ARC Journal of Ophthalmology
Volume 4, Issue 2, 2019, PP 13-15
www.arcjournals.org

Inflammatory Pseudotumor of the Orbit: Inaugural Feature of Hyper 'igg4' Syndrome

Mouna Snoussi[1*], Yosra Bouattour[1], Faten Frikha[1], Moez Jallouli[1], Chifa Damak[1], Ghribi Mariem[1], Raida Ben Salah[1], Sameh Marzouk[1], Jamel Feki[2], Zouhir Bahloul[1]

[1]*Department of internal medicine Hedi Chaker Hospital Sfax Tunisia*

[2]*Department of ophthalmology Habib Bourguiba Hospital Sfax Tunisia*

Corresponding Author: *Mouna Snoussi, *Department of internal medicine Hedi Chaker Hospital Sfax Tunisia.* ***Email:*** *mounasnoussi23@gmail.com*

Abstract: *Hyper IgG4 syndrome is a chronic condition characterized by fibro-inflammatory infiltration of the several organ systems. It leads to mass forming lesions and organ damage mimicking malignancy, inflammatory or infectious disorders. Hyper IgG4 syndrome is commonly misdiagnosed because of the lack of reliable biomarkers for this condition. We represent here a new case of a recurrent pseudotumor of the orbit revealing the diagnosis of hyper IgG4 syndrome. Relapses were managed by high dose corticosteroid therapy.*

Keywords: *Exophthalmos, pseudotumor, orbit, IgG4*

1. Introduction

Hyper-IgG4 syndrome was first described by Japanese researchers in 2001 in a group of patients with autoimmune pancreatitis [1]. Then extra-pancreatic fibro-inflammatory lesions with elevated serum IgG4 were identified [2]. In 2013, a diagnosis classification was established for the disease [3]. We report a case of an orbital pseudotumor as an unusual first manifestation of IgG4 syndrome.

2. Case Report

A 50-year-old female white patient with no significant medical history was referred on July 2010 for bilateral eyelid swelling that has worsened over the six previous months. The patient also suffered from right sided proptosis, burning sensation, excessive tearing and diplopia. There was no rhinorrhea, bleeding, fever or other associated signs. Her ophthalmic examination concluded to right exophtalmos with bilateral palpebral oedema (figure1).

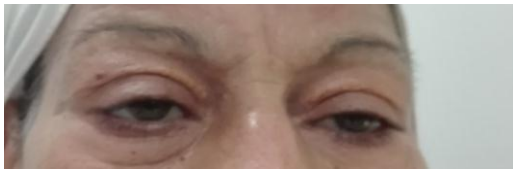

Figure1. *Bilateral Palpebral Swelling with Predominant Right Exopthlamos Before Treatment*

The ocular motricity was preserved, the vision and intraocular pressure were normal in both eyes. There was neither uveitis nor vasculitis. A computed tomography (CT) scan of the orbit showed bilateral hypertrophy of the oculomotor muscles marked in the right side. The orbital magnetic resonance imaging (MRI) concluded to bilateral hypertrophy of oculomotor muscles particularly lateral rectus. (figure2).

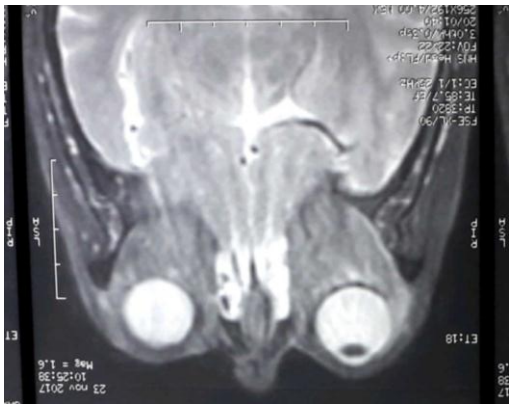

Figure2. *Orbit MRI: bilateral inflammation of ocular muscles predominant in the right side*

