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Spinal cord compression by cystic IgG4-related spinal pachymeningitis mimicking neurocysticercosis: a case report

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Abstract

Background To report a case of IgG4-related pachymeningitis presenting with cystic lesions mimicking neurocysticercosis.

Case presentation A 40-year-old female patient with tetraparesis, dysphagia and dysphonia was evaluated with clinical examination, magnetic resonance imaging, and meningeal biopsy. Magnetic resonance imaging (MRI) revealed diffuse pachymeningeal enhancement involving the cranial, cervical, thoracic, and lumbar segments with spinal cord compression and cystic lesions. CSF immunology was initially positive for *cysticercus cellulosae*. After disease progression a meningeal biopsy was compatible with IgG4 related disease. The patient had partial response to rituximab and needed multiple surgical procedures for spinal cord decompression and CSF shunting.

Conclusions This case highlights the possibility of IgG4-related disease in patients with diffuse pachymeningitis causing spinal cord compression, even with cystic lesions on MRI. Diagnosis of IgG4-related pachymeningitis is paramount due to the possibility of treatment response to immunotherapy, particularly to anti-CD20 agents.

Keywords Immunoglobulin G4-related disease, Pachymeningitis, Neurocysticercosis, Spinal cord, Neuroimmunology

This work was conducted at the Neurology Department of Hospital Universitário Walter Cantidio, Federal University of Ceara, Fortaleza, Brazil.

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Background

IgG4 related disease (IgG4-RD) is a multisystemic disease that is characterized by storiform fibrosis associated with fibrogenic cytokines and IgG4 tissue deposition [1]. Manifestations of IgG4-RD in isolated organs have been reported for many decades and were thought to represent several distinct disorders. Only in 2003, the shared disease features, common natural history and response to immunosuppression culminated in the recognition of IgG4-RD as a systemic disorder [2, 3].

The condition usually presents with tumor-mimicking lesions, more often affecting lacrimal glands, orbits, major salivary glands, pancreas, bile ducts, retroperitoneum, lungs, kidneys, aorta, pachymeninges and thyroid gland [3]. Previous studies reported that up to 35% of patients with IgG4-RD present with pachymeningitis, a chronic inflammatory process of the dura mater that usually presents as headache and cranial nerve palsy [4]. This number is thought to be yet underestimated, since an increasingly proportion of cases of hypertrophic pachymeningitis once considered idiopathic are being studied and reclassified as IgG4-RD [5, 6].

Pachymeningitis is an inflammatory process affecting the dura mater (pachymeninx) that can be caused by various disorders. Magnetic resonance studies usually reveal focal or diffuse signs of meningeal thickening and contrast enhancement. The neurological symptoms depend on the topography of lesions and the adjacent structures impaired. The most common etiologies of pachymeningitis include chronic infectious diseases such as mycobacterium tuberculosis, syphilis, Lyme disease, fungal infection and cysticercosis; malignancies and autoimmune/inflammatory diseases, such as granulomatosis with polyangiitis (GPA), sarcoidosis, and IgG4-related disease [1, 7, 8].

Case reports are important tools to improve our understanding of diseases, particularly their atypical manifestations. Our goal was to report a distinct case of a patient suffering from severe cystic spinal IgG4-related pachymeningitis. This complex condition led to spinal cord compression and obstructive hydrocephalus. Intriguingly, the initial diagnosis pointed to neurocysticercosis, illustrating the challenges associated with identifying and diagnosing this rare presentation of IgG4-RD.

Case presentation

A 40-year-old female patient initially presented to a neurosurgery outpatient clinic with imbalance and shuffling gait in 2016. Brain magnetic resonance imaging (MRI) revealed hydrocephalus and a ventriculoperitoneal shunt was placed. No cerebrospinal fluid (CSF) or blood workup results are available from this first presentation. Pachymeningitis was not reported in the initial MRI. She had moderate improvement in gait and balance afterward.

Four months later, in April 2017, she reported progressive weakness in her left arm and leg, followed by dysphagia and inability to walk. Neurological examination revealed atrophy of the deltoid, supraspinalis and infraspinalis muscles with muscle strength grade 3 in upper limbs and grade 4 in lower limbs, as well as fasciculations observed in deltoid muscles. There was hyperreflexia with bilateral extensor plantar responses in the lower limbs. No cervical weakness was observed, suggesting a C4 motor level. There were no sensory abnormalities and no well-defined sensory level.

Spinal cord MRI showed extensive pachymeningitis with cysts associated with spinal cord compression (Fig. 1A). Meningeal biopsy revealed nonspecific inflammatory changes. At this time, immunohistochemical staining for IgG4 was not performed and storiform fibrosis was not reported.

