A tumor of IgG4-related skin disease on a forehead with relapse 3 years after resection

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INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is a condition involving the formation of nodules or plaques comprising accumulated IgG4-producing plasma cells. The diagnostic criteria for this new disease, which was identified in Japan, were established in 2011.[1] The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease have been developed and validated in a large cohort of patients.[2] A case of IgG4-RD manifesting as skin lesions was first reported in 2009.[3] Pseudolymphoma of this disease is characterized by the following three features: 1) Lesions in the head and neck region, particularly in the periauricular, buccal, and mandibular areas; 2) accumulation of lymphocytes, mainly plasma cells, and prominent fibrosis; and 3) masses or elevated lesions in the affected region.[4]

Here, we report a relatively rare case of a 56-year-old man with a mass in the forehead, which was postoperatively identified as IgG4-related skin disease, and which relapsed 3 years after complete resection.

Abbreviation used:

IgG4-RD: Immunoglobulin G4-related disease

CASE REPORT

A 56-year-old man presented with a 5-cm pulsating tumor on his right forehead (Fig 1). The lesion first appeared as a 1.5-cm nodule 4 years previously and gradually increased in size. The patient had a medical history of hypertension but no autoimmune disease. The patient had no symptoms or physical findings other than the tumor. Contrast-enhanced computed tomography revealed that superficial temporal artery branches were spread out within the tumor (Fig 2), leading to a preoperative diagnosis of hemangioma and subsequent extirpation. Pathological analysis revealed noticeable infiltrating lymphocytes and plasma cells around blood vessels. Approximately 70% of the IgG^+ plasma cells were found to be IgG4-producing cells (Fig 3). The patient's serum IgG4 level was 109 mg/dL. Whole-body contrast-enhanced computed tomography examination to evaluate for involvement by other organs was performed and was unremarkable. The concentration of C-reactive protein was 0.03 mg/dL, and tests for autoantibodies, including antinuclear antibodies, were negative. Based on comprehensive diagnostic criteria for IgG4-RD, the patient was

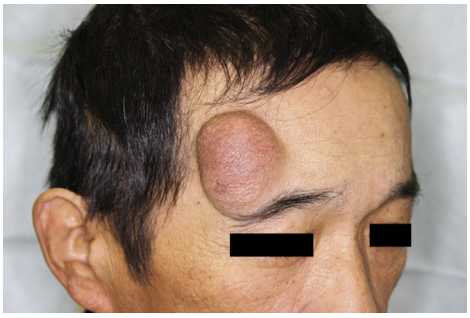

Fig 1. A 56-year-old man presented with a 5-cm in diameter, elastic, slightly solid tumor with good mobility on his forehead.

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diagnosed with probable IgG4-RD given the following findings: 1) Involvement of a single organ, 2) serum IgG4 higher than normal but not meeting criterion for elevated serum IgG4 ($\geq$135 mg/dL), and 3) features of marked infiltration of lymphocytes and plasma cells with fibrosis and infiltrating $IgG4^+$ plasma cells on histopathology.

Although the patient's serum IgG4 level had decreased to a normal level of 72.9 mg/dL at 6 months after surgery, it gradually increased thereafter. Approximately 3 years after surgery, a subcutaneous tumor (2 cm in size) again developed in the operated region, and the patient's serum IgG4 had increased to 91.4 mg/dL. The tumor was resected again with clear margins. Pathological analysis revealed infiltration of lymphocytes and plasma cells around blood vessels as in the previous specimen, consistent with recurrence. Currently, 6 years after the initial surgery, no new lesions have developed.

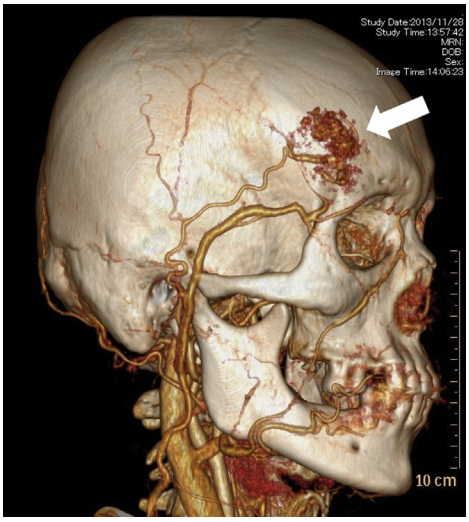

Fig 2. Contrast-enhanced computed tomography examination: Superficial temporal artery branches are spread from the deeper part of the center to the inside of the tumor (*arrow*).

