Medical Science

pISSN 2321–7359; eISSN 2321–7367

IgG4 related cranial pachymeningitis and extraocular muscle paralysis

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To Cite:
Balambighai V, Dhanaraj M. IgG4 related cranial pachy meningitis and extraocular muscle paralysis. Medical Science 2022; 26:ms357e2349. doi: https://doi.org/10.54905/disssi/v26i127/ms357e2349

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Peer-Review History
Received: 11 June 2022
Reviewed & Revised: 15/June/2022 to 31/August/2022
Accepted: 01 September 2022
Published: 08 September 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

In this case report we discuss a case of IgG4 related cranial pachymeningitis with isolated extraocular muscle paralysis in a middle aged woman. MRI Brain showed thickened and enhancing pachymeninges and superior recti muscles, with raised serum IgG4 levels. A diagnosis of "possible" IgG4 Related pachymeningitis was considered, and was treated with steroids. She responded well over a period of two months. At the end of two months, the clinical response was good and serum IgG4 levels became normal. IgG4 RD may be considered as a possible differential in all cases of idiopathic pachymeningitis in view of excellent therapeutic response to steroids.

Keywords: IgG4 related cranial pachymeningitis, extraocular muscle paralysis, corticosteroids

1. INTRODUCTION

IgG4- RD is a rare immune - mediated disorder involving multiple organs (eg: Pancreas, salivary glands) characterized by swelling of involved organs, lymphoplasmocytic infiltrates with IgG4 positive plasma cells, characteristic "storiform" fibrosis with obliterative phlebitis, elevated serum IgG4 levels (Kamisawa et al., 2003; Kim et al., 2011). Central nervous system involvement occurs primarily due to pachymeningitis of cranium and spine. Cranial Pachymeningitis can involve structures in the anterior and posterior cranial fossa and the symptoms will depend on the structures affected and spinal Pachymeningitis commonly presents as compressive myelopathy (Walsh et al., 2017; Mohanasundaram et al., 2016). In Indian literature, while isolated case reports of spinal pachymeningitis presenting as compressive myelopathy have been reported, no publication is available about cranial pachymeningitis. Extraocular muscle paralysis can occur either due to ocular nerve involvement or due to extraocular muscle involvement (Abdel Razek et al., 2018). Here, we describe a case of isolated intracranial pachymeningitis which manifested as extraocular muscle paralysis.

2. CASE REPORT

A woman in her late forties presented with drooping of both eyelids, since last two and half months, without history of double vision, diurnal variation, headache, neck pain, or vomiting. She is a known case of Acyanotic congenital

heart disease (subaortic VSD).There was no history suggestive of any other system involvement. Her general examination was unremarkable. Cognitive functions were normal. Both optic fundi were normal with equally reacting pupils. There was bilateral Ptosis (Left > Right) with mild Left Medial Rectus weakness. Other cranial nerves, Spino motor, Sensory, Cerebellar, Autonomic, Extrapyramidal systems were normal. Routine blood reports were unremarkable except for a high ESR of 94. Repetitive Nerve Stimulation showed no decremental response. MRI brain and Orbit(Plain & Contrast) revealed thickened and enhancing meninges along left cavernous sinus extending upto superior orbital fissure anteriorly along sphenoid wing and posteriorly upto retroclival regions. Thickened pachymeninges was noted along the left fronto temporo parietal convexity, tentorium, cerebellar convexity with maximum thickness of 7mm along temporal convexity. Similar changes were noted on the right side with minor degree as shown in figure 1A & 1B, figure 2A & B. Bilateral superior recti muscles appeared thickened and edematous as shown in figure 3 A & 3B.