Laboratory testing was negative for rheumatologic diseases (antinuclear antibodies, rheumatoid factor, anti-Ro, anti-La, anti-DNA, anti-phospholipid antibodies) and infectious etiologies (VDRL, anti-HIV, serology for tuberculosis - interferon-gamma release assays or IGRA). CSF analysis revealed normal cell count and protein content, and screening for infectious agents, including HSV, CMV, tuberculosis and syphilis was negative. Serum and cerebrospinal fluid ELISA for *Cysticercus cellulosae*, which were positive. The patient lived in a rural area and had the habit of eating vegetables grown by the local community and drinking water from household wells. Given these findings and a high epidemiological risk factor, a diagnosis of pachymeningitis associated with cysticercosis was suspected. She was treated with albendazole, praziquantel, and intravenous methylprednisolone (IVMP) 1 g/day for 5 days. There was partial improvement after treatment; she regained the ability to walk with unilateral assistance, and her dysphagia also improved.

In September 2017, she was admitted to a neurology ward with dysphagia, dysphonia and tetraparesis. Muscle strength was grade 3 in upper limbs and grade 4 in lower limbs. Hyporeflexia and fasciculations were found in the upper limbs, and hyperreflexia, spasticity, clonus, and bilateral extensor plantar responses were present in the lower limbs. Lhermitte´s sign was also present.

MRI revealed diffuse cervical pachymeningeal enhancement with spinal cord compression, central T2/FLAIR hyperintensity of the spinal cord, and cysts in the lumbar pachymeninges (Figs. 1B, 2 and 3).

Posterior fossa decompression and multilevel cervical laminectomy with dural excision were performed in October 2017. Histopathological examination of the dural samples revealed a substantial number of IgG4-positive plasma cells and storiform fibrosis, with no

