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Case Report

Immunoglobulin G4-related disease manifesting as peripheral neuropathy: A rare clinical symptom due to rare autoimmune disease

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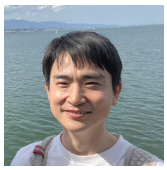

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ABSTRACT

Background: Nervous system involvement in immunoglobulin G4-related disease (IgG4-RD) has been rarely reported.

Case Description: We describe an unusual case of IgG4-RD manifested as paresthesia in the right lower extremity. A 51-year-old male presented with paresthesia in the right S1–S3 regions. A neurological examination revealed peripheral neuropathy. Blood examination results were normal, barring slightly elevated IgG levels. Initial magnetic resonance imaging of the swollen right S1 and S2 nerve roots revealed lymphoma, schwannoma, and sarcoidosis. However, following the biopsy, the pathological findings were not typical of these diseases. Abdominal computed tomography revealed perirenal lesions, and IgG4-RD was suspected. The patient had a serum IgG4 level of 724 mg/dL. Additional pathological evaluations of the swollen S1 nerve revealed findings that corresponded to the diagnostic criteria for IgG4-RD. Oral steroid therapy was initiated, which improved paresthesia, and the swollen S1 nerve root gradually shrank.

Conclusion: This report highlights a rare case of IgG4-RD involving nerve roots that neurosurgeons should consider.

Keywords: Immunoglobulin G4-related disease, Nerve root, Pathology, Peripheral neuropathy, Spine

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is characterized by tumefactive lesions from underlying autoimmune fibroinflammatory conditions, mainly involving the pancreas, bile duct, lungs, and rarely the nervous system.[1,3,7,8,10] Radiologically, IgG4-RD mimics a malignancy and is difficult to differentiate from other diseases.[10] Pathologically, IgG4-RD is associated with dense lymphoplasmacytic infiltration, fibrosis in a storiform pattern, obliterative phlebitis, and IgG4-positive plasma cells.[1] Recently, IgG4-RD lesions along the spinal structure have been described but seem unusual.[4,6,7,10,11] Reports documenting multiple spinal nerve root involvement in IgG4-RD mimicking peripheral neuropathy are scarce. Herein, we report a rare case of IgG4-RD involving multiple sacral nerve roots.

CASE PRESENTATION

A 51-year-old male presented to our neurosurgery department complaining of numbness in the right lower extremity that had gradually worsened over a year. He had undergone surgery for pneumothorax and had varicose veins and emphysema but was not taking any medication. Neurological examination revealed paresthesia in the medial-posterior side of the right leg and buttock and the absence of the right Achilles tendon reflex. The paresthesia region appeared to correspond to the dermatome of left S1–S3. No neurological deficits were observed. We hypothesized that the patient's neurological symptoms could be attributed to peripheral neuropathy. Blood and cerebrospinal fluid samples revealed no abnormalities in rheumatoid factor, antinuclear antibodies, human immunodeficiency virus, syphilis antibodies, or malignancies. Serum IgG levels were slightly elevated at 1974 mg/dL (normal range: 870–1700 mg/dL). Pelvic magnetic resonance imaging (MRI) was performed to rule out paresthesia caused by the mass. The right S1 and S2 nerve roots appear swollen and homogeneously enhanced on T1-weighted gadolinium-enhanced imaging. The dura appeared partially hypertrophic and enhanced [Figures 1a and b]. Based on radiological findings, schwannoma, lymphoma, or sarcoidosis were suspected. Given that the hypertrophic dura did not compress the spinal cord, we predicted that it would be irrelevant to paresthesia. A biopsy of the swollen S1 nerve root was performed to rule out malignancy or inflammatory disease. A soft, reddish lesion of the S1 nerve root was sampled for pathological evaluation [Figure 1c]. The harvested tissue showed the presence of aggregated lymphocytes, surrounded by diffusely growing fibrous tissue, and was positive for CD3 and CD20 [Figures 1d-g]. These findings are not typical of lymphoma, raising the suspicion of an alternative malignancy or inflammatory disease. Abdominal contrast-enhanced computed tomography (CT) was performed to rule out an abdominal lesion and revealed a dilated left ureter and bilateral