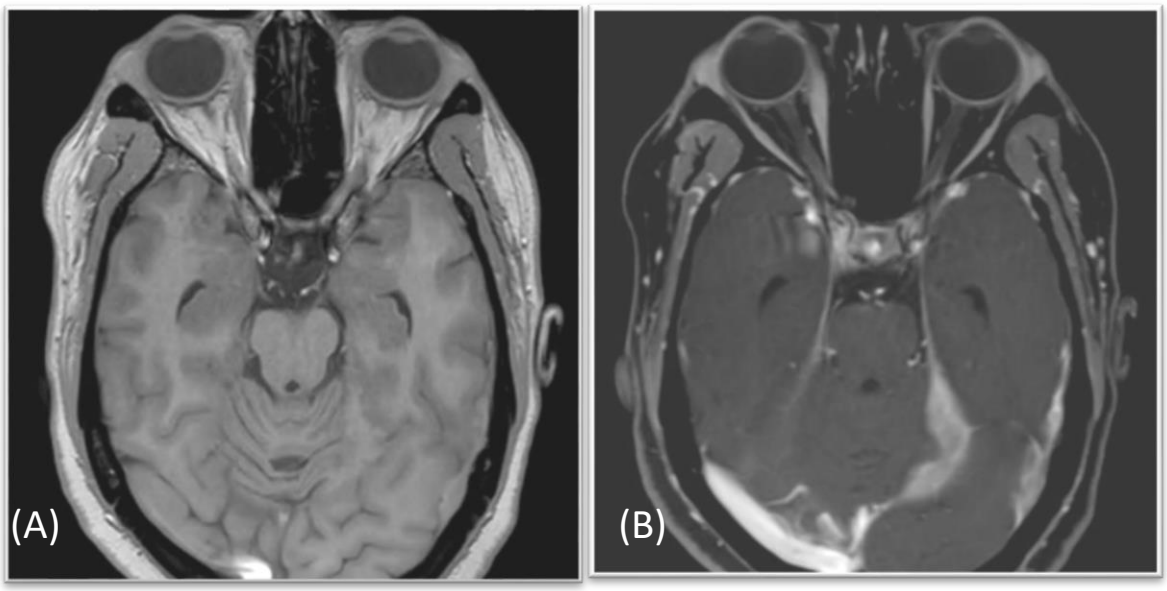

Figure 1 MRI Brain Plain (A) and contrast (B) showing bilateral enhanced and thickened meninges

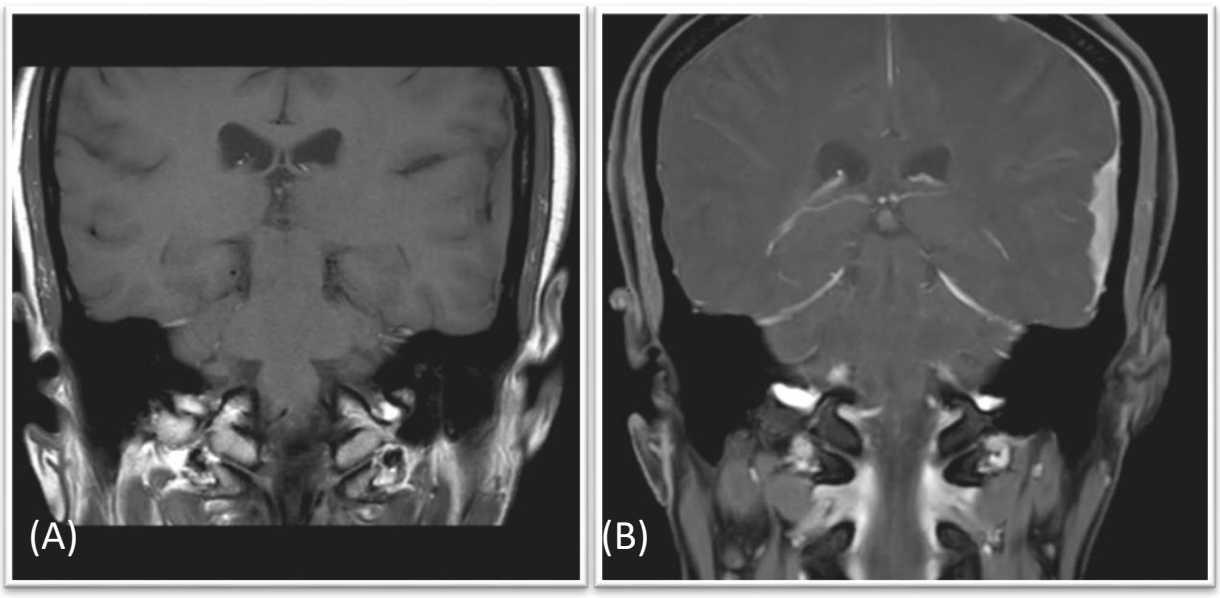

Figure 2 MRI Brain A (plain) & B (contrast), coronal sections showing enhanced meninges