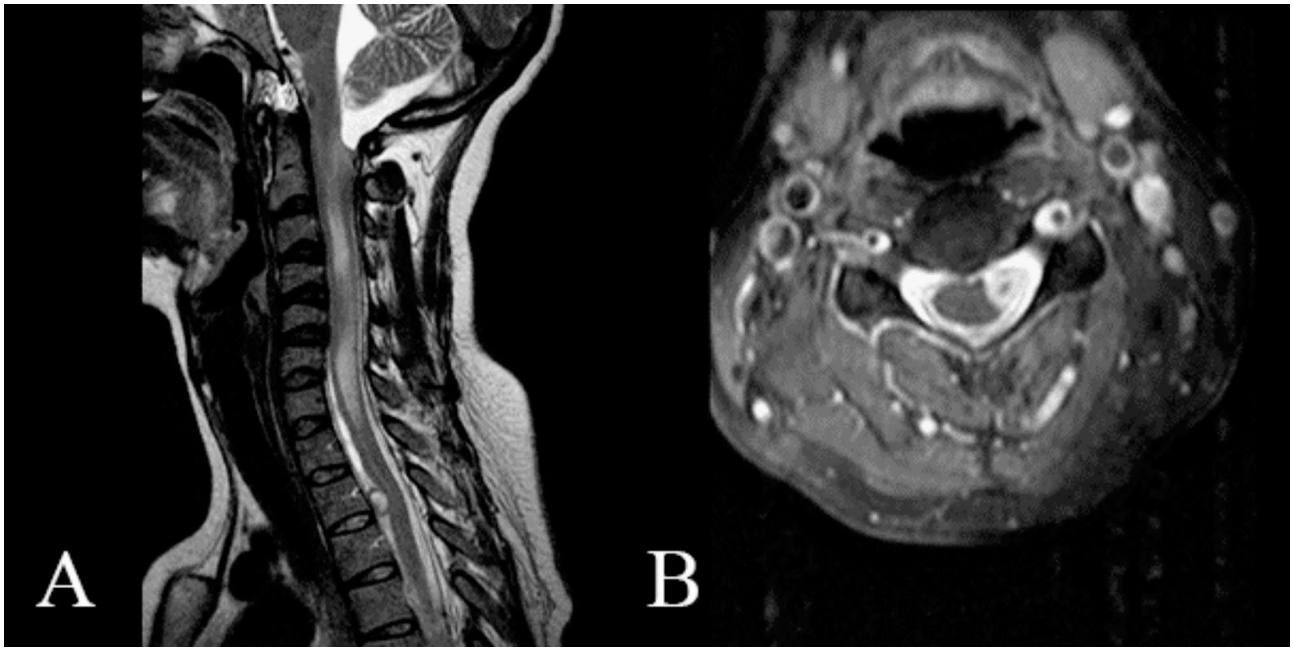

Fig. 1 Spinal cord MRI. (**A**) There is dural thickening with extensive spinal cord T2 hyperintensity, absence of the normal CSF column with enlargement of the cisterna magna, and an intradural oval image with peripheral T2 hyposignal and gadolinium enhancement in the topography of the C3-C4 intervertebral disc, measuring about 7.3 × 4.6 mm. (**B**) Axial image of the cervical spine showing diffuse circumferential pachymeningeal enhancement and an oval intradural image, with peripheral contrast-enhancement, measuring about 12.0 × 8.0 mm, on the topography of the intervertebral disc T2-T3

evidence of cysticercosis. A diagnosis of IgG4-associated pachymeningitis was made and a new course of IVMP 1 g/day for 5 days was given, followed by cyclophosphamide 1 g. The patient had no evidence of other organ involvement.

One month after surgery her symptoms worsened, and she was unable to walk. Rituximab 1 g divided in two doses of 500 mg 15 days apart was added to her treatment regimen. After 3 months there was an improvement in motor functions, and the patient was able to walk with unilateral assistance. She remained stable using oral prednisone, azathioprine, and semestral rituximab infusions until 2019 when progressive dysphagia and dysarthria recurred, and she needed another neurosurgical approach for cervical spinal cord decompression.

In April 2022, five years after the initial pachymeningitis presentation, advanced invasive ductal carcinoma of the breast was diagnosed, and the patient died of sepsis and multiple organ failure two months later in June 2022.

A complete timeline of the patient medical history is shown in Fig. 4.

Discussion and conclusions

We reported a case of cystic IgG4-RD spinal pachymeningitis leading to cervical spinal cord compression. Due to its atypical presentation, the condition was initially misdiagnosed with neurocysticercosis. As a result, considerable delay in the start of immunotherapy occurred.

Pachymeningitis is a rare condition that requires a comprehensive diagnostic approach due to its association with various underlying conditions such as tuberculosis, syphilis, neoplasia, and cysticercosis [1, 7, 8]. Diagnostic methods include imaging techniques like MRI and CT scans to identify dural thickening and enhancement. Serological tests and cerebrospinal fluid (CSF) analysis are essential to detect infections like tuberculosis and syphilis [1, 7, 8]. Biopsy of the dura mater is often considered the gold standard for diagnosis, providing definitive histopathological evidence, and enabling the identification of specific causes, including neoplastic and parasitic infections like cysticercosis. This multimodal approach ensures accurate diagnosis and guides appropriate treatment strategies [1, 7, 8].

Tuberculosis, a common infectious cause of hypertrophic pachymeningitis, can lead to chronic granulomatous inflammation of the dura, often requiring long-term antimicrobial therapy. Syphilis is another infection that can present as pachymeningitis. The diagnosis can be achieved through immunological testing and the disease is responsive to penicillin treatment. Primary or metastatic tumors can mimic inflammatory pachymeningitis, making biopsy crucial for distinguishing malignant cells and inflammatory processes. Cysticercosis, a parasitic infection caused by Taenia solium larvae, leads to granulomatous inflammation as the body's immune response to the parasitic cysts in the dura, requiring both antiparasitic treatment and management of inflammatory

