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**NOTE**

# A Case of Suspected Lymphocytic Hypophysitis and Organizing Pneumonia during Maintenance Therapy for Autoimmune Pancreatitis Associated with Autoimmune Thrombocytopenia

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**Abstract.** A 75-year-old man with a medical history of autoimmune pancreatitis associated with autoimmune thrombocytopenia was emergently admitted to our hospital because of anorexia, vomiting, and transient loss of consciousness. Serum sodium was 115 mEq/l and the endocrinologic data indicated impaired secretion of ACTH, TSH, and gonadotropin, a preserved GH response, and increased PRL. Dynamic magnetic resonance imaging revealed marked swelling of the pituitary gland and stalk, with enhancement on early phase. The findings were consistent with lymphocytic hypophysitis according to the diagnostic criteria. Chest computed tomography revealed consolidation adjacent to the pleura in the right upper lobe, lower lobe, and left lower lobe. Because lymphocytic hypophysitis and associated organizing pneumonia were suggested, 50 mg of prednisolone was started and the dose was tapered. Swelling of the pituitary gland, lung lesion, and the LH and FSH response on the stimulation test were all markedly improved. Autoimmune pancreatitis, pituitary lesion, and organizing pneumonia might all be components of a systemic autoimmune fibrosclerosing disease in our case, although further studies are required to confirm this hypothesis.

*Key words*: Lymphocytic hypophysitis, Organizing pneumonia, Autoimmune pancreatitis

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**AUTOIMMUNE** pancreatitis is a special form of chronic pancreatitis, characterized by extensive fibrosis and lymphocyte infiltration in the exocrine pancreas, together with responsiveness to corticosteroid therapy [1, 2]. This disease often involves extrapancreatic organs, including salivary glands, thyroid gland, bile duct, gallbladder, and retroperitoneal fibrosis concomitantly or metachronically [2–6]. Involvement of the pituitary gland, however, has not been reported. We report a case of suspected lymphocytic hypophysitis and organizing pneumonia during maintenance therapy for autoimmune pancreatitis.

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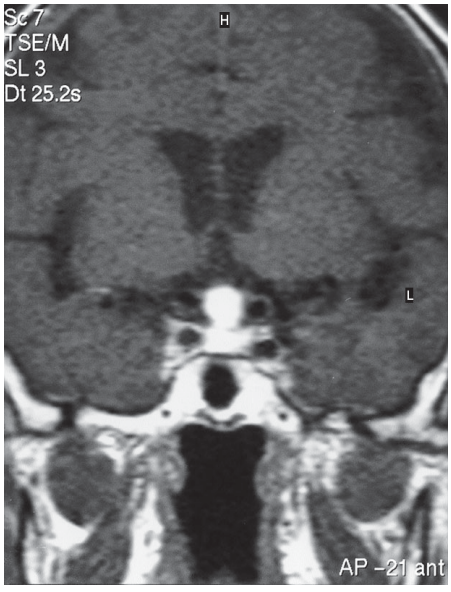
## Case Report

A 75 year-old man was emergently admitted to our hospital because of anorexia, vomiting, and transient loss of consciousness. He had a medical history of autoimmune pancreatitis associated with autoimmune thrombocytopenia, as we reported previously [7]. At the age of 66, he was admitted to our hospital because of a mass at the head of the pancreas with diffuse narrowing of the main pancreatic duct on endoscopic retrograde cholangiopancreatography. Anti-nuclear antibody and anti-SSA antibody were positive and the serum IgG level was elevated to 6040 mg/dl. On the 14th hospital day, petechiae developed and thrombocytopenia (1000/μl) with positive anti-platelet antibodies and component consumption were observed. Both autoimmune pancreatitis and thrombocytopenia were remedied by 60 mg/day prednisolone, which was tapered to 5 mg.

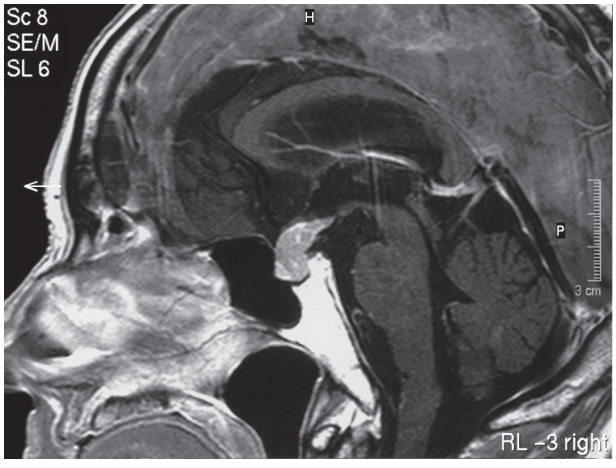
At the age of 69, he had uveitis, which was remedied by increasing the prednisolone to 30 mg, and then the dose was tapered. He was taking 2.5 mg/day prednisolone for the last 15 months. He had body weight loss from 2 months before.

