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Case Report

Igg4 Related Granulomatous Spinal Pachymeningitis with Cord Compression – A Multisystem Disorder Presenting as Tumor Mimic

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Abstract: IgG4 Related Disease (IgG4 RD) is a comparatively new multisystem disorder associated with elevated levels of IgG4. It includes a number of disorders which were previously thought to be idiopathic or autoimmune. This is a rare condition and can affect any organ system in the body with IgG4 Related pachymeningitis having even lesser incidence. In this case report we present a patient who had chronic low back ache, who on evaluation was found to have a mass compressing on the spinal cord at the thoracic level, requiring surgical decompression. Biopsy and immunological testing were suggestive of IgG4 related pachymeningitis. We describe the diagnosis, medical management, and follow up of this patient, with discussion on how timely diagnosis and management will help in preventing further episodes and help in recovery. This case reiterates about medical conditions presenting as tumor mimics.

Keywords: Autoimmune disease, Chronic inflammatory meningitis, Immunoglobulin, Immunoglobulin G4 meningitis, Multisystem disorder, Rituximab.

INTRODUCTION

IgG4 Related Disease (IgG4 RD) is a recently described systemic disorder which includes a spectrum of disorders that are associated with IgG4, though the majority of the single organ manifestations of this disease has been described since the 19th century. This disease is more commonly seen in men and the incidence peaks between the fifth and seventh decade [1-5]. The etiology is unclear but is thought to be of autoimmune origin. This disease is described as an immune mediated fibro-inflammatory disorder characterized by dense lymphoplasmacytic infiltrates with a high percentage of IgG4 bearing plasma cells, abundant storiform fibrosis, obliterative phlebitis and frequent tissue eosinophilia. The diagnosis is based on clinical criteria, immunologic criteria, and pathologic criteria. Due to the rarity of this disease in itself, there is an even greater paucity of data regarding the Central Nervous system involvement of this disease. In this following case report, we describe a case of IgG4 related pachymeningitis with spinal cord compression, its diagnosis and its management.

CASE REPORT

A 57-year-old male patient with no previous comorbidities came with complaints of mid back pain for one year. The pain was dull in character, insidious in onset, gradually worsening, not relieved with analgesics and was associated with gait imbalance. There was no history of bladder and bowel disturbance. There was no history of previous similar episodes. No similar history in family members. Neurological examination showed decreased motor power at the right ankle along with right lower limb paraesthesia. Deep tendon reflexes were exaggerated in both lower limbs at all joints. Plantar response was extensor in both lower limbs. Romberg's sign was positive. Gait examination showed ataxic gait. Higher mental functions, cranial nerves and cerebellar examination were normal. An upper motor neuron lesion was suspected and imaging was done.

Magnetic Resonance Imaging (MRI) of dorsal spine was showing an anteriorly located epidural mass lesion in the spinal canal from T5 to T7 levels, with thecal sac and cord compression along with cord edema. Post contrast images showed striated appearance of the lesion (Figure 1). In view of cord compression and symptoms, the patient was taken up for emergency surgery-T5 to T7 dorsal laminectomy and decompression of the intradural extramedullary lesion (Figure 2). Postoperatively, he was admitted in the ICU and he showed gradual neurological improvement with supportive care and physiotherapy. Histopathological

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examination of the specimen showed fibrocollagenous tissue with dense infiltrates of lymphocytes, plasma cells and hisiocytes centered around blood vessels – suggestive of granulomatous pachymeningitis with the possibility of an autoimmune etiology. The specimen was negative for acid fast bacilli and fungi. Evaluation showed raised IgG and IgG4 levels, with raised ESR and CRP. Initial IgG4 was 342 mg/dL (Laboratory reference value <201 mg/dL), Serum IgG4/IgG ratio 16 %. The 2019 ACR EULAR criteria score was >20. Diagnosis of IgG4 RD was made.