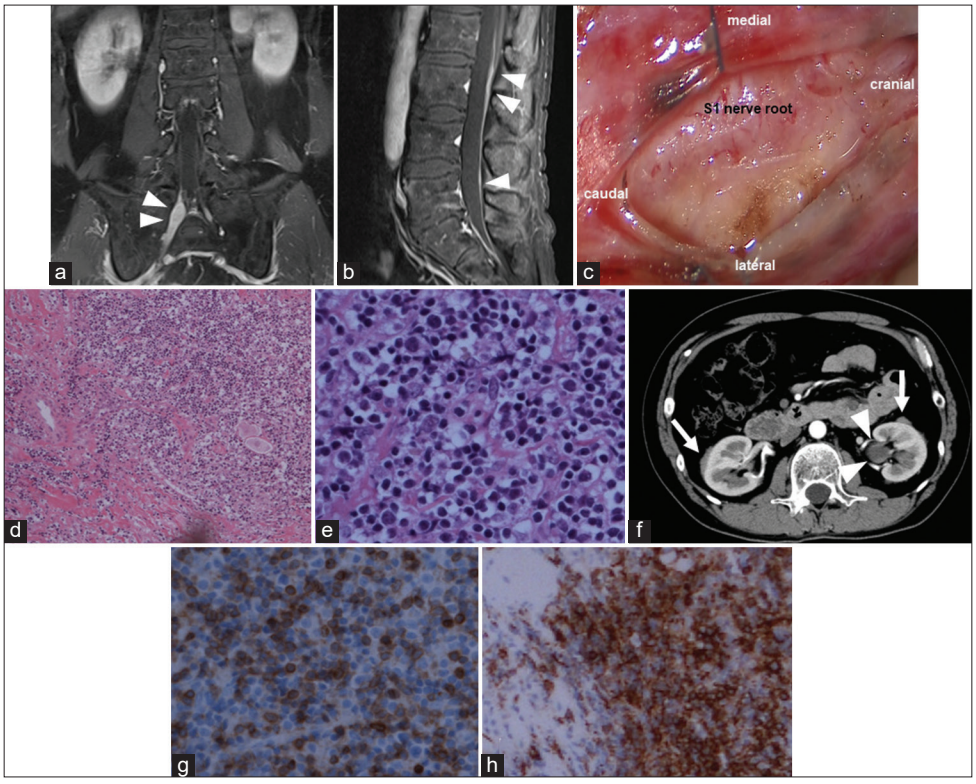

Figure 1: (a and b) The right S1 and S2 nerve roots (white arrowheads) appear swollen and enhanced with the contrast agent. The hypertrophic lumbar dura (white arrowhead) appears partially enhanced (a) coronal T1-weighted gadolinium-enhanced image and (b) sagittal T1-weighted gadolinium-enhanced image. (c) Intraoperatively, reddish and swollen S1 nerve roots can be observed on opening the dura; (d and e) lymphocyte aggregation was accompanied by the diffuse growth of fibrous tissue (hematoxylin-eosin staining with original magnification ×100 (d) and original magnification ×400 (e). (f and g) The specimen is positive for CD3 (original magnification, ×400) and CD20 (original magnification, ×200). (h)The left dilated ureter (white arrowheads) and bilateral perirenal lesions (white arrows) can be observed on contrast-enhanced computed tomography.

perirenal lesions [Figure 1h]. These findings were indicative of IgG4-RD.[9] The serum IgG4 level was 724 mg/dL (normal range: 4.8–105 mg/dL). Moreover, examination of perirenal lesion samples collected laparoscopically by a urologist revealed the presence of lymphocytes, fibrous tissue, and plasma cells. The ratio of IgG4-positive plasma cells to IgG-positive cells exceeded 0.5. Based on these findings, the perirenal tissue was identified as retroperitoneal fibrosis due to IgG4-RD. Immunostaining was performed to confirm this diagnosis, which led to the detection of plasma cells, aggregated lymphocytes, and fibrous tissues. Storiform patterns of collagen fibers and obliterating phlebitis were observed [Figure 2].[1,9] Consequently, we deduced that the S1 and S2 nerve root involvement in IgG4-RD could cause paresthesia. Oral steroid therapy (prednisolone, 30 mg/day) was prescribed. After that, the serum IgG4 level decreased, and the neurological symptoms improved. In addition, the swollen S1 and S2 nerve roots had shrunk on the follow-up MRI. Eighteen months after initiating steroid therapy, the symptoms did not relapse, and prednisolone therapy (8 mg/day) was continued.

DISCUSSION

Here, we describe a rare case of IgG4-RD involving the S1 and S2 nerve roots. After initially suspecting peripheral neuropathy due to paresthesia in the right S1-S3 region, biopsy and pathological examination of the involved S1 nerve root and perirenal lesion revealed IgG4-RD. Due to the rarity of IgG4-RD involving the nerve roots, diagnosis can be challenging.

