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Case Presentation

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Sclerosing Mesenteritis Associated with IgG4 Immunopathy - A Case Report

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Abstract

Sclerosing mesenteritis is a rare disease characterized by its fibrosis due to the presence of fatty tissue and chronic inflammation within it. Histologically and immunologically associated with IgG4 immunopathy. The clinical picture depends on the affected organ, and one of the most common locations is the abduction. In this article, we describe a patient with severe sclerosing mesenteritis.

Keywords: IgG4-related diseases; Sclerosing mesenteritis

Introduction

IgG4-Related Diseases (IgG4 - RD; IgG4 - related diseases) are a group of diseases characterized by a chronic, recurrent course with typical inflammatory and fibrosing infiltrates in various tissues and organs leading to their impaired function. For the diagnosis of IgG4-RD the result of histopathological examination of the involved organ or tissue should be interpreted in the clinical context. Neither the clinical picture nor the result of the microscopic examination alone can provide a reliable diagnosis of IgG4-RD **[1].** Most patients have elevated serum IgG4 concentration, which is now considered more as a disease marker than an aetiological factor. The clinical manifestation depends on the affected organ **[2].** One of the common locations involves the digestive tract **[3].** These diseases can also present as IgG4-Related Pseudotumors (IgG4-RPT; IgG4-related pseudotumors). Sclerosing mesenteritis was first described in the literature in 1924. It is a rare disease characterized by fibrosis with adipose tissue necrosis and chronic inflammation **[4].** Histological and immunological sclerosing inflammation is associated with IgG4 (IgG4-RD) immunopathy **[5-7].** On imaging, MS most often appears as a nodular mass in the mesentery, which may be misdiagnosed as malignant **[8].**

Case Presentation

A 38-year-old patient was admitted to the Department of Internal Medicine for diagnosis of systemic connective tissue disease. The first symptoms, the low-grade fever and joint pain appeared 4 years earlier, but despite being hospitalized in two departments of internal medicine, including a rheumatology department, no diagnosis was made, and carious changes in teeth were considered as the most probable cause of the ailments. Two years later, he was admitted to the Department of Internal Medicine due to high fevers (up to 40 Celsius degrees), headaches and abdominal pain. In laboratory tests, abnormalities revealed increased activity of transaminases, increased CRP concentration (19.27 mg/dl); D-dimer to 2819.29 ng/ml; total IgE (151.6 IU/ml), leukocytosis (WBC over 12.0x10^9/L) with a left shift, increased concentration of procalcitonin (0.72 ng/ml), increased activity of lactate dehydrogenase, amylase and lipase, decreased total calcium and iron, elevated creatinine, blood gas abnormalities (decreased pO2 to 43.60 mmHg, pCO2 to 32.5 mmHg, SaO2 to 80%, with normal pH of 7.42). Despite the applied treatment, including antibiotics, the patient's condition deteriorated and with symptoms of septic shock, the cardiorespiratory failure was transferred to the Intensive Care Units (ICUs) for further treatment. The patient required mechanical ventilation and infusion of catecholamines. There was an enlarged submandibular lymph node, hepatosplenomegaly, jaundice and positive meningeal signs. Due to the severe condition of the patient in the ICU's as well as in the department of internal medicine, a wide differential diagnosis was conducted by performing numerous additional laboratory tests, as well as imaging tests. A lumbar puncture was done and a cloudy fluid with high cytosis was revealed. The bronchial secretion, spinal fluid, blood and urine cultures were negative. Tests for Legionellosis, AH1N1 flu, HIV, Listeriosis and parasites were also negative. Diagnose for systemic connective tissue diseases was also performed, and despite positive anti-nuclear antibodies, the patient did not meet the criteria for any systemic connective tissue disease. The chest CT showed inflammatory changes in the apical segments of the lungs and ground glass opacity. There were no enlarged lymph nodes or pleural effusion. In the CT scan of the abdomen and pelvis, apart from uncharacteristic, borderline intra- and retroperitoneal lymph nodes, a small amount of fluid and increased adipose tissue density, no pathology was found. Groups of normotypic lymphocytes were found in the biopsy of the enlarged submandibular lymph node. The patient was also consulted haematologically, without finding the cause of severe clinical condition. On the 10th day of hospitalization, symptoms of critical state delirium occurred, which subsided on the 14th day of treatment. The most probable cause of septic shock was Yersinia (positive p/c IgA, IgG, negative IgM). The treatment included broad-spectrum antibiotic therapy and steroid therapy.

