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Case study

Hypophysitis presented as inflammatory pseudotumor in immunoglobulin G4-related systemic disease

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Summary Immunoglobulin (Ig) G4–related systemic disease is a recently characterized entity. The best-known manifestation is pancreatitis. Other systemic involvements are also described. Three cases of this disease with hypophyseal involvement have been reported in the literature, all diagnosed clinically. We herein present the first case of IgG4-related hypophysitis diagnosed histopathologically. The patient is a 77-year-old Chinese man with a pituitary tumor. Histologic examination of the resected tumor showed hypophysitis with features of inflammatory pseudotumor. Clinical review showed history of pancreatitis and cholecystitis 4 years ago. The pancreatic biopsy and gall bladder specimens obtained previously had the same pathologic features of inflammatory pseudotumor. Immunohistochemistry highlighted abundant IgG4-positive plasma cells in all 3 specimens. Serum IgG4 level was also elevated. A diagnosis of IgG4-related systemic disease was confirmed. This is the first case of intracranial inflammatory pseudotumor shown to be associated with IgG4-related systemic disease.

1. Introduction

Hypophysitis is a rare inflammatory disorder, which can mimic pituitary tumor clinically and radiologically [1]. The causes are heterogeneous and can be idiopathic or secondary to other systemic diseases. Hypophysitis featuring inflammatory pseudotumor (IPT) has not been described pathologically. A subgroup of IPT is associated with immunoglobulin (Ig) G4–related systemic disease. This autoimmune disease has a variety of clinical manifestations depending on which organ systems are involved [2,3], but they all share the same histopathologic features of IPT, which consist of dense lymphoplasmacytic infiltration with sclerosis and phlebitis [4]. One specific feature is the presence of abundant IgG4-secreting plasma cells in the infiltrates. The serum IgG4 level during the active phase of the disease is also elevated. IgG4–related systemic disease with hypophysitis has been described, but the cases were all diagnosed clinically [5-7]. We describe here the first case of pathologically proven IgG4-related hypophysitis with features of IPT. This is also the first reported case of intracranial IPT associated with this systemic autoimmune disease.

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2. Case report

A 77-year-old Chinese man presented with blurred vision for several months. Physical examination showed a pale optic disc. Computer tomographic scan and magnetic resonance imaging showed a pituitary tumor (1 × 1 × 0.8 cm) with suprasellar extension and optic nerve compression. Laboratory tests revealed hypogonadism, with a low testosterone level (1.48 nmol/L; reference range, 12.00-34.00 nmol/L), but other pituitary hormones were within the normal range. Transphenoidal tumor resection was performed, and the visual symptoms subsided after surgery. The patient was then prescribed hydrocortisone and thyroxine replacement therapy. Pathologic examination showed hypophysitis with features of IPT. Clinical review showed a medical history of obstructive jaundice 4 years before this episode. Computer tomographic imaging showed a prominent pancreatic uncinate process with suspected distal common bile duct and ampulla of Vater tumor. The tumor was biopsied, and pancreatitis was diagnosed at that time. Choledochojejunostomy and cholecystectomy were performed. Retrospective examination of the pancreatic biopsy and cholecystectomy specimen showed the same pathologic features of IPT. The serum IgG and IgG4 level was measured using blood preserved before steroid replacement therapy. The IgG4 serum level was elevated (720 mg/dL; reference range, 0-291 mg/dL), and the IgG serum level was normal (13.3 g/L; reference range, 7.51-15.55 g/L), with a ratio of IgG4 to IgG of 0.54. The diagnosis of IgG4-related systemic disease was confirmed.

