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Case Report

Neuro-surgical considerations for treating IgG4-related disease with rare spinal epidural compression

Maia Winkel, Cort D. Lawton[1], Olabisi R. Sanusi[2], Craig M. Horbinski[3], Nader S. Dahdaleh[2], Zachary A. Smith[2]

Department of Neurological Surgery, Chicago Medical School At Rosalind Franklin University of Medicine and Science, North Chicago, Departments of [1]Orthopedic Surgery, [2]Neurological Surgery and [3]Neurological Surgery and Pathology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

E-mail: Maia Winkel - maia.winkel@my.rfums.org; Cort D. Lawton - cort.lawton125@gmail.com; Olabisi R. Sanusi - olabisi.sanusi@northwestern.edu; Craig M. Horbinski - craig.horbinski@nm.org; Nader S. Dahdaleh - nader.dahdaleh@nm.org; *Zachary A. Smith - zsmith1@nm.org
*Corresponding author

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Abstract

Background: Immunoglobulin G4-related disease (IgG4-RD) is a group of distinct autoimmune disorders affecting nearly every organ system in the body. Although central nervous system involvement is quite rare, it may present as hypertrophic pachymeningitis more frequently affecting the brain than the spine. In this study, we provide a case of spinal IgG4-RD pseudotumor resulting in cord compression, and a comprehensive review of the literature.

Case Description: A patient presented with an extradural mass causing spinal cord compression at the L2-L3 level. Pathologically this proved to be an IgG4-RD pseudotumor. The patient was treated with thecal sac decompression and post-operative steroids that resulted in complete resolution of his symptoms.

Conclusion: IgG4-RD is typically under-recognized and under-reported in the spinal literature. The clinical spinal presentation and non-surgical vs. surgical treatment are relatively straightforward. Although most cases can be managed with a course of steroids, surgical decompression may be required in patients presenting with spinal cord and/or nerve root compression. The differential diagnoses for these spinal tumors or pseudotumors should include IgG4-RD. Early detection and appropriate treatment can lead to satisfactory outcomes.

Key Words: Hypertrophic pachymeningitis, IgG4-RD, IgG4-RD pseudotumor, IgG4-related disease, pachymeningitis

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INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is a family of orphan, autoimmune diseases, which share key features affecting nearly all systems throughout the body.[1,20] IgG4-RD is rarely found in the central nervous system, and it is more frequently found intracranially rather than in the spine.[9,16] In the spine, IgG4-RD typically presents as a pachymeningitis that may cause spinal cord and/or nerve root compression.[2,3,12,18,19,22,25]

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In total, 15 such cases have been reported in the literature.[2,3,8-10,12,15-18,21,23,25]

In this study, we summarized 15 cases of spinal IgG4-RD found in the literature and added our case of IgG4-related spinal pachymeningitis contributing to spinal cord compression. The patient presented responded well to surgical decompression and post-operative steroid administration. This highlights how important it is for spine surgeons to consider this disease, as early detection and treatment result in improved outcomes.

CASE REPORT

Clinical background

A 48 year-old female presented with 8 weeks of lower back pain, neurogenic claudication, and right lower extremity radiculopathy. On examination, she was neurologically intact.

Imaging

The MRI of her lumbar spine with and without contrast showed an enhancing extradural mass at the L2-L3 level extending into the right neural foramen, contributing to severe central and right L2-L3 foraminal stenosis [Figure 1]. MRI studies of the cervical and thoracic spine were negative, as was the CT of her chest, abdomen, and pelvis.

Surgical technique

The patient underwent central and right neural foraminal decompression at the L2-L3 level. The tumor capsule was clearly defined. Tumor originated from the right lateral recess-L2-L3 neural foramen. An excisional biopsy provided the histopathological diagnosis on frozen section of a lymphoproliferative tumor. According to the intra-operative frozen section, the tumor was debulked allowing for decompression of the thecal sac. Additional samples were subsequently sent for a lymphoma panel evaluation.

