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LETTER TO THE EDITOR

Therapeutic strategies for durable response in plasma cell granulomas in the central nervous system

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Dear Editor,

Plasma cell granuloma or inflammatory myofibroblastic tumor (IMT) is a rare histopathologic diagnosis characterized by heavy lymphoplasmacytic inflammatory infiltration with myofibroblastic spindle cells [1–3]. Here, we present a challenging case of IMT with exceptional response to therapy using Rituximab that reveals information regarding the pathobiology of IMT.

A 62-year-old male presented with a 6-week history of progressive right-sided headaches. His medical history was significant for pulmonary nodules biopsied with inconclusive results. Imaging was suggestive for mastoiditis with temporal leptomeningeal enhancements (Fig. 1a, b). With persistent symptoms a month later, a temporal lobe and dural biopsy performed revealed a CD138+ polyclonal plasma cells with CD20+ B-lymphocytic infiltrate in the background of reactive myofibroblastic spindle cells (Fig. 2). Staining for ALK rearrangement was negative. There were no features of infection or granulomas suggestive of sarcoid and IgG4 staining was not present.

Bone marrow biopsy did not reveal any clonal plasma cells or blasts and PET CT did not reveal any abnormal marrow enhancements or metastatic involvement. The pulmonary nodules previously noted in his medical history were no longer present.

All studies obtained supported the diagnosis of IMT.

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IMT in adults often present with pulmonary lesions and less commonly extrapulmonary manifestations, including central nervous system (CNS) involvement have been described [3–5]. As in our patient, it was suspicious that his past pulmonary nodules represented early IMT.

Definitive surgical resection is the treatment for IMT, with radiotherapy a second option for localized or low tumor burden [4–7].

Management in patients with inoperable or metastatic disease remains challenging and with few options. Immunohistochemical studies on pulmonary and extrapulmonary IMT have cited rearrangements of the ALK locus on chromosome 2p23 in 50% of cases which have led to reports of partial responses after the use of Crizotinib for 4 months [8]. Two case reports of ALK-negative IMT demonstrated a partial response in treatment with Methotrexate and Vinorelbine [5, 7]. Methylprednisolone has been used for growth suppression and *Garcia* et al. demonstrated Rituximab as an effective adjunct to steroid therapy, with even sustained radiologic response in IMT [4, 6].

Given the extent of CNS involvement in our patient, surgical resection or targeted radiotherapy was not an appropriate treatment option. The patient received Rituximab infusion every 2 weeks and high-dose prednisone tapered over 2 months. Surveillance MRI 1 year later had shown interval decrease in temporal-dural thickening and near-complete radiographic remission (Fig. 1c, d).

This is the first case of IMT in a patient with inoperable CNS disease benefitting from a long-term durable response to Rituximab therapy. B-lymphocytes are present within all biopsy specimens and despite their low percentage, may have a role in inflammatory recruitment and development of plasmacytic granulomas [1, 4, 9]. This may explain our patient's remarkable response to Rituximab therapy. Interestingly, recent pathologic studies demonstrate a high degree of programmed cell death-1 ligands (PD-1/PDL-1) staining in ALK-negative IMT [10]. This further lends to the possibility of immune-mediated dysfunction in the development

