A 68-YEAR-OLD WOMAN WITH A LEFT ORBITAL AND TEMPORAL MASS

Luca Bertero[1], Francesco Zenga[2], Francesca Maletta[3], Rebecca Senetta[4], Paola Cassoni[1]

1 Division of Pathology, Dept. of Medical Sciences, University of Turin, Turin, Italy

2 Division of Neurosurgery, Dept. of Neurosciences, University of Turin, Turin, Italy

3 Division of Pathology, Città della Salute e della Scienza University Hospital, Turin, Italy

4 Division of Pathology, IRCCS Candiolo, Candiolo (Turin), Italy

Corresponding Author:

Dr. Luca Bertero

Division of Pathology, Dept. of Medical Sciences

University of Turin

Via Santena 7

10126 Turin

Italy

Telephone: +39-011-6335438

Fax: +39-011-6334633

Email: luca.bertero@live.it

CLINICAL HISTORY AND IMAGING

A 68-year-old woman was admitted to the Department of Neurosurgery because of sudden development of fluent aphasia after a history of about 20 days of right inferior-temporal quadrantanopia with left eye sight deterioration. MRI found a 3 cm hyperintense, contrast-enhancing mass in the left posterior-lateral orbital wall protruding through the optic foramen and displacing the temporal lobe (Fig. 1). A meningioma was suspected and patient underwent left pterional craniotomy combined with a lateral orbitotomy in order to remove both the intraorbital and the intradural components of the tumor. The mass showed neither a clear dural implant, nor a well-defined dissection plan from the brain parenchyma, raising the suspicion of a lymphoproliferative disorder. Since the intraoperative pathological findings from frozen sections were suggestive for an inflammatory disease, only a partial resection was achieved to avoid damage to the optic nerve. The patient recovered well and was discharged with a left eye sight improvement.

PATHOLOGICAL FINDINGS

Haematoxylin and eosin (H&E) intraoperative frozen sections showed a sclerotic tissue with a chronic inflammatory infiltrate without significant atypia, mitoses or necrosis. Further resection of the lesion was therefore completed and more pathological material was submitted. Histological examination after FFPE processing showed a fibrotic tissue with storiform pattern, a chronic inflammatory infiltrate with a background of numerous plasma cells with a balanced Kappa/Lamba *ratio* and a high count of IgG4-positive elements (up to 40/HPF) (Fig. 2).

Examination of the additional submitted samples pointed out a significantly different finding: H&E sections showed a hypercellular connective tissue with numerous histiocytes, with large nuclei and wide, foamy or eosinophilic, cytoplasms, arranged in small groups (Fig. 3). Emperipolesis was diffusely observed (Fig. 4) and S100 staining was positive in these cells. A background of small lymphocytes and numerous IgG4-positive plasma cells (Fig. 5), as on the frozen sections, was also present, with an average IgG4+/IgG+ ratio > 40% by counting the IgG4+ “hot spots”.

What’s your diagnosis?

DIAGNOSIS

Rosai-Dorfman meningeal disease with IgG4-related disease histological features.

DISCUSSION

Rosai-Dorfman (RD) disease, also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a rare condition of unknown etiology caused by a non-clonal proliferation of S100-positive histiocytes (1). It can present in nodal or extranodal sites, the latter including meninges and orbit. Emperipolesis is a histological hallmark.

IgG4-related disease is a chronic inflammatory condition characterized by tissue infiltration by IgG4-positive plasma cells and lymphocytes leading to tissue sclerosis. Possible disease sites are very broad, also including orbit and meninges. A consensus statement including diagnostic criteria has been published: diagnosis is based on morphological findings, the presence of IgG4-positive plasma cells and a IgG4+/IgG+ *ratio* > 40% (2). The three major morphological features are: a dense lymphoplasmacytic infiltrate, fibrosis, arranged at least focally in a storiform pattern, and obliterative phlebitis. In case of meningeal disease, > 10 IgG4-positive plasma cells/HPF together with the presence of at least 1 morphological feature has been proposed as sufficient for a diagnosis of “Probable histological features of IgG4-related disease”. No criteria for a diagnosis of “Histologically highly suggestive of IgG4-related disease” have been defined for the meningeal site because of the limited data available. IgG4 serum levels have been investigated as a possible diagnostic aid, but their use is limited by their unsatisfactory sensitivity and specificity.

In our meningeal RD disease case, criteria for a diagnosis of probable histological features of IgG4-related disease were also met. Increased IgG4-positive plasma cells in RD disease have been extensively reported in literature, but the question wherever a true association between these entities exist or if it is a mere non-specific coincidental finding remains open (4). This can be especially true in meningeal disease, since, as previously described, diagnostic criteria for meningeal IgG4-related disease are less defined and this could lead to overdiagnosis of this condition.

RD disease treatment approach is mainly based on general clinical conditions, sites involved and disease progression. After diagnosis and disease staging, a close follow up can be suggested for patients without symptoms or critical organs involvement. If active treatment is indicated, steroids are the first-line option and are sufficient to achieve disease control in most of the cases. Surgery, radiotherapy and chemotherapy can be taken into consideration in specific situations (1). Steroids are the mainstay treatment for IgG4-related disease too and improvement is usually rapid: however, early diagnosis and prompt treatment are important because sclerosis and organ damage can be irreversible (3).

As a concluding remark, the different histological findings between the material submitted for intraoperative examination and the additional tissue samples highlight the limits of intraoperative diagnoses and the importance of adequate sampling.

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