3. Pathologic findings

Two pieces of tan-colored tissue specimens, each measuring 4 to 5 mm, were received for pathologic examination. One was submitted for frozen section, and the other was submitted for permanent section. Microscopic examination showed prominent plasmacytic infiltration with a sprinkle of lymphocytes and an area of sclerosis (Fig. 1A and C). The plasma cells showed no atypia, and there was no granulomatous inflammation, significant histiocytic infiltration, or

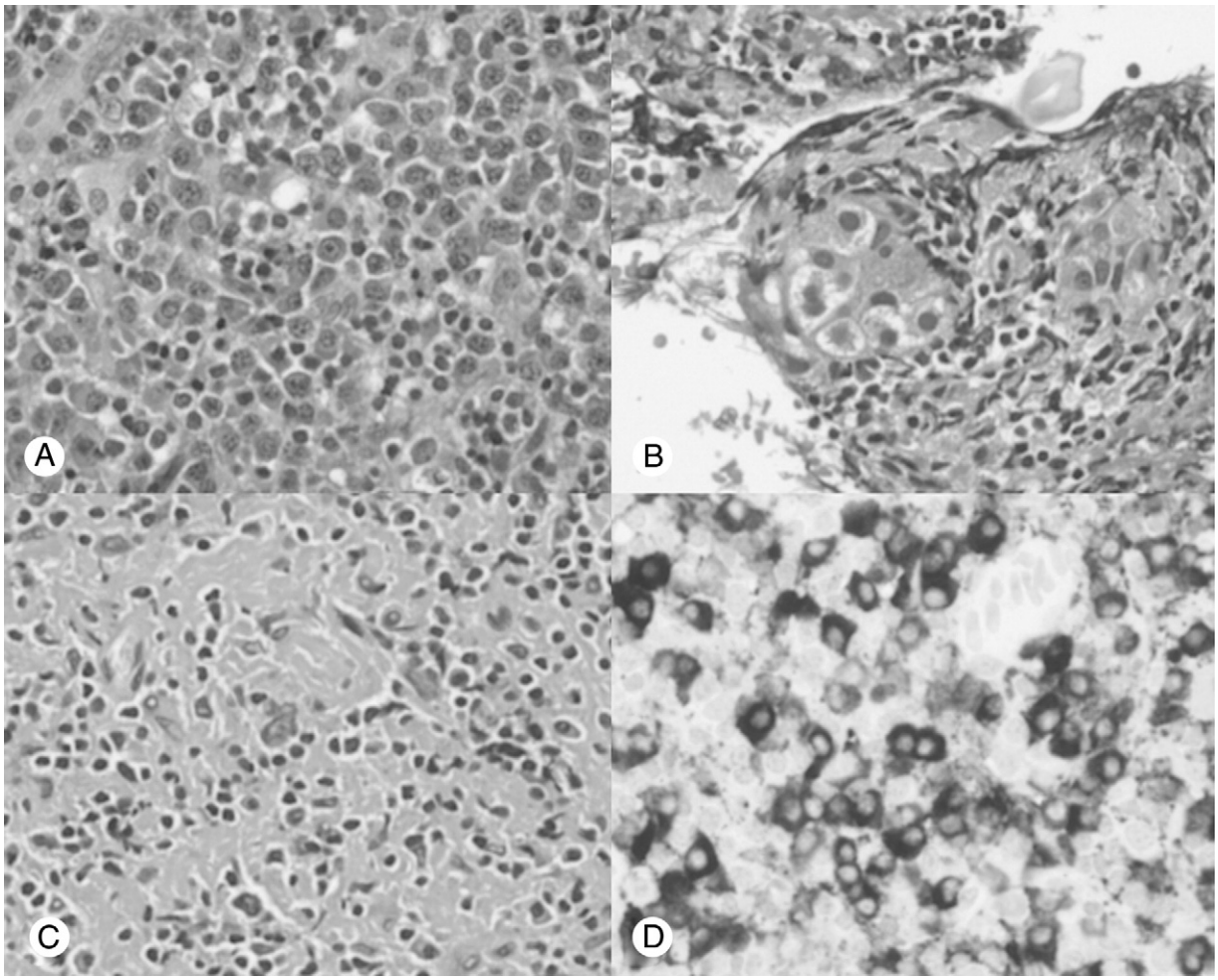

Fig. 1 Histopathology of the pituitary tumor showed dense plasmacytic infiltration (A), residual nests of adenohypophyseal cells (B), and area of sclerosis (C). Immunohistochemistry for IgG4 highlighted numerous positive plasma cells (D).