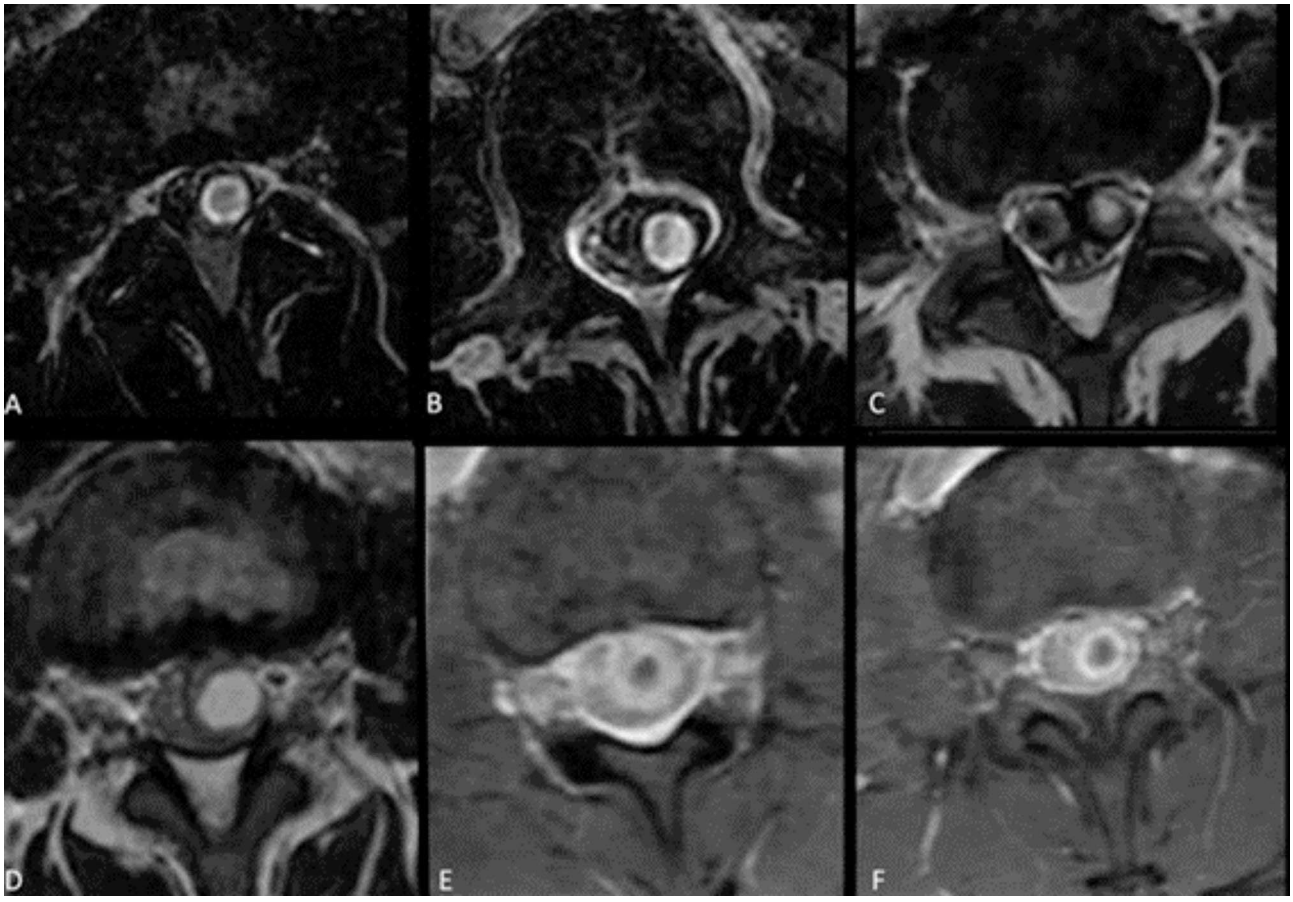

Fig. 2 Spinal cord MRI. Axial images of the thoracolumbar spine. **A**- T2 Fat Sat, **B** & **C**-T2. Lower row post-contrast, **D**-T1, **E** & **F**-T1 Fat Sat. There are nodular intradural extra-axial lesions with heterogeneous T2 signal and variable enhancement (solid in D, peripheral in E and F)