Postoperative course

Postoperatively, she was started on 4 mg of intravenous dexamethasone every 6 h. The postoperative lumbar MRI showed the thecal sac, and neural elements at the L2-L3 level was adequately decompressed [Figure 2]. However, there was a small amount of residual tumor ventral to the thecal sac extending laterally into the right L2-L3 neural foramen. A PET CT scan later confirmed her known residual spinal disease, but without evidence of hypermetabolism/disease elsewhere. After 5 days of intravenous dexamethasone, she was discharged home with a 2-week oral steroid taper.

Histopathological diagnosis

The patient's lymphoma panel was negative. Rather, the final pathology report showed dense mixed lymphoplasmacytic and histiocytic inflammatory infiltrate with marked stromal fibrosis and a large number of IgG4+ plasma cells with an IgG4/IgG ratio of 27% [Figure 3]. Her serum IgG4 level was normal. Furthermore, a bone marrow biopsy obtained as an outpatient was negative for lymphoproliferative disorder or plasma cell dyscrasias with absent IgG4+ plasma cells.

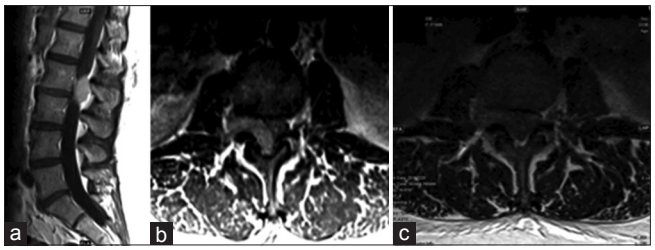

Figure 1: MRI of the lumbar spine. (a) Sagittal postcontrast scan showing an enhancing mass at the L2-3 level. (b) Axial postcontrast scan showing a right-sided mass extending into the right neural foramen causing foraminal expansion and canal stenosis. (c) Axial T2 showing severe central stenosis

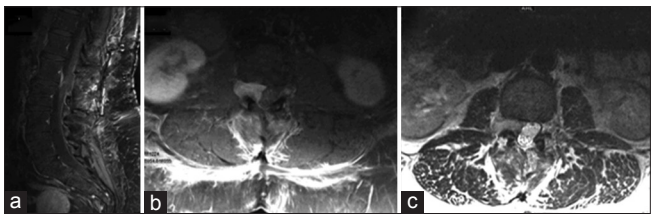

Figure 2: Postoperative MRI. (a) Sagittal contrast enhancing scan showing residual tumor ventral to the thecal sac. (b) Axial contrast-enhancing scan showing residual tumor extending laterally into the neural foramen. (c) Axial T2 image showing adequate decompression of the thecal sac

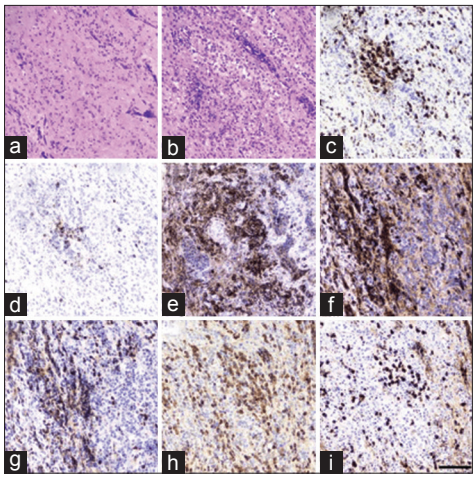

Figure 3: Histopathology slides. (a) Hematoxylin and eosin showing mixture of inflammation and fibrosis. (b) Hematoxylin and eosin showing areas of more extensive mononuclear inflammation. (c) CD3, numerous T-cells. (d) CD20, relatively fewer B-cells. (e) CD138, heavy plasma cells. (f) Kappa light chain. (g) Lambda light chain. (h) IgG. (i) Scale bar = 50 microns; IgG4

One-year follow-up

The patient continued to improve clinically. At her 1-year follow-up, she remained clinically asymptomatic without evidence of recurrent disease. Her treatment plan is for continued conservative management. Should her symptoms recur, she would be a candidate for the re-initiation of steroids.