Nervous system involvement is a rare manifestation of IgG4-RD.[10] Hypertrophic pachymeningitis is a frequent manifestation of IgG4-RD of the nervous system and is often observed in intracranial lesions. However, the spinal cord and nerve roots may also be affected.[11] Inoue *et al*. described two cases of IgG4-RD involving the cervical, lumbar, and sacral nerve roots. However, a pathological examination was not performed.[2] In addition, Williams *et al*. described a case of cervical and thoracic paraspinal lesions secondary to IgG4-RD, and findings from a CT-guided biopsy of the lesion corresponded to IgG4-RD.[10] In the current case, the paraspinal lesion was in the extradural space rather than the intradural S1 and S2 nerve roots. The hypertrophic dura, although asymptomatic, could have resulted from IgG-RD. IgG4-RD lesions can be radiologically misdiagnosed as lymphomas.[8] Before the pathological examination, lymphoma was suspected due to atypical radiological findings in the right S1 and S2 nerve roots. However, the pathological findings of the S1 nerve root biopsy were not typical of lymphoma but were immunologically positive for CD3 and CD20 and typically positive for T-cell lymphoma and B-cell lymphoma, respectively.[9]

The diagnostic criteria for IgG4-RD include one or more organs manifesting a nodular or swollen shape (lymph node swelling should be omitted), elevated serum IgG4 level (>135 mg/dL), and pathological diagnosis.[9] Two of the following three criteria should be fulfilled: (a) dense lymphocyte and plasma cell infiltration with fibrosis, (b) IgG4-positive plasma cell to IgG-positive

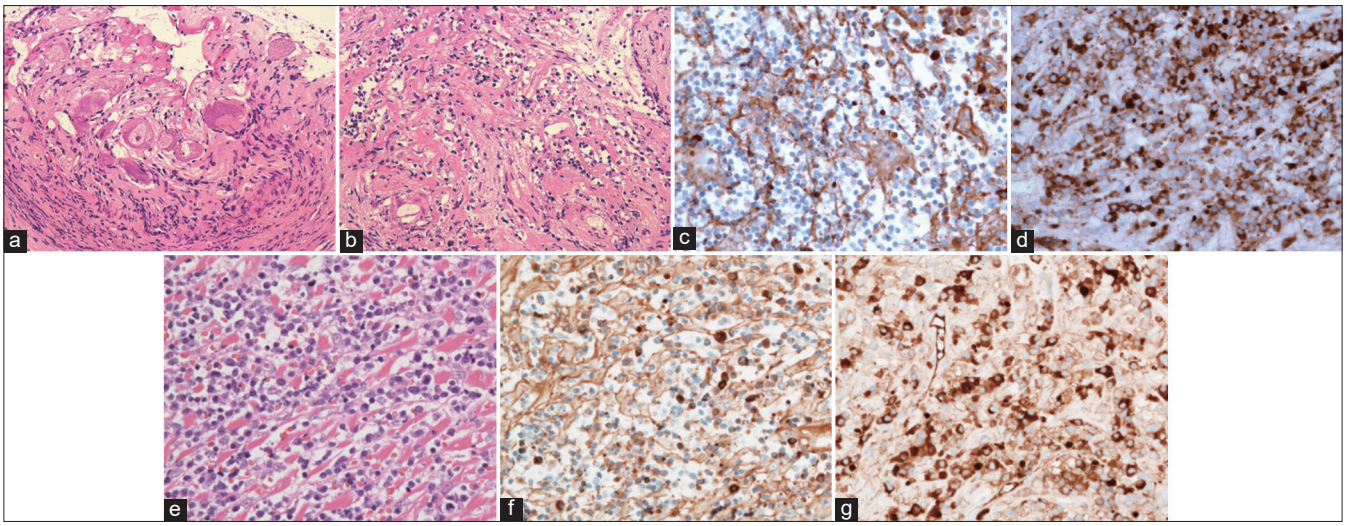

Figure 2: (a and b) The specimen of the right S1 nerve exhibits dense lymphoplasmacytic infiltration, obliterative phlebitis, and storiform growth of collagen fibers (a and b: hematoxylin-eosin staining, original magnification ×100). (c and d) The specimen is positive for immunoglobulin G (IgG) (c: original magnification ×200) and IgG4 (d: original magnification ×200), and more than half of the tissue positive for IgG is positive for IgG4. (e-g) The ureter specimen shows similar findings on hematoxylin-eosin staining (e), immunostaining of IgG (f), and that of IgG4 (g) (original magnification ×200).

cell ratio exceeding 40%, and (c) typical tissue fibrosis (particularly storiform fibrosis) or obliterative phlebitis.[9] In addition to the swollen S1 and S2 nerve roots, the patient presented a serum IgG4 level of 724 mg/dL. The pathological examination revealed aggregated lymphocytes, plasma cell infiltration, and storiform fibrosis. The proportion of IgG4-positive to IgG-positive plasma cells exceeded 50%. In the current case, given that sufficient nerve root and ureter specimens could not be obtained, we did not evaluate the positive/negative expression of CD138 to support the diagnosis of IgG4-RD.[5] However, similar pathological findings in the nerve root were observed in the ureteral specimen. Therefore, the diagnosis of IgG4-RD was appropriate.

CONCLUSION

Neurosurgeons should consider the possibility of a rare entity, such as IgG4-RD, that mimics peripheral neuropathy accompanied by atypical radiological findings. To rule out IgG4-RD occurring in rare regions such as nerve roots, abdominal CT screening can aid in the diagnosis of typical IgG4-RD-related findings.

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Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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