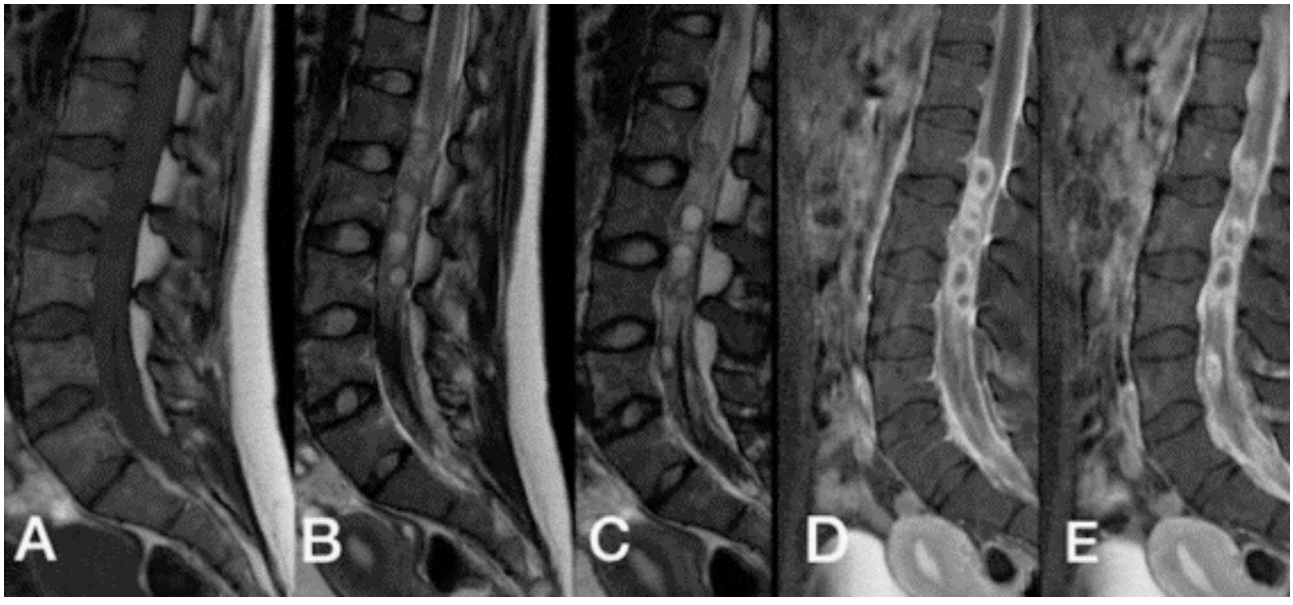

Fig. 3 Spinal cord MRI. Longitudinal images of thoracolumbar spine. **A** - **E**. Diffuse enhancement of the dura mater, evident in the thoracic and lumbar segments. Pachymeningeal enhancement and cystic formations with thick enhancement in the lumbar region

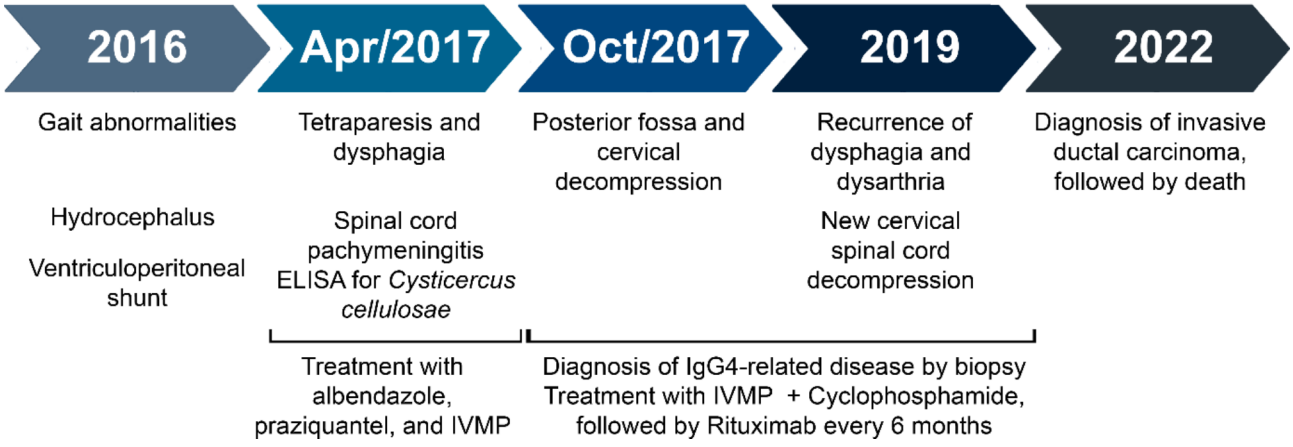

Fig. 4 Case report timeline

symptoms. Each of these clinical entities demands a targeted therapeutic approach following accurate diagnosis, highlighting the importance of comprehensive diagnostic methods in effective disease management [7, 8].

IgG4-RD pachymeningitis typically manifests with headache (67%), cranial nerve palsy (33%), motor weakness (15%) and limb numbness (12%)[9]. IgG4-RD is one of the main etiologies implicated in non-malignant cranial pachymeningitis [1]. However, IgG4-RD may also present as subacute to chronic myelopathy due to compression by spinal cord pachymeningitis [9].

A review of published cases of spinal IgG4-RD pachymeningitis suggests that this presentation is more common in middle-aged males [10]. Moreover, most cases of spinal IgG4-RD pachymeningitis occur at cervical or thoracic spinal cord levels. A challenge for the diagnosis of spinal IgG4-RD pachymeningitis encompasses the cases without extra-neurological manifestations of IgG4-RD. Classicaly, a vast majority of patients with IgG4-RD were reported to present with elevation of serum IgG4 levels. However, more recent studies revealed that normal IgG4 serum levels may occur in up to 40% of cases, being neither sensitive nor specific to the diagnosis of IgG4-RD, and requiring a robust clinical background to be associated with the occurrence of the disease [10, 11]. Thus, only a pathological examination of spinal dura mater may definitely diagnose IgG4-RD in this scenario. Despite this, early diagnosis is crucial because patients with IgG4-RD spinal pachymeningitis tend to exhibit good, albeit partial, response to steroids and to anti-CD20 therapy [12].