On the present admission, body mass index was 19.2 kg/m$^2$ and blood pressure was 118/83 mmHg, serum sodium was 115 mEq/l, serum potassium was 3.7 mEq/l, plasma glucose was 125 mg/dl, white blood cell count was 3700/μl (neutrophils 65%, eosinophils 3%, monocytes 12%, lymphocytes 20%). Plasma ACTH was 5 pg/ml, serum cortisol was 0.6 μg/dl, GH was 0.27 ng/ml (normal range, <1.46), LH was less than 0.5 mIU/ml (normal range, 1.1–8.8), FSH was 0.6 mIU/ml (normal range, 1.8–13.6), PRL was 13.6 ng/ml (normal range, 1.5–9.7), TSH was 0.64 μIU/ml (normal range, 0.3–4.0), free T3 was 2.5 pg/ml (normal range, 2.5–4.3), free T4 was 0.7 ng/dl (normal range, 1.0–1.8), and anti-diuretic hormone was 1.4 pg/ml (normal range, 0.8–6.3), plasma osmolality was 253 mOsm, urinary osmolality was 501 mOsm. The serum cortisol level 30 min after administration of 0.25 mg synthetic ACTH was 4.2 μg/ml. These data indicated secondary adrenal insufficiency and subsequent SIADH. A stimulation test with combined thyrotropin releasing hormone, luteinizing hormone releasing hormone, and growth hormone releasing hormone indicated an impaired LH, FSH, and TSH response (peak value; 1.2 mIU/ml, 1.9 mIU/ml, and 5.16 μIU/ml, respectively), normal GH response (13.56 ng/ml) , and increased PRL response (33.8 ng/ml). Although we performed a TRH test to differentiate the type of thyroid dysfunction, which might be risky in a patient with angina, we opted not to perform a CRH test, which would further increase the risk to the patient.

Anti-nuclear antibody was positive (1 : 80). Dynamic magnetic resonance imaging revealed marked swelling of the pituitary gland and stalk, with enhancement on early phase (Fig. 1). There was no high intensity signal of the posterior lobe observed on T1 weighted image. The patient's findings corresponded to a suspected case of lymphocytic hypophysitis according to the diagnostic criteria (guidelines of diagnosis and treatment of anterior pituitary dysfunction by the research committee of the Ministry of Health, Labor, and Welfare of Japan). Biopsy of the pituitary gland was not performed because of the patient's advanced age.




A




B

**Fig. 1.** Dynamic magnetic resonance image of the pituitary gland on admission (A: coronal section, B: sagittal section). The pituitary gland and stalk are swollen and enhanced on the early phase.

Chest computed tomography revealed consolidation adjacent to the pleura in the right upper lobe, lower lobe, and left lower lobe (Fig. 2). Tuberculin skin test was negative, and serum angiotensin-converting enzyme was normal. Mycobacterium tuberculosis DNA was not detected by polymerase chain reaction using a bronchial alveolar lavage sample (BAL). Histology from segment 2b of the right lobe obtained by transbronchial lung biopsy showed marked thickening of the alveolar septum with marked infiltration of plasma cells and lymphocytes. There was no granuloma. The

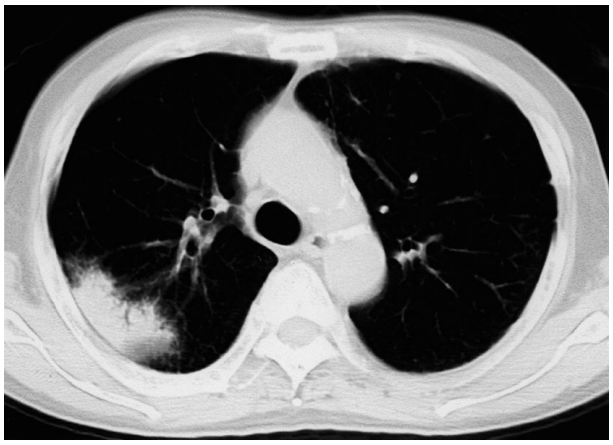


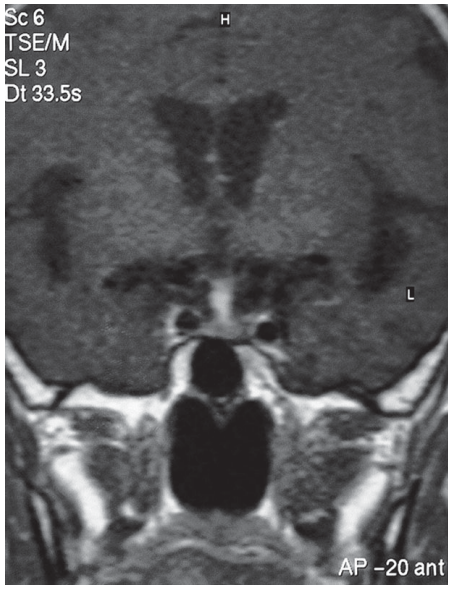
**Fig. 2.** Chest CT on admission. There is consolidation adjacent to the pleura in the right upper lobe.

CD4/CD8 ratio of the lymphocytes derived from BAL was 8.18.

