymphoma, and 1 each with rheumatoid arthritis, giant cell arteritis, and sarcoidosis. Two of the cases could not be diagnosed more precisely and were classified as undifferentiated HP. Clinical history, serologic tests, cerebrospinal fluid studies, and radiology alone could not identify the cause of HP. Rather, biopsy with histopathology and immunostaining was necessary to reach an accurate diagnosis. Significant IgG4+ plasma cell infiltrates were observed in rheumatoid arthritis, granulomatosis with polyangiitis, and lymphoma, underscoring the importance of histopathology in making the diagnosis of IgG4-RD.This case series demonstrates that IgG4-RD may be the most common etiology of noninfectious HP and highlights the necessity of biopsy for accurate diagnosis [9].

Case reports

IgG4-related hypertrophic pachymeningitis case reports

1)
Yu Y, Lv L, Yin SL, Chen C, Jiang S, Zhou PZ. Clivus-involved immunoglobulin G4 related hypertrophic pachymeningitis mimicking meningioma: A case report. World J Clin Cases. 2022 Jun 26;10(18):6269-6276. doi: 10.12998/wjcc.v10.i18.6269. PMID: 35949844; PMCID: PMC9254204.
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9)

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