The identification of IgG4-related disease as a distinct immune-mediated condition encompassing disorders that were traditionally seen as idiopathic has been a revolution in the diagnostic and therapeutic algorithm in several medical fields. This condition usually involves multiple organs (isolated organ involvement is uncommon except in the pancreas) with characteristic histopathological findings. We report a case that was assessed due to abdominal pain and subsequently diagnosed with IgG4-related sclerosing mesenteritis. A comprehensive work-up of the case ruled out other conditions and a diagnosis of IgG4-related sclerosing mesenteritis was made according to radiographic and histopathological criteria.

Key words: IgG4-related disease. IgG4-related sclerosing mesenteritis. Abdominal pain. Storiform fibrosis. IgG4 plasma cells.

INTRODUCTION

IgG4-related disease is a chronic systemic disorder characterized by specific histopathological findings in involved organs. These include lymphoplasmacytic infiltration with IgG4 plasma cells, storiform fibrosis, obliterative phlebitis and tissue eosinophilia (1). The involvement of the digestive system includes type-1 autoimmune pancreatitis (AIP), IgG4-related sclerosing cholangitis, IgG4-related retroperitoneal fibrosis, sclerosing mesenteritis, IgG4-related pseudotumor of the gallbladder or cholecystitis, gastrointestinal involvement and IgG4-related hepatitis (2,3). Sclerosing mesenteritis is an inflammatory, fibrosing condition of an unknown origin. Cases have recently been reported with tissue infiltration by IgG4 plasma cells. This might be considered part of the IgG4-related disease spectrum, although further studies are required (4,5). Herein we report a case of IgG4-related sclerosing mesenteritis in a young male.
abundant eosinophils. Immunohistochemistry identified > 50 IgG4 plasma cells per high-power field (HPF) and an IgG4/IgG ratio of > 80% (Figs. 2 and 3).

According to these findings, the patient was diagnosed with IgG4-related sclerosing mesenteritis (as per the criteria established by Okazaki et al.) (6) as it was deemed to be the most likely diagnosis according to the radiographic and histological criteria. The symptoms relapsed following surgery (primarily abdominal pain) and corticosteroid treatment (deflazacort 45 mg) was initiated, following a descending schedule until an eventual discontinuation and symptom clearance over the subsequent weeks. Due to the good clinical response and asymptomatic status, no further therapy was given and the patient underwent a regular follow-up. A further corticosteroid therapy course followed by maintenance regimens was considered in the case of symptom recurrence.

DISCUSSION

Sclerosing mesenteritis is a rare condition characterized by inflammation (panniculitis), necrosis (lipodystrophy) and fibrosis (scarring-retraction) of the adipose component of the intestinal mesentery (7). The prevalence ranges from 0.16% to 7.8% and cases are usually male (3:1) and older than 50 years of age, although younger cases have been reported (8). The etiology is unknown but has been related to mechanisms such as abdominal trauma, surgery, autoimmunity, ischemia, infection and paraneoplastic syndrome (7).

It was recently suggested that most sclerosing “idiopathic” conditions might belong within the IgG4-related disease spectrum (2,3,9). This is an immune-mediated systemic disorder characterized by the presence of lymphoplasmacytic infiltration rich in IgG4 plasma cells, storiform fibrosis, obliterative phlebitis and tissue eosinophilia (1). The pathogenesis remains unknown but the presence of a type of trigger has been suggested, which stimulates B-cell infiltration. These cells then differentiate into IgG4 plasma cells in response to mediators (IL-4 and IL-13) secreted by Th2 lymphocytes. B-cells and plasmablasts act as antigen-presenting cells to CD4+T-cells, which in turn release the substances that cause fibrosis (3,5). The pancreas is the most commonly affected organ in 60% of systemic cases (type-1 AIP). However, other organs may be affected in an isolated, synchronous or metachronous fashion, including the biliary tree, kidney, retroperitoneum (Ormond’s disease),
mesentery, thyroid gland (Riedel’s thyroiditis), lacrimal and salivary glands (Mikulicz’s disease) and the gastrointestinal tract, among others (2,6).