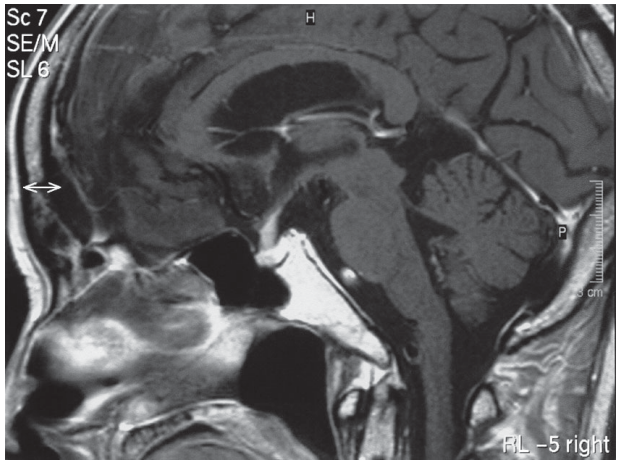
Because lymphocytic hypophysitis and associated organizing pneumonia were suggested, 50 mg of prednisolone was administered for 1 week and the dose was tapered.

There was marked improvement of the swelling of the pituitary gland (Fig. 3) and lung lesion (Fig. 4) after 2 weeks. On stimulation test, LH and FSH responses were also improved (peak value, 11.5 mIU/ml and 14.9 mIU/ml, respectively). Diabetes inspidus was not observed before or after steroid treatment.

Seven months later, when prednisolone was tapered to 10 mg/day, organizing pneumonia recurred in the left lower lobe and pituitary swelling recurred, both of which were improved by increasing the prednisolone to 50 mg/day. The patient is currently in remission on 20 mg/day prednisolone.




**A**




**B**

**Fig. 3.** Dynamic magnetic resonance image of the pituitary gland after steroid treatment (A: coronal section, B: sagittal section). Swelling of pituitary gland and stalk was improved.

## Discussion

Autoimmune pancreatitis is a recently described clinical entity, characterized by swelling of the pancreas, diffuse narrowing of the main pancreatic duct on endoscopic retrograde cholangiopancreatography, increased serum gammaglobulin or IgG, extensive fibrosis, and lymphocyte and plasma cell infiltration in the exocrine pancreas, together with responsiveness to corticosteroid therapy [1, 2]. Because autoimmune pancreatitis often involves extrapancreatic organs, including salivary glands, thyroid gland, bile duct, gallbladder, and retroperitoneal fibrosis, Kamisawa *et al.* postulated that this disease is a part of a systemic fibrosclerosing disease known as multifocal idiopathic fibrosclerosis [3].

Lymphocytic hypophysitis is a cause of hypopituitarism characterized by pituitary enlargement with infiltration of lymphocytes and occasional plasma cells. Its association with other autoimmune diseases suggests an autoimmune etiology [8]. Because this disease mainly presents in women during late pregnancy or during the postpartum period, the demographic data

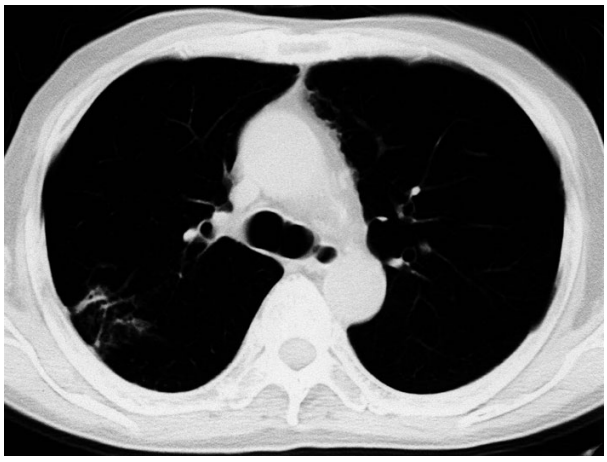


**Fig. 4.** Chest CT after steroid treatment. Consolidation in the right upper lobe improved.

of our present case are atypical. Rather, the demographic data are compatible with autoimmune pancreatitis. The endocrinologic data, however, such as impaired secretion of ACTH, TSH, and gonadotropin, preserved GH response, increased PRL, and magnetic resonance imaging findings and history of autoimmune disease, suggested lymphocytic hypophysitis. The dramatic response to corticosteroid therapy supports the diagnosis.

In the present case, the CD4/CD8 ratio of lymphocytes derived from BAL was high, atypical of idiopathic bronchiolitis obliterans organizing pneumonia. Rather, it suggests that the lung lesion was associated with autoimmune disease.

Autoimmune pancreatitis is associated with autoimmune diseases, including retroperitoneal fibrosis [4–6] and bronchiolitis obliterans organizing pneumonia [6], concomitantly or metachronically. There are reports of an association between lymphocytic hypophysitis and retroperitoneal fibrosis [9, 10]. Taken together, autoimmune pancreatitis, pituitary lesion, and organizing pneumonia might all be components of a systemic autoimmune fibrosclerosing disease in our case, although further studies are required to confirm this hypothesis.

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