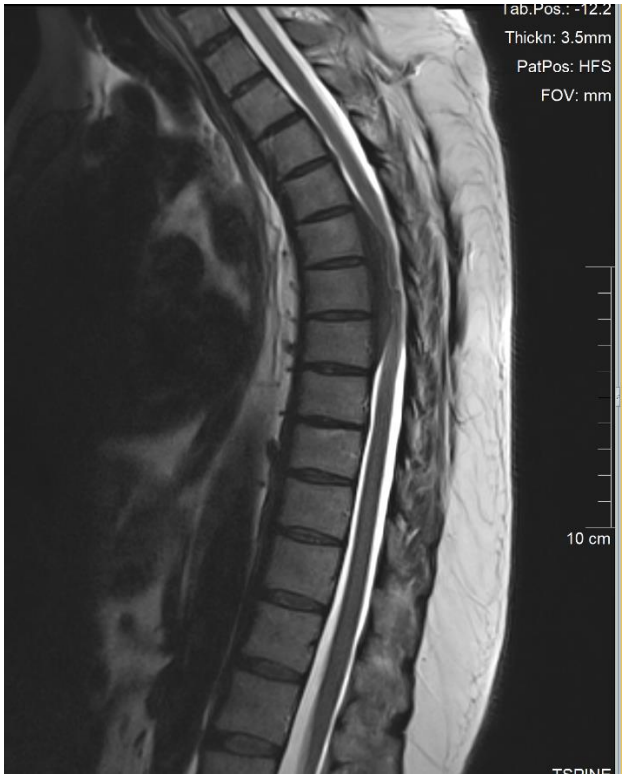

Figure 1: MRI showing anteriorly located Epidural mass lesion from T5 to T7

He was discharged and was managed in the outpatient department with steroids and mycophenolate mofetil. Steroid was started with 40 mg prednisolone and reduced to 5 mg per day. Repeat MRI performed at 6 months postoperatively showed improvement. The patient was continued on Mycophenolate mofetil and his IgG4 levels showed a decreasing trend.

A year later, the patient presented once again with a similar episode of mid back pain for 5 days associated with sudden onset progressive weakness of both lower, urinary retention and not being able to stand. Examination showed decreased power with increased tone in both the lower limbs. Deep tendon reflexes were exaggerated. There was hypoesthesia below the D5 level, with reduced joint position sense. MRI of the dorsal spine showed a strip of hypointensity extending from D2 to D10 levels, more prominent in the D5 to D7 levels, with cord compression and cord edema, probably due to recurrence (Figure 4). He was taken for emergency re-exploration – D1 to D9 laminectomy and posterior decompression of the intradural extramedullary lesion. Postoperatively, he was managed in intensive care and improved neurologically with supportive care. He required suprapubic catheterisation for neurogenic hypocontractile bladder. Positron Emission Tomography and Computed Tomography (PET-CT) scan was done in the postoperative period which showed metabolically active mural thickening in the brachiocephalic artery, arch of aorta, pulmonary trunk and thoracic aorta, likely representing arteritis, which required no active intervention. Three months later he developed holocranial headache associated with mood changes, rituximab option was given but patient denied, and hence was continued on mycophenolate mofetil. Further evaluation showed hydrocephalus on CT scan and he underwent ventriculo-peritoneal codman shunt surgery for the same. He was discharged after postoperative ICU monitoring and physiotherapy.

Patient was started on 1mg/kg steroids with rituximab 2 gm infusion. He received a total of 4 rituximab doses – 1 gm every 6 months and now on 500 mg maintenance dose. Patient started improving symptomatically with improvement in muscle power and tone. IV steroid (methylprednisolone was given daily for 3 days and then continued on 32 mg.) Neurosensory functions also started showing improvements. Bilateral plantar reflexes remained positive. Patient was being maintained with low dose steroids upon discharge at home. During subsequent follow up, the patient was able to walk without support and able to control the

bladder. He is planned for a follow-up for total duration of 3 years.

DISCUSSION

IgG4 related disease is an immune mediated and multisystemic disorder which was recently described and includes a spectrum of various diseases previously considered idiopathic. The Older terminologies of this disease include IgG4 related systemic disease, IgG4 related sclerosing disease, IgG4 – positive multiorgan lymphoproliferative disorder [6, 7]. The formal name "IgG4 Related Disease" was named by Takahashi *et al.*, in 2010 [8]. Even though this name IgG4 RD is relatively new, many of the single organ disorders in this spectrum have been described since the 18th century or before. This disease was initially reported more in the Japanese population but is now being described in other ethnic groups as well. The disease peaks between the fifth and seventh decade with a clear male predominance (61-80%) [5, 6, 9-11].