DISCUSSION

IgG4-RD mainly affects middle-aged to elderly men, and the detailed etiology is still unknown.[1,5] Due to the high incidence in Asia, the involvement of autoimmune reactions by activation of the innate immune response based on the genetic background has been reported.[1,5] Tokura et al[4] categorized the skin lesions into seven subtypes: (1) Cutaneous plasmacytosis (multiple papulonodules or indurations on the trunk and proximal part of the limbs), (2) pseudolymphoma and angiolymphoid hyperplasia with eosinophilia (plaques and papulonodules mainly on the periauricular, cheek, and mandible regions), (3) Mikulicz disease (palpebral swelling, sicca syndrome, and exophthalmos), (4) psoriasis-like eruption (strikingly mimicking psoriasis vulgaris), (5) unspecified maculopapular or erythematous eruptions, (6) hypergammaglobulinemic purpura (bilateral asymmetrical palpable purpuric lesions on the lower extremities) and urticarial vasculitis (prolonged urticarial lesions occasionally with purpura), and (7) ischaemic digit (Raynaud phenomenon and digital gangrene). Here we described a case of pseudolymphoma according to the classification of IgG4-related skin disease that relapsed 3 years after complete resection. The most common site of pseudolymphoma is the head and neck, especially around the pinna, cheeks, and mandible, which form a mass or elevated lesions.[4] Because only some cases of primary cutaneous-type IgG4-related pseudolymphoma with skin lesions without plasma cells infiltrating into other organs are known, it may be necessary to include this condition in the differential

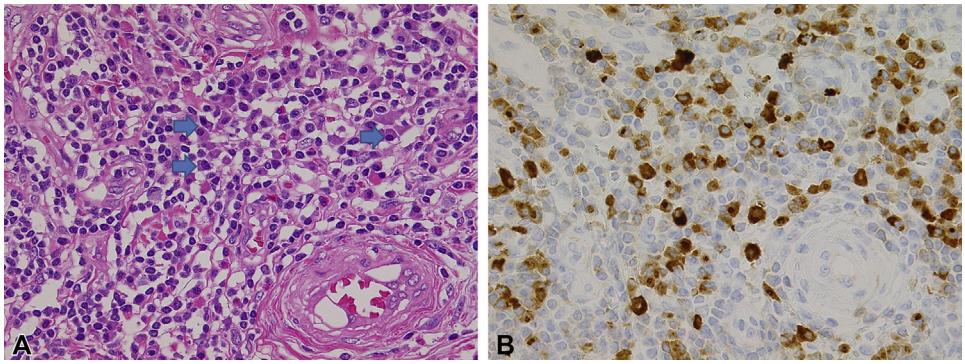

Fig 3. Pathological examination: Many plasma cells (*arrows*) are observed, and $IgG4^+$ accounts for approximately 60%–70% of the IgG^+ cells. **A**, Hematoxylin-eosin staining, original magnification ×400. **B**, Immunostaining for IgG4, original magnification ×400.

diagnoses for facial tumors in the future.[6] In particular, given the high specificity of serum IgG4 in blood tests, preoperative testing with the possibility of IgG4-RD may be helpful for diagnosis.[7]

Administration of oral glucocorticoids is the current first-line therapy for IgG4-related skin disease.[7] Because our patient had no evidence of involvement of organs other than the skin, he was not treated with any systemic therapy. In our case, the mass was completely removed for cosmetic reasons; however, a previous report has argued that complete removal is often not required, even when tumors remain, although no clear treatment guidelines exist.[8] The decision to treat surgically should be based on evidence from other sites, including serum IgG4 levels and imaging. Long-term postoperative follow-up is necessary because recurrence is a possibility, as was the case for our patient.

Conflicts of interest

None disclosed.

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