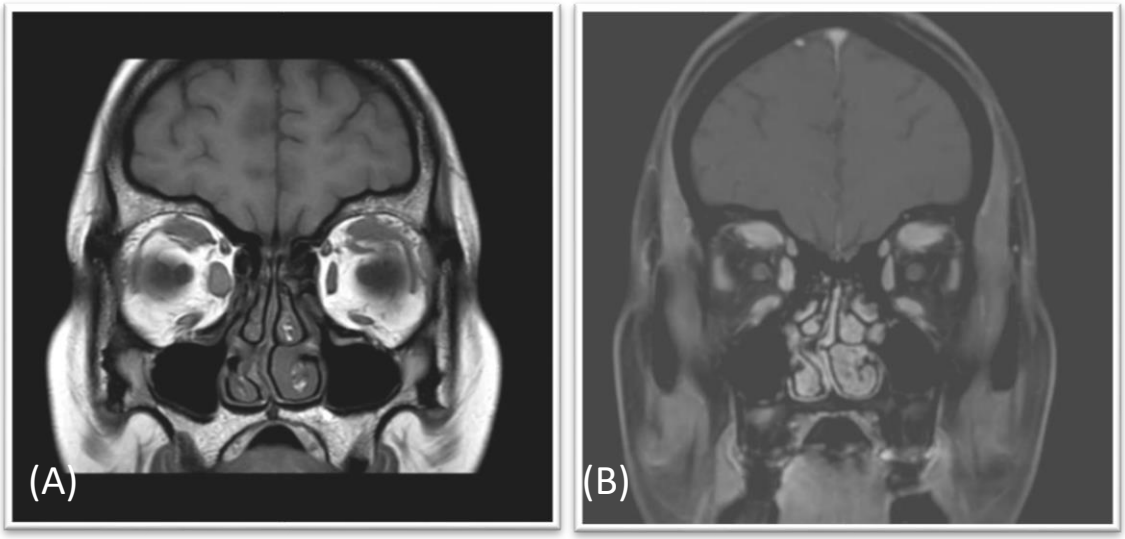

Figure 3 MRI Brain A (plain) & B (contrast), showing thickened and enhancing superior recti muscles

Serum electrophoresis showed albumin- globulin reversal, and `Serum protein immunotyping showed polyclonal increase of IgG. Vasculitis workup showed positive ANA (4+). Serum ACE level was normal (48U/L). CSF analysis was normal except for raised Protein levels (97.4 mg/dl). Cytology was negative for malignant cells. Serum IgG4 level was 243 mg/dl (Normal 2-121). She denied consent for meningeal biopsy. A diagnosis of "possible "IgG4 related Pachymeningitis along with extraocular muscle paralysis was made based on her radiological features of pachymeningitis and superior recti muscle involvement and raised serum IgG4 levels. She was started on I.V. Methyl prednisolone 1gm OD for three days followed by oral Prednisolone 60mg OD. On follow up after 2 months, she recovered well. Serum IgG4 level was reduced to 78mg/dl and the dose of steroid was gradually tapered and was maintained on small dose and then stopped.

3. DISCUSSION

IgG4 related isolated intracranial involvement with orbital disease is not frequently reported in literature. IgG4 related isolated orbital disease, hypophysitis, parenchymal brain infiltrates, and peripheral nerve disease and spinal pachymeningitis have been reported. In this case, the patient presented as extraocular muscle paralysis, and on further workup found to have intracranial pachymeningitis. Japan reported the first case of IgG4 – RD in 2003 which manifested as pancreatic involvement (Kubota et al., 2012). The other organs involved are salivary gland, retroperitoneum, biliary tract, lymphnodes, sinuses, kidneys, lungs, prostate, testis and thyroid (Lu et al., 2014). The actual data for incidence and prevalence of IgG4 RD was underestimated. In a Japanese survey, the reported incidence was 8.8%. There is a male preponderance with average age at diagnosis being 35 years. The pathophysiology behind IgG4 RD seems to be antigen driven process and is due to interaction between B cell lineage (both B lymphocytes and plasmablasts), and two CD4+ T lymphocytes, the T-follicular helper (CD4 +Tfh)cells, CD4+ cytotoxic T lymphocytes (CD4+ CTC). The antigen initiating the process remains unclear. The various manifestations of IgG4 related orbital disease include dacryoadenitis, involvement of optic & trigeminal nerves, orbital bone & soft tissues, sclera, eyelids and extraocular muscles. In our patient, though she had extensive pachy meningeal thickening, ptosis was probably due to extraocular muscle involvement rather than due to cranial nerve involvement. Inspite of meningeal thickening, she does not have headache or any other symptoms (Chan et al., 2009).