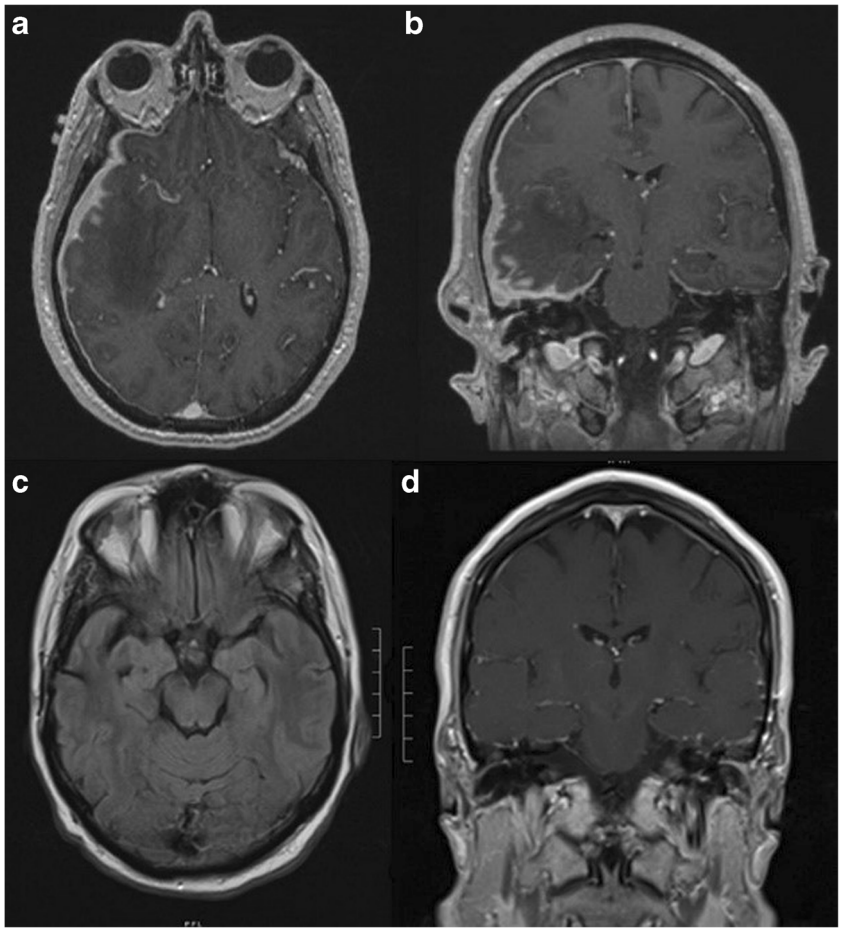

Fig. 1 Magnetic resonance imaging of IMT noted in transverse (**a**) and sagittal (**b**) images. Radiographic improvement after 6 cycles of rituximab and prednisone with near-complete radiographic resolution of IMT tumor burden (**c**, **d**)

of IMT [1, 2, 4]. In addition, PD-1/PD-L1 staining may point to efficacy with the use of immunotherapy in the future.

Our patient with IMT represents a challenging case that continues to have a durable response of greater than 28 months. We suggest Rituximab therapy may have a significant efficacious role in the treatment owing to B lymphocyte-mediated inflammatory recruitment in plasma cell granulomas.

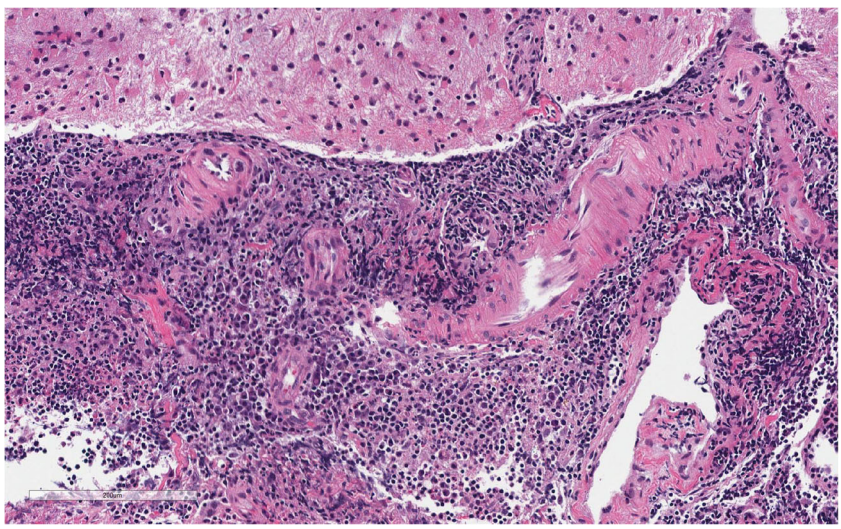

Fig. 2 Pathologic interpretation of temporal lobe biopsy with hematoxylin and eosin stain demonstrates myofibroblastic proliferation with significant plasma cell and lymphoid infiltration

Authors' contribution All authors were involved in patient care, participate in collecting and interpreting data, and writing the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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