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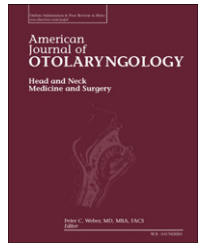

Case reports

Immunoglobulin G4-related disease of the orbital cavity, cervical lymph nodes and greater auricular nerve: case report☆,☆☆,★

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ABSTRACT

IgG4-related disease (IgG4-RD) is a novel clinicopathological entity characterised by elevated tissue levels of IgG4-positive plasma cells. It can present in almost every organ systems. We present a case of a 48 year-old man with recurrent intra-orbital and cervical lymph node swelling and found to have greater auricular nerve involvement intraoperatively during open surgical biopsy. Histopathological evaluation of biopsied specimens from these lesions yielded IgG4-positive plasma cell infiltration on immunohistochemistry. Key pathological features such as prominent lymphoplasmacytic population, storiform fibrosis and obliterative phlebitis were also seen. A diagnosis of IgG4-RD was made. Oral prednisone therapy ameliorated the symptoms and patient remained in remission at followup. Literature review indicated that IgG4-RD is a rare condition that seldom occurs concurrently in the orbital cavity, cervical lymph nodes and involving the greater auricular nerve. The condition may often masquerade as malignancy or infection due to formation of tumefactive lesions but tend to respond favourably to glucocorticoid or immunosuppressants. The differential diagnosis of unusual mass lesions in these locations should include IgG4-RD. The otolaryngologist, as well as other health professionals, should be familiar with this novel disease to ensure timely diagnosis and treatment.

1. Introduction

IgG4-related disease (IgG4-RD) is a novel clinicopathological entity characterised by elevated tissue levels of IgG4-positive plasma cells [1–3]. Multi-organ involvement is common, and symptomatology can often be attributed to compression from formation of mass lesions in the affected organs [1–5]. In the clinical setting, patients with this condition often undergo biopsy in order to rule out lymphoma, lymphoproliferative disorders or other malignancies. Notwithstanding the organ

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systems affected, IgG4-RD shares key pathological features such as prominent lymphoplasmacytic population, storiform fibrosis and obliterative phlebitis [1,2]. The diagnosis and management of this condition require a multidisciplinary effort involving the physician, pathologist and radiologist. The literature is replete with papers supporting the effectiveness of glucocorticoids and immunosuppressives in the management of IgG4-RD although reports of long-term studies are scarce. We describe a patient with IgG4-RD manifesting as recurrent intra-orbital and cervical lymph node swelling and found to have greater auricular nerve involvement intraoperatively.

2. Case report

A 48-year old man presented with a six-month history of left-sided proptosis (7 mm on Hertel's exophthalmometry) and bilateral non-tender cervical lymphadenopathy. He had intact visual acuity and full extra-ocular motility. Physical examination and flexible fibreoptic endoscopy of the upper aerodigestive tract was normal. His past medical history was unremarkable.

Computed tomography (CT) scan showed a large homogeneous mass with intra and extra-conal components extending into the left orbital apex (Fig. 1). Swelling of the left infraorbital nerve, inferior rectus muscle and lacrimal gland was noted. Enlarged lymph nodes (up to 27 mm) were observed along the deep cervical chains bilaterally.

Fine-needle aspirations (FNAs) of the cervical lymph node were inconclusive. The patient underwent an open orbital biopsy. Histologically, florid lymphoid infiltrate with focal fibrosis was seen. Numerous plasma cells were observed within the infiltrate, with at least 40% of the plasma cells being positive for IgG4 on immunohistostaining.

An open cervical lymph node biopsy in the form of a selective neck dissection (levels II–III) was undertaken. Intra-operatively, the greater auricular nerve was noted to be abnormally and irregularly thickened. An incisional biopsy was taken of one of the prominent deposits in the nerve; the nerve itself was preserved and remained intact in the postoperative course. Histological examination of the cervical lymph node showed areas reminiscent of Castleman's disease-like changes and other areas showing inter-follicular expansion by heavily infiltrating lymphoplasmacytes (Fig. 2). Immunohistochemical-staining confirmed clusters of plasma cells that do not demonstrate kappa or lambda light chain restriction. The ratio of IgG4-positive cells amongst total IgG-positive cells was approximately 40% (Fig. 3). These findings are compatible with IgG4-related lymphadenopathy.