Clinical manifestations – the clinical manifestations of the disease depend on the organ involved. It can be either single organ involvement or multi organ involvement. Based on the organs involved, 4 clinical phenotypes of the disease are identified (Table 1) [12]. IgG4 RD has been described involving lacrimal glands, salivary glands, thyroid gland, lungs, aorta, pancreas & biliary ducts, kidney, retroperitoneal region, lymph nodes, skin, pituitary gland, prostate, etc.

Table 1: Clinical Phenotypes of IgG4 RD [12]

Type 1	Pancreato – Hepato – Biliary
Type 2	Retroperitoneum and aorta
Type 3	Head and neck – limited
Type 4	Mikulicz and systemic

In order to help with disease recognition, the American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) released a set of classification criteria for IgG4 RD. Patients reaching a score of more than or equal to 20 points are classified as having IgG4 RD. Recent study showed that this classification algorithm proved replicable and user friendly when adopted by experienced clinicians [13].

The diagnosis is based on clinical criteria, immunologic criteria, and pathologic criteria (Table 2) [1]**.** This illness is diagnosed as possible, probable or definite IgG4-RD based on the above three criteria. Nevertheless, Gold standard for diagnosis is histopathology and immunohistochemistry.

Table 2: Diagnostic Criteria [1]

1.	Clinical examination (History, examination, imaging)	1+2 = Possible IgG4 RD
2.	Immunological examination (IgG4 in serum >135 mg/dL or elevated IgG4/IgG ratio; optionally accompanied by other laboratory alterations like in IgE, Gamma globulin or complement)	1+3 = Probable IgG4 RD
3.	Histopathologic examination: lymphoplasmocytic infiltration with storiform fibrosis and obliterative phlebitis, infiltration bt IgG4+ plasma cells (IgG4+/IgG >40%)	1+2+3 = Definitive IgG4 RD

Levels of IgG and IgG4 – majority of cases are characterized by elevated serum levels of IgG and IgG4, but it can remain within the normal ranges in 30% and 8% of patients, respectively [14-16]. CSF examination of cells, proteins and glucose usually don't have any specific signs. Analysis of CSF for intrathecal IgG4 production and IgG4 index is a useful, non-invasive and cost affordable tool that may be a choice for the diagnosis of IgG4 related diseases. Meningeal biopsy is usually required for final diagnosis, but is not easy to implement in all patients.

Thoracic spinal cord compression caused by IgG4 related disease is extremely rare. Due to nonspecific clinical and radiologic features of this disease, early diagnosis is difficult and hence treatment may get delayed [17]. In our patient, there was neurological involvement with compression symptoms requiring surgical decompression. Differential diagnosis mainly includes Granulomatosis with Polyangitis, lymphoma and neurological tumors. They are distinguished based on the other organ system involvement and on histopathological staining techniques.

IgG4 related pachymeningitis is rare condition and was first reported in 2009 [18]. As one of the main causes of meningeal inflammatory disease, it is mainly characterized by the lack of extra neurologic organ involvement and systemic signs. HPE should be carried out, if possible, as it is essential for final diagnosis because serum markers are rarely useful.

All symptomatic and active IgG4 related diseases need timely treatment. For the primary treatment, glucocorticoids are the first choice. Poor response to glucocorticoids and recurrence, addition of immunosuppressors may be required. Currently there is no specific treatment for IgG4 related pachymeningitis. Short term efficacy of surgery in single organ IgG4 related disease is good and, in some cases, may be sufficient to achieve remission. Post-surgical steroids and immunosuppressants may be required, and occasionally surgery for recurrence may be required. Intrathecal rituximab can also be considered [19].

Our patient also had features of arteritis and urethritis which is also possibly due to IgG4 RD for which he did not require any intervention and was medically managed.

CONCLUSION

The clinical presentations and radiological features of IgG4 related CNS diseases are nonspecific. Definitive diagnosis should depend on histopathology and immunohistochemistry. Spinal cord involvement with neuro symptoms is rare and may progress rapidly, leading to severe neurological deficits. Timely surgical decompression with postoperative steroids and immunosuppressors is required for successful management.

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