According to a data from France, the incidence for IgG4-related ophthalmic disease (IgG4-ROD) was 17% with a male preponderance. The average age during diagnosis was around 55 years. In IgG4 related ophthalmic disease, lacrimal gland was the most commonly involved (68.4%), followed by soft tissue (57.5%), extra-ocular muscles (36.8%), optic nerve, orbital bone, and trigeminal nerve. Bilateral involvement was seen 57.9% of cases. Around 78.9% of the cases had Extra-ophthalmic manifestations (Ebbo et al., 2017). Hypertrophic Pachymeningitis can present as focal or widespread involvement and can involve cranial nerves, cavernous sinus, superior orbital fissure, brain stem and the symptoms depends on the structures involved. Our Patient had diffuse involvement of Meninges and B/L superior recti muscles were oedematous and contrast enhancing and presented as Ptosis. MRI Brain with contrast remains the standard modality of imaging to look for dural thickening, involvement of optic nerve & chiasm, brain stem, and base of skull. Pachymeninges appears as hypo intense lesion with foci of hyper intensity in T2 weighted images,

suggestive of inflammation which is confirmed by T1 weighted Gadolinium enhanced MRI (Wallace et al., 2013; Takeuchi et al., 2014).

Recent imaging modalities like SPECT, Carbon 11-labelled methionine and FDG PET-CT (2-[18F]-fluoro-2-deoxy-D-glucose positron emission tomography– computed tomography), are used for both diagnostic and monitoring purposes. Raised ESR & CRP are seen in IgG4 RD. Polyclonal gammopathy with elevated serum IgG & IgE levels and low complement levels are also seen. The characteristic feature of IgG4 RD is markedly elevated serum IgG4 levels which is also used for monitoring disease prognosis and relapses. Elevated serum IgG4 levels are also seen in healthy people, parasitic disease and in autoimmune diseases like ANCA related vasculitis, Rheumatoid arthritis, Castleman's disease and in some malignancies like pancreatic cancer (Kosakai et al., 2010). In patients suspected to have IgG4 RD with normal levels of serum IgG4 and in whom biopsy is not possible, serum plasmablast count can be useful for diagnosis and response to treatment.

CSF examination in patients with IgG4 RD will show normal glucose levels and a slight increase in protein concentration and predominant lymphocytes. IgG4 levels in CSF may be useful in some cases when it is correlated with serum levels. For the definitive diagnosis of IgG4 RD, histology continues to be the gold standard. Comprehensive clinical diagnostic criteria for IgG4-RD includes: (1) Localised / Diffuse masses or swellings in single or multiple organs; (2) Raised serum IgG4 levels; (3) Histology showing lymphocytic infiltrates and plasmacytes with IgG4 rich plasma cells and fibrosis.

The diagnosis is deemed "definite" if all the above mentioned criteria are present, "probable" if criteria 1 and 3 are present, and possible if criteria1 and 2 are present. In our case, intracranial pachymenigitis along with oedematous superior recti muscles (Criteria-1) with elevated IgG4 levels (Criteria -2) were present and hence a diagnosis of "possible IgG4-RD" was made. The mainstay of therapy in IgG4 RD is Corticosteroids. Response is usually seen well within two weeks. Early diagnosis and initiation of treatment is important for response to steroids and to prevent fibrosis (Baptista et al., 2017; Andrew et al., 2013). Our patient responded well to parenteral steroids followed by oral steroids with significant reduction in symptoms with decline in IgG4 levels. Steroid withdrawal, tapering of glucocorticoids may result in disease relapse. The dosage of corticosteroids and total duration of treatment is still on debate. One recommended treatment regimen is with Prednisolone 0.6-1 mg/ kg/ day for a period of 2–4 weeks, followed by a tapering dose over a period of 3–6 months and maintained on 2.5-5 mg/day for a period of 3 years. The second line of management includes Methotrexate, Cyclophosphamide, Azathioprine, 6-mercaptopurine, Mycophenolate mofetil, Rituximab and Tacrolimus. The clinical, radiological features along with IgG4 levels are used for assessing prognosis.

4. CONCLUSION

Idiopathic pachy meningitis cases should be evaluated for IgG4RD pachymeningitis as a possible differential diagnosis as the disease is not uncommon. Case reports have been published on IgG4 related CNS/PNS involvement. If diagnosed early, IgG4 RD can be managed with specific treatment plans and hence long term complications can be prevented.

Acknowledgement

We thank the patient and her family for the support during treatment and follow up sessions. We also thank the publication desk for their help in publishing this article.

Authors' Contributions

Dr. Balambighai collected the patient details, followed up the case and wrote the article and collected the references. Dr. Dhanaraj proof read the article and reviewed.

Informed Consent

Written & Oral informed consent was obtained from the patient in case report.

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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