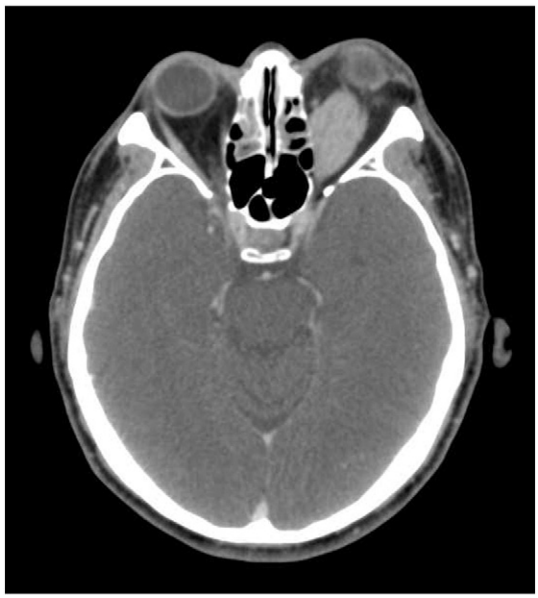

Fig. 1 – Axial-view of contrast-enhanced computed tomography showing a left intra-orbital mass lesion with displacement of globe.

The nerve biopsy histology showed lobulated aggregates of lymphocytes admixed with plasma cells with surrounding sclerotic fibrous bands and ectatic blood vessels. Immunohistochemistry studies confirmed an elevated IgG4 to IgG ratio with up to 30 IgG4-positive plasma cell per high power field (hpf).

A diagnosis of IgG4-related disease (IgG4-RD) involving the orbit, cervical lymph nodes and greater auricular nerve was made. Serum IgG4 was 30 (normal 5–125 mg/dl). He was started on prednisone at 40 mg daily initially. This was gradually titrated down given that there was clinical regression of his proptosis and cervical lymphadenopathy. He remained in remission when seen in the outpatient visits.

3. Discussion

IgG4-related disease (IgG4-RD) is an inflammatory condition characterized by a propensity to form tumefactive lesions. Histologically, dense lymphoplasmacytic infiltrate with a predominance of T-cells, obliterative phlebitis and storiform fibrosis is often seen [1,6]. Elevated numbers of IgG4-positive plasmacytes are needed to make the diagnosis; although the precise number per high power field (hpf) and the ratio of IgG4-positive plasma cells to total IgG-positive plasma cells vary based on the organ systems involved. IgG4-positive cell number and its ratio to IgG-positive cells are regarded as less important as opposed to the histological morphology of the lesion [1,4,6,7].

IgG4-RD commonly affects the head and neck [1,6,7]. It is increasingly being accepted that this condition is not as rare as previously thought, and with greater understanding and awareness of this condition, the number of cases being diagnosed will steadily increase.

Lymph node involvement is frequent in IgG4-RD, however, the histopathological features is often not as clear-cut when compared to other extranodal sites [4,7,8]. To prevent over-diagnosis of this condition, Cheuk et al have proposed a number of clinical and histological criteria for IgG4-related lymphadenopathy [8]. Clinically, constitutional symptoms are often absent in IgG4-related lymphadenopathy. Lymph node enlargement can manifest synchronously or metachronously alongside other organ systems involvement, usually subacutely. Serum IgG4 concentrations may or may not be raised. Histologically, unique features of inflammation such as dense lymphocytic infiltrate with storiform fibrosis like those seen in the salivary gland are typically not seen in the lymph nodes [2,8]. Rather, the morphologic manifestations can be classified into five distinct subtypes: (i) Castleman's disease-like, (ii) follicular hyperplasia,