The incidence of isolated IgG4-related sclerosing mesenteritis remains unknown, although it is uncommon. A search of PubMed using “IgG4” and “sclerosing mesenteritis” returned ten definite/probable cases. Avincsal et al. (9) reported three cases classified as idiopathic sclerosing mesenteritis when considering that IgG4 plasma cell infiltration is usually > 50/HPF and the IgG4/IgG ratio is usually > 40% in order to distinguish IgG4-related sclerosing mesenteritis from other conditions. All three cases had increased IgG4 plasma cell levels but the IgG4/IgG ratio was < 40%. Chen et al. (4) reported nine cases of sclerosing mesenteritis, six of which had lymphoplasmacytic infiltration of > 10 IgG4 plasma cells/HPF (> 100 in two). In 2011, Vlachou et al. (10) published a series of 57 patients with type-1 AIP, two with mesenteric involvement.

Clinical presentation varies according to disease extent, abdominal pain is the most common symptom (70%) followed by a palpable mass (20-50%), changes in bowel habit and hydropneumosis, among others. Up to 10% of cases are asymptomatic and incidental findings (8). Increased IgG4 serum levels (> 135 mg/dl) and an IgG4/IgG ratio of 40% (normal < 5%) are found in 60-85% of cases. However, this does not represent a specific finding as this is also found in other conditions such as sarcoidosis, systemic lupus erythematosus (SLE), Castelman’s disease, cholangiocarcinoma and granulomatous polyangiitis (1,6). In addition, levels below the cut-off do not exclude a diagnosis. Five of ten reported cases of IgG4-related sclerosing mesenteritis had levels > 135 mg/dl.

Imaging techniques are key for a diagnosis. Abdominal CT is the most sensitive method and may detect mesenteric fat hyperattenuation, calcification and retroperitoneal/mesenteric lymph-node involvement (4). Both the “fat ring” sign and tumoral pseudocapsule are highly specific (7). The differential diagnosis is complex and usually requires biopsy samples. The diagnosis includes mesenteric conditions such as neoplasms (lymphoma, carcinomatosis, mesothelioma), infiltrative disorders (amyloidosis, sarcoidosis), infection (mycobacteria) or vasculitis (granulomatous polyangiitis, SLE), among others (5,8,9).

There are no internationally accepted criteria for diagnosis. However, the Japanese Research Committee for IgG4-related Systemic Sclerosing Disease (6) proposed the following criteria in 2009:

1. Radiographic criteria: an increase in size or focal or diffuse lesions in one or more organs.
2. Serologic criteria: serum IgG4 > 135 mg/dl.
3. Histological criteria: a) lymphoplasmacytic infiltration with fibrosis and no neutrophils; b) > 10 IgG4 plasma cells/HPF and/or an IgG4/IgG ratio > 40%; c) storiform fibrosis; and d) obliterator phlebitis.

A diagnosis is made when any of the following combinations are found: 1 + 2, 1 + 3 (a + b), 2 + 3 (a + b) or 3 (a + b + c + d). The case reported here met criteria 1 + 3 (a + b + c + d). Other authors only consider a diagnosis as definite when all three criteria are met (radiographic, serological and histological), as probable when radiographic and histological criteria are met, and as possible when only radiographic and serological criteria are met (3). Response to corticosteroids supports a diagnosis for probable/possible cases.

Treatment is based on clinical experience as studies are limited. Asymptomatic forms may remain untreated and cases of spontaneous regression have been reported (9). Surgery is indicated for complications such as obstruction, suspicion of alternate diagnosis (mainly neoplasms) or predominant fibrosis (3,5). Glucocorticoids represent the primary means of medical therapy and are used when inflammation predominates and early use is associated with an improved response and prognosis (1). The recommended dose of AIP is 0.6 mg/kg/day or 40 mg/day of prednisone for four weeks, followed by dose reductions until discontinuation (Mayo Clinic scheme) or maintenance with 2.5-5 mg/day (Japanese scheme). Immunosuppressants are usually included for refractory cases and azathioprine is most commonly used. Other treatments include methotrexate, cyclophosphamide, tacrolimus and mycophenolate (1). Rituximab has proven useful for induction and/or maintenance against resistance/ intolerance to steroids or immunosuppressants in type-1 AIP (3).

REFERENCES