Due to non-specific changes in the lungs, a positive QuantiFERON test and the symptom of stiff neck and impaired consciousness, tuberculous meningitis was suspected and full anti-mycobacterial treatment was initiated. After multidirectional treatment, the patient's condition improved and he was transferred to outpatient treatment. In the course of the diagnostics, negative results of subsequent blood and urine cultures and cerebrospinal fluid tests for PCR for tuberculosis of the nervous system were obtained. The therapy continued with glucocorticoids treatment and several months of anti-tuberculosis treatment, and the patient was under the supervision of the Immune and Pulmonology Clinic. Due to persistent abdominal symptoms despite chronic steroid therapy and the patient's lack of full recovery, a control CT scan of the abdomen was performed one year after the onset of multiple organ failure and a spiky focal lesion approximate size 3.5 cm was revealed. Increased adipose tissue density was adhere to the superior mesenteric artery and vein. In the control MRI of the abdomen at the level of the L3-L4 bodies, within the mesenteric artery a focal lesion (3.5x2.5 cm) with low signals in the

T1 and T2 sequences was found. The lesion had a spiky outline and, in its vicinity, there was a significant increase in the signal of the mesenteric adipose tissue, as in the case of inflammatory lesions. The described abnormalities surrounded the branches of the superior mesenteric vein and artery. On the basis of the MR image, sclerosing mesenteritis was suspected and the patient was referred to the Department of Gastroenterology for further diagnosis. The colonoscopy showed no pathology, but an elevated concentration of IGG 4 (2.47 g/l N: 0.19-1.13) was found. The treatment was continued with prednisone at a dose of 10-15 mg/day.

The overall clinical history, non-specific course and good response to steroid therapy suggested IgG4-associated sclerosing mesenteritis. The infiltration of the mesenteric artery led to periodic flow disturbances and resulted in abdominal discomfort. Intestinal ischemic changes enabled systemic infection with Yersinia, which resulted in sepsis complicated by septic shock and its consequences in the form of multiple organ failure. After a two-year use of prednisone, complete remission of the disease was not achieved and the therapy with azathioprine and then mycophenolate mofetil was started, simultaneously reducing the dose of prednisone. The patient was also directed to collect a fragment of the tumor for histopathological examination, which revealed inflammatory infiltrates and IgG4(+) cells. Follow-up imaging studies showed no significant differences in the picture of sclerosing mesenteritis compared to previous studies. The lesion occupied a similar area, but was more consolidated with the duration of the disease. The patient was again referred for surgical treatment - fragments of the tumor were removed and the histopathological result of adipose tissue inflammation with fibrosis was obtained. Due to the incomplete response to the previous treatment, the patient was consulted at the Rheumatology Department and rituximab was added to the treatment in the immunological protocol (two infusions of 1000 mg, followed by repeated cycles every 6 months). In subsequent abdominal imaging studies, a gradual remission of the inflammatory changes and a reduction in the mass of the tumor within the mesentery were observed. Currently, the patient is after the third cycle of rituximab.

Discussion

Sclerosing Mesenteritis (MS) is a rare disease characterized by fibrosis, inflammation and necrosis of adipose tissue, occurring spontaneously in the mesentery of the small intestine. Clinically, MS patients mainly complain of chronic, severe pain and other non-specific symptoms such as nausea, vomiting, diarrhoea, weight loss and fever. Histologically there is fibrosis with adipose tissue necrosis, chronic inflammation, especially around the vessels and focal calcifications. Histological features of IgG4-RSM include lymphoplasmacytic infiltration, fulminant fibrosis and phlebitis obliterans. The immunological criterion is the presence of IgG4-positive cell infiltration (IgG4-positive/IgG-positive > 40%). However, this ratio is considered secondary to the histological picture. It is important to link the clinical history with the histopathological picture and to differentiate it from neoplastic disease **[9-11].**

Many patients go into spontaneous remission, but most require immunosuppressive therapy. Most patients with IgG4-mediated disease show a rapid clinical improvement after the use of glucocorticoids **[12].** The initial dose of prednisone of 30–40 mg/day should be maintained for 2–4 weeks and then gradually reduced. Many authors describe a poor response to treatment and even no remission, which prompts the prolongation of treatment or the addition of another immunosuppressive treatment **[13].** These include: azathioprine, mycophenolate mofetil, 6-Mercaptopurine (6-MP), methotrexate, tacrolimus and cyclophosphamide. In patients not responding to standard treatment, rituximab therapy has been shown to be effective, especially in the refractory and relapsed form **[14].**

Conclusion

We presented a case of a patient with IgG4 immunopathy-associated sclerosing mesenteritis. The patient's condition at the beginning of the diagnosis was severe, and tumor-like lesions in the abdominal cavity required differential diagnosis, including neoplastic diseases. The rarity of the disease, especially in Europe, limits its unambiguous characterization and more cases are needed to make recommendations for both diagnosis and treatment.

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