Table 1: Case reports of immunoglobulin G4-related disease causing spinal cord compression

Author	Year published	Age (years)	Sex	Symptom duration (weeks)	Site of spinal lesion	Neurological symptom (s)	IgG4/ IgG ratio (%)	IgG4 + plasma cells/hpf	Serum IgG4 (mg/ dl)	CSF IgG4 index	Treatment	Symptomatic outcome at final follow-up
Our case	NA	48	Female	8	L2-L3	LBP Neurogenic claudication; RLE radiculopathy	27	NR	Normal	NR	Surgical decompression and steroids	Complete resolution
Williams *et al*.	2017	46	Female	16	C4-T1	Neck pain; BL UE paresthesia and weakness	NR	10	38 (RR 5-140)	NR	Steroids and azathioprine	Marked improvement
Rumalla *et al*.	2017	50	Male	12	T4-T6	LBP; BL LE weakness; T6 sensory level	NR	Increased	Normal	NR	Surgical decompression and steroids	Near complete resolution
Radotra *et al*.	2016	50	Male	24	L1-L2	NR	50	120-130	NR	NR	Steroids	Marginal improvement
Radotra *et al*.	2016	19	Male	24	L2-L3	NR	40	140-150	NR	NR	Steroids	Complete resolution
Ferreira *et al*.	2016	57	Female	156	T10-T12	BL radiculopathy	NR	>50%	66.2 (RR 1-291)	NR	Surgical decompression and steroids	Improvement
Lu *et al*.	2016	55	Male	24	C2-T9	BL UE and LE numbness and weakness; Constipation; Dysuria	40	>10	82.2 (RR 3.0-201)	9.1	Steroids and cyclophosphamide	Improvement
Gu *et al*.	2016	43	Male	2	C4-T2	Neck pain; BL LE numbness and weakness; Bowel and bladder dysfunction	40	>50	976 (RR 800-1600)	NR	Surgical decompression, steroids, mannitol, and neurotrophic drugs	Near complete resolution
Kim *et al*.	2014	52	Female	0.5	C7-T5	BL LE numbness and weakness; Inability to void	NR	Many	NR	NR	Surgical decompression and steroids	Little improvement
Ezzeldin *et al*.	2014	55	Male	2	T2-T3	Paraplegic weakness; T4/T5 sensory level	NR	2	512 (RR 7-89)	NR	Surgical decompression and steroids	Improvement
Wallace *et al*.	2013	32	Male	NR	L5	RLE radiculopathy; RLE numbness and weakness	35	10	NR	NR	Surgical decompression	NR
Tajima and Mito	2012	64	Male	4	T2-T8	Dysphagia Cranial nerve palsies	NR	NR	221 (RR <104)	NR	Steroids	Marked improvement
Lindstrom *et al*. .	2010	55	Male	NR	C3-C7	NR	60	46.6	NR	34.30	Steroids and radiation therapy	Complete resolution
Lindstrom *et al*.	2010	63	Male	NR	C2-C3	BL hand numbness	30	11.8	NR	NR	Surgical decompression	NR
Choi *et al*.	2010	46	Female	2	T9-T11	BL LE weakness	NR	>20	90 (RR 8-140)	NR	Surgical decompression and steroids	Complete resolution
Chan *et al*.	2009	37	Male	2	T5-T10	BL LE numbness and weakness	70	310	NR	NR	Surgical decompression	NR

NA: Not available, LBP: Low back pain, RR: Risk ratio, IgG4: Immunoglobulin G4, IgG: Immunoglobulin, CSF: Cerebrospinal fluid, RLE: Right lower extremity, BL: Bilateral, UE: Upper extremity, LE: Lower extremity, NR: Not reported

DISCUSSION

Clinical presentation of IgG4-RD

The PubMed database was utilized to identify 15 cases in 13 publications (2000–2017) of IgG4-RD causing spinal cord and/or nerve root compression [Table 1].[2,3,8-10,12,15-18,21,23,25] Patients averaged 48.25+/–11.50 years of age [Table 1]. Lesions were more common in males (2.2:1) and were more frequently seen in the thoracic spine, followed by lumbar spine, cervicothoracic junction, and cervical spine (ratio 3:2:2:1).