In biological tests, the blood cell count and the level of C - reactive protein were normal. Renal function and hepatic enzymes were in the normal range. Laboratory tests of thyroid function and anti-thyroglobulin autoantibodies were normal. The measurement of antinuclear antibodies (ANA) levels, anti-SSA/Ro, and antineutrophil cytoplasmic antibodies (ANCA) levels were negative. Viral serologies (hepatitis B, hepatitis C and HIV) and tuberculosis investigations were negative. The patient was treated with High-dose corticosteroid therapy with a favourable course and a total regression of exophthalmos in clinical and radiological control. Eight years later, the patient presented for eye dryness, a bilateral

palpebral oedema and recurrence of exophthalmos mainly in the right eye (figure1) with parotid and submandibular swelling. The echography showed the hypertrophy of the parotid and submaxillary glands. The orbital MRI concluded that the rectus and oblique muscles of the two orbits were enlarged associated to intra-conical fat infiltration (figure2). Laboratory tests were all negative including new infectious and immunological investigations. biopsy of salivary gland did not reveal any abnormality. The coexistence of salivary gland hypertrophy and orbital inflammatory pseudotumour evoked the hyperIgG4 syndrome. The diagnosis was confirmed by the IgG4 test raised to 6,8g/l (normal: 0.039 to 0.86 g/l). The patient was treated with high-dose corticosteroid therapy with a favourable course (figure3).

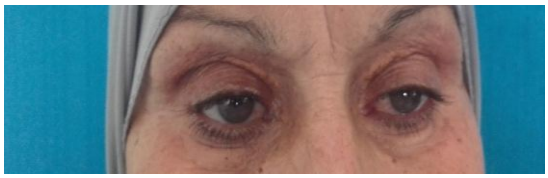

Figure3. *Amelioration of Exopthlamos After Treatment*

3. DISCUSSION

Hyper IgG4 is a recent entity of unknown etiology. It was first described in Japan with an incidence of 0.28–1.08/100,000 [4]. Old men of the sixth decade are more affected by the disease. Several organs could be involved and the most frequent one is the pancreas [4-5-6]. Clinical features described are sclerosing cholangitis, glomerulonephritis, dacryoadenitis and sclerosing sialadenitis, idiopathic fibrosis (retroperitoneal, mediastinal, and thyroid), pulmonary inflammatory pseudotumors, interstitial pneumonitis, pachymeningitis, and hypophysitis [5-6-7-8]. Ocular involvement in this pathology is less frequent reported with a prevalence of 3.6–12.5%. the most common patterns are dacryoadenitis that may be accompanied with salivary gland swelling or Mickulicz disease, enlarged orbital nerves, Orbital fat involvement, orbital myositis, scleritis and less commonly sclerosing orbital inflammation without lacrimal gland involvement [8].

Clinical presentations of ocular manifestation are usually nonspecific as unilateral or bilateral swelling of the eyes like in our patient [3]. Ocular muscles enlargement is common in this disease and more than one muscle is affected. Oculomotor muscles enlargement reported in order of frequency was inferior rectus, followed by superior rectus–elevator complex, lateral rectus, medial rectus, inferior oblique, and superior oblique. In Ig G4 syndrome, stabism is less seen graves orbitopathy despite the very large muscles involvement [9].

MRI helps with the diagnosis of IgG4 syndrome. In reported studies, lesions were well defined and showed isointensity on T1-weighted images and hypointensity on T2-weighted lesions, which were all homogeneous [10].

It is difficult to make the differential diagnosis with other inflammatory diseases such as granulomatosis with polyangiitis which is associated with destructive polysinusitis [11]. Another Differential diagnosis is the MALT lymphoma. the most common type is marginal zone B-cell lymphoma, occurs in the conjunctiva, lacrimal gland, orbit, eyelids, and other parts of the eye. Histological investigation is necessary in confusing cases. In inflammatory pseudotumor, there is a moderate amount of lymphocyte and plasma cell infiltration, with significant spindle cells (myofibroblasts and spindle cells), without phlebitis, immunohistochemical staining of spindle cells that are actin positive or CD68 positive, and no increase in the number of IgG4-positive plasma cells [12]. Nevertheless, A small number of cases of lymphoma arising in patients with IgG4 syndrome has been reported, and it seems likely that this disease increases the risk of development of lymphoma and the physiopathology of this association is unknown [9].

In our case, the clinical and radiological presentation were reassuring and against tumoral process. The coexistence of salivary glands swelling evoked also the Sjogren Syndrome and the diagnosis was ruled out with the normality of salivary gland biopsy and the negativity of antinuclear antibodies.