One additional diagnostic hurdle is the clinical and radiological similarity of IgG4-related pachymeningitis to other etiologies of pachymeningitis, which include infectious diseases (neurosyphilis, tuberculosis, cysticercosis), other inflammatory disorders (neurosarcoidosis), neurohystiocitosis [13] and malignant neoplasms [6]. The definitive diagnosis of IgG4-RD usually requires histopathological confirmation, characterized by "storiform" (similar to a woven mat) fibrosis pattern, phlebitis obliterans (possibly a rarer finding in meningitis compared to other organs) and dense lymphoplasmacytic infiltrate with infiltration of IgG4 plasma cells [14–16]. A significant number of plasma cells (usually greater than 40%) stain positively for IgG4[15].

A rare variant called "Racemose cysticercosis" or "Extraparenchymal cysticercosis" involves the development of cysts that are unusually large, multilobular, and clustered; they may lack scolex and contrast-enhancing in imaging studies. This form occurs in non-confining extraparenchymal sites (e.g., ventricles, subarachnoid space). Mixed parenchymal and extraparenchymal disease can occur [17, 18]. This form could be compatible with the lesions found in the lumbar region of this patient, but meningeal biopsy of that site revealed findings consistent with IgG4 deposition and no evidence of cysticercosis tissue. In racemose cysticercosis, the scolex cannot be identified but the typical three-layered membrane wall often allows the correct identification of the parasite [19].

The diagnosis of IgG4-RD remains challenging. Clinical assessments, laboratory evaluations, and imaging studies often are not sufficient to distinguish IgG4-RD from neoplastic, inflammatory and infectious mimickers. Current diagnostic criteria for IgG4-RD [16] are shown in Fig. 5.

In our case, the atypical presentation of cystic pachymeningitis and the positivity of serum and cerebrospinal fluid ELISA for Cysticercus cellulosae resulted in a misdiagnosis of neurocysticercosis. In accordance, the