Ratio of IgG4-RD, symptoms, and treatment options

The IgG4/IgG ratio was greater than 40% in 3 of 9 cases (33.3%). Serum IgG4 was elevated in 2 of 9 cases (22.2%). Only 2 cases reported an elevated CSF IgG4 index. Treatment options varied; these included surgical decompression, application of glucocorticoids, and use of immunosuppression therapy. All cases reported improvement in symptoms, with 4 cases reporting complete resolution of symptoms at final follow-up.

Autoimmune IgG4-RD

IgG4-RD is a collection of autoimmune disorders, which have recently been grouped together because of their unique manifestations. IgG4-RD presents in nearly all organ systems but remains rare in the central nervous system.[1,19] Only 15 cases of IgG4-RD causing spinal cord and/or nerve root compression have been reported in the literature [Table 1].[2,3,8-10,12,15-18,21,23,25]

Presentation of IgG4-RD in the central nervous system

In the central nervous system, IgG4-RD manifests primarily as hypertrophic pachymeningitis, and may be misdiagnosed as lymphoma given its pseudotumor appearance.[20] The current diagnostic criteria for IgG4-RD require at least two of the three following conditions: lymphoplasmacytic infiltrate, fibrosis in a storiform pattern, and obliterative phlebitis.[7] Additional criteria in IgG4-RD affecting other organ systems include elevated serum IgG4 levels, a ratio of IgG4/IgG greater than 40%, and infiltration of organs with IgG4+ plasma cells.[6,7,14] Analysis of data from Table 1 shows only 22.2% of patients with IgG4-related pachymeningitis causing spinal cord and/or nerve root compression had elevated serum IgG4 levels, with only 33.3% of patients having a ratio of IgG4/IgG greater than 40%. These findings are consistent with those reported by Lu *et al*. and Kosakai *et al*.[13,16]

CSF IgG4 index

Della-Torre *et al*. utilized a CSF IgG4 index for diagnosing and monitoring patients with IgG4-related pachymeningitis.[5] The CSF IgG4 index indicated intrathecal IgG4 synthesis and was useful for assessing patients diagnosed with IgG4-related pachymeningitis. Only 2 patients in the series reviewed had a CSF IgG4 index, which was elevated in both cases [Table 1]. More data are required to determine the sensitivity and specificity of this measure in diagnosing patients with IgG4-RD of the spine.

Histopathology and immunohistochemistry of IgG4-RD

Histopathological and immunohistochemical staining from a biopsied specimen showing a lymphoplasmacytic inflammatory infiltrate, fibrosis, and IgG4+ plasma cells remains the gold standard for diagnosing IgG4-RD. Similar to patients with IgG4-RD in other organs, patients with IgG4-related spinal pachymeningitis respond favorably to glucocorticoid treatment, which typically reduces the IgG4-RD pseudotumor mass and controls the inflammatory processes.[4,11,20,24] Glucocorticoid administration offers a non-invasive and highly effective treatment option for patients presenting with this rare diagnosis. Only patients with severe spinal cord and/or nerve root compression or progressive neurological decline may require surgical decompression with tumor debulking, followed by a course of glucocorticoid treatment to reduce the residual tumor burden.

CONCLUSION

Prompt diagnosis and early administration of glucocorticoid treatment may result in the avoidance of surgical decompression in the very rare patients with IgG4-RD spinal tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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