The assessment of serum levels of IgG4 is used as a diagnostic criterion. The relation of serum IgG4/total IgG higher than 8% as a high sensitive and a specific criterion mainly in cases of immunodeficiency [8].

Glucocorticoids are used as first-line therapy to IgG4 syndrome with rapid and excellent response but relapseas in our patient is common even after many years. A maintenance low dose of corticosteroid of 5mg/j is preferable and reduces significatively the relapses [2-13-14]. Azathioprine, methotrexate, and mycophenolate are used with unsatisfactory results in patients with corticosteroid dependency. Rituximab was

effective the latter cases [3]. In case of resistance to therapy, a search of differential diagnosis particularly the malignancy is mandatory. Our patient is another case report of this disease presenting with a recurrent pseudotumor of the orbit. The outcome was favorable with steroids. Nevertheless, the diagnosis was made lately in the second relapse.

4. CONCLUSION

IgG4-related disease is associated with polymorphous and non specific manifestations. Through our case report, we emphasize on the necessity to evoke this diagnosis in idiopathic recurrent orbital inflammation. Treatment is based on Corticosteroids, but relapses are frequent on ceasing or tapering treatment. In this situation, rituximab is a promising therapy basing on the pathogenesis pathways of the disease.

REFERENCES

[1] Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, et al. High Serum IgG4 Concentrations in Patients with Sclerosing Pancreatitis. N Engl J Med. 8 mars 2001;344(10):732‑8.

[2] Kamisawa T, Egawa N, Nakajima H. Autoimmune pancreatitis is a systemic autoimmune disease. Am J Gastroenterol. déc 2003;98(12):2811‑2.

[3] Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol. févr 2012;22(1):21‑30.

[4] Kamisawa T, Okamoto A. IgG4-related sclerosing disease. World J Gastroenterol. 2008;14(25):3948.

[5] Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. Mod Rheumatol. févr 2012;22(1):1‑14.

[6] Brito-Zerón P, Ramos-Casals M, Bosch X, Stone JH. The clinical spectrum of IgG4-related disease. Autoimmun Rev. déc 2014;13(12):1203‑10.

[7] Neild GH, Rodriguez-Justo M, Wall C, Connolly JO. Hyper-IgG4 disease: report and characterisation of a new disease. BMC Med [Internet]. déc 2006 [cité 29 août 2019];4(1). Disponible à: http://bmcmedicine.Biomed central.com/articles/10.1186/1741-7015-4-23

[8] Origuchi T, Yano H, Nakamura H, Hirano A, Kawakami A. Three cases of IgG4-related orbital inflammation presented as unilateral pseudotumor and review of the literature. Rheumatol Int. nov 2013;33(11):2931‑6.

[9] McNab AA, McKelvie P. IgG4-Related Ophthalmic Disease. Part II: Clinical Aspects. Ophthal Plast Reconstr Surg. 2015;31(3):167‑78.

[10] Song YS, Choung H-K, Park S-W, Kim J-H, Khwarg SI, Jeon YK. Ocular adnexal IgG4-related disease: CT and MRI findings. Br J Ophthalmol. avr 2013;97(4):412‑8.

[11] Carbone T, Azêdo Montes R, Andrade B, Lanzieri P, Mocarzel L. Orbital Pseudotumor: Uncommon Initial Presentation of IgG4-Related Disease. Case Rep Rheumatol. 2015;2015:1‑4.

[12] Geyer JT, Ferry JA, Harris NL, Stone JH, Zukerberg LR, Lauwers GY, et al. Chronic Sclerosing Sialadenitis (Küttner Tumor) Is an IgG4-associated Disease: Am J Surg Pathol. févr 2010;34(2):202‑10.

[13] Khosroshahi A, Stone JH. Treatment approaches to IgG4-related systemic disease: Curr Opin Rheumatol. janv 2011;23(1):67‑71.

[14] Hirano K, Tada M, Isayama H, Yagioka H, Sasaki T, Kogure H, et al. Long-term prognosis of autoimmune pancreatitis with and without corticosteroid treatment. Gut. 1 déc 2007; 56(12):1719‑24.

Citation: *Mouna Snoussi et al, Inflammatory Pseudotumor of the Orbit: Inaugural Feature of Hyper 'igg4' Syndrome. ARC Journal of Ophthalmology. 2019, 4(2): 13-15.*