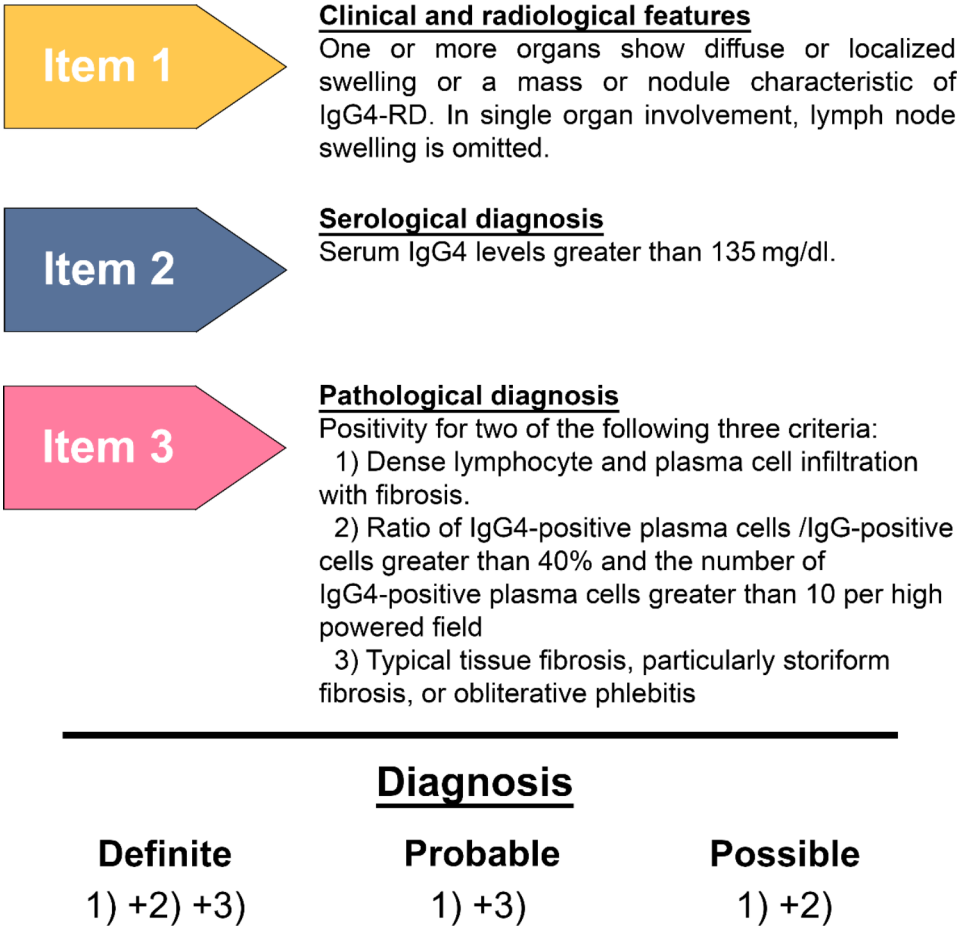

Fig. 5 The 2020 Revised comprehensive diagnostic (RCD) criteria for IgG4-RD

guideline of the diagnosis of neurocysticercosis by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH) suggests that caution is required when testing for neurocysticercosis using ELISA methods, due to considerable risk of false positive results [20].

Spinal IgG4-RD pachymeningitis with spinal cord compression is exceedingly rare. Differentiating it from infectious diseases, including cysticercosis, is vital to prevent misdiagnosis. Prompt diagnosis of spinal IgG4-RD pachymeningitis is essential as these conditions typically respond favorably to corticosteroids and anti-CD20 agents, thus averting further neurological disability [21, 22].

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Author contributions
All authors made substantial contributions to the production of this report. D.A.B.S. Araujo, P.L.G.S.B. Lima, R.M. Ribeiro, D.C. de Queiroz and P.R. Nobrega were enrolled in the conceptualization, methodology, and clinical data collection of this report. C.D. Nogueira was responsible for the pathological examination of the biopsy material of the patient. P.P. Coimbra and B.M. carried out the neuroimaging review, as well as selecting the neuroradiology figures for the manuscript. All authors contributed to the early writing of the manuscript. P.L.G.S.B. Lima, P. Braga Neto, G.D. Silva and P.R. Nobrega were the main reviewers of the final version of the manuscript. P.L.G.S.B. Lima was responsible for the submission of the report.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Written informed consent was obtained from the parents of the patient for publication of this case and accompanying images.

Consent for publication
Written informed consent was obtained from the parents of the patient for publication of this case and accompanying images.

Competing interests
The authors declare no competing interests.

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References

1. AbdelRazek MA, Venna N, Stone JH. IgG4-related disease of the central and peripheral nervous systems. Lancet Neurol [online serial]. Lancet Neurol; 2018;17:183. Accessed at: https://pubmed.ncbi.nlm.nih.gov/29413316/. Accessed May 29, 2024.
2. Stone JH, Khosroshahi A, Deshpande V et al. Recommendations for the nomenclature of IgG4-related disease and its individual organ system manifestations. Arthritis Rheum [online serial]. Arthritis Rheum; 2012;64:3061–3067. Accessed at: https://pubmed.ncbi.nlm.nih.gov/22736240/. Accessed May 29, 2024.
3. Perugino CA, Stone JH. IgG4-related disease: an update on pathophysiology and implications for clinical care. Nature Reviews Rheumatology. 2020 16:12 [online serial]. Nature Publishing Group; 2020;16:702–714. Accessed at: https://www.nature.com/articles/s41584-020-0500-7. Accessed May 29, 2024.
4. Takahashi H, Yamashita H, Morooka M et al. The utility of FDG-PET/CT and other imaging techniques in the evaluation of IgG4-related disease. Joint Bone Spine [online serial]. Joint Bone Spine; 2014;81:331–336. Accessed at: https://pubmed.ncbi.nlm.nih.gov/24568886/. Accessed May 29, 2024.
5. Lindstrom KM, Cousar JB, Lopes MBS. IgG4-related meningeal disease: Clinico-pathological features and proposal for diagnostic criteria. Acta Neuropathol [online serial]. Springer; 2010;120:765–776. Accessed at: https://link.springer.com/article/10.1007/s00401-010-0746-2. Accessed May 29, 2024.
6. Lu LX, Della-Torre E, Stone JH, Clark SW. IgG4-related hypertrophic pachymeningitis: clinical features, diagnostic criteria, and treatment. JAMA Neurol [online serial]. American Medical Association; 2014;71:785–793. Accessed at: https://jamanetwork.com/journals/jamaneurology/fullarticle/1859983. Accessed May 29, 2024.
7. Mekinian A, Maisonobe L, Boukari L et al. Characteristics, outcome and treatments with cranial pachymeningitis: a multicenter French retrospective study of 60 patients. Medicine (United States) [online serial]. Lippincott Williams and Wilkins; 2018;97. Accessed at: https://journals.lww.com/md-journal/fulltext/2018/07270/characteristics,_outcome_and_treatments_with.16.aspx. Accessed May 29, 2024.
8. Fain O, Seror O, Wirth JF, et al. Les pachyméningites crâniennes. Rev Med Interne Elsevier Masson. 1999;20:234–46.
9. Slade SJ, Bauer EM, Stone VV, Dave AJ. Spinal IgG4-related hypertrophic pachymeningitis with spinal cord compression: case report and literature review. World Neurosurg [online serial]. World Neurosurg; 2019;130:65–70. Accessed at: https://pubmed.ncbi.nlm.nih.gov/31254697/. Accessed May 29, 2024.
10. Lu Z, Tongxi L, Jie L et al. IgG4-related spinal pachymeningitis. Clin Rheumatol [online serial]. Clin Rheumatol; 2016;35:1549–1553. Accessed at: https://pubmed.ncbi.nlm.nih.gov/26567899/. Accessed May 29, 2024.
11. Wallace ZS, Stone JH. An update on IgG4-related disease. Curr Opin Rheumatol [online serial]. Curr Opin Rheumatol; 2015;27:83–90. Accessed at: https://pubmed.ncbi.nlm.nih.gov/25415530/. Accessed May 29, 2024.
12. Choi SH, Lee SH, Khang SK, Jeon SR. IgG4-related sclerosing pachymeningitis causing spinal cord compression. Neurology [online serial]. Neurology; 2010;75:1388–1390. Accessed at: https://pubmed.ncbi.nlm.nih.gov/20938032/. Accessed May 29, 2024.
13. Nóbrega PR, Rodrigues PGB, de Sousa Pereira I et al. Steroid responsive cavernous sinus syndrome due to Rosai-Dorfman disease: beyond Tolosa-Hunt syndrome - a case report. BMC Neurol [online serial]. BMC Neurol; 2021;21. Accessed at: https://pubmed.ncbi.nlm.nih.gov/34225703/. Accessed May 29, 2024.
14. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med [online serial]. N Engl J Med; 2012;366:539–551. Accessed at: https://pubmed.ncbi.nlm.nih.gov/22316447/. Accessed May 29, 2024.
15. Radotra BD, Aggarwal A, Kapoor A, Singla N, Chatterjee D. An orphan disease: IgG4-related spinal pachymeningitis: report of 2 cases. J Neurosurg Spine [online serial]. J Neurosurg Spine; 2016;25:790–794. Accessed at: https://pubmed.ncbi.nlm.nih.gov/27391401/. Accessed May 29, 2024.
16. Umehara H, Okazaki K, Kawa S et al. The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. Mod Rheumatol [online serial]. Mod Rheumatol; 2021;31:529–533. Accessed at: https://pubmed.ncbi.nlm.nih.gov/33274670/. Accessed May 29, 2024.
17. Mahale RR, Mehta A, Rangasetty S. Extraparenchymal (Racemose) neurocysticercosis and its multitude manifestations: a comprehensive review. J Clin Neurol [online serial]. J Clin Neurol; 2015;11:203–211. Accessed at: https://pubmed.ncbi.nlm.nih.gov/26022457/. Accessed May 29, 2024.
18. Marcin Sierra M, Arroyo M, Cadena Torres M et al. Extraparenchymal neurocysticercosis: demographic, clinicoradiological, and inflammatory features. PLoS Negl Trop Dis [online serial]. PLoS Negl Trop Dis; 2017;11. Accessed at: https://pubmed.ncbi.nlm.nih.gov/28599004/. Accessed May 29, 2024.
19. Yang C, Liu T, Wu J et al. Spinal cysticercosis: a rare cause of myelopathy. BMC Neurol [online serial]. BioMed Central Ltd; 2022;22:1–11. Accessed at: https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-022-02589-2. Accessed May 29, 2024.
20. White AC, Coyle CM, Rajshekhar V et al. Diagnosis and treatment of neurocysticercosis: 2017 clinical practice guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). Clin Infect Dis [online serial]. Clin Infect Dis; 2018;66:e49–e75. Accessed at: https://pubmed.ncbi.nlm.nih.gov/29481580/. Accessed May 29, 2024.
21. Fernández-Codina A, Orozco-Gálvez O, Martínez-Valle F. Therapeutic options in IgG4-related disease. Current Treatment Options in Rheumatology 2020 6:3 [online serial]. Springer; 2020;6:191–204. Accessed at: https://link.springer.com/article/10.1007/s40674-020-00147-w. Accessed May 29, 2024.
22. Wu S, Wang H. IgG4-related digestive diseases: diagnosis and treatment. Front Immunol [online serial]. Frontiers Media SA; 2023;14. Accessed at: /pmc/articles/PMC10585276/. Accessed May 29, 2024.

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