Published in final edited form as:

Pancreas. 2013 January ; 42(1): 175–177. doi:10.1097/MPA.0b013e3182546e37.

Autoimmune Chronic Pancreatitis with IgG4-Related Pancreatic Pseudocyst in a Patient Undergoing Total Pancreatectomy Followed by Autologous Islet Transplantation:

A Case Report

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To the Editor

Autoimmune pancreatitis (AIP), a rare type of chronic pancreatitis, has been recognized as an IgG4-related pancreatic disease, and the International Association of Pancreatology presented a set of diagnostic criteria for AIP recently.^{1,2} Although patients with AIP have an excellent response to steroid therapy, a relapse rate of 92% within 3 years has been reported, suggesting the need for further treatment options.³

A total pancreatectomy with islet autotransplantation (TP-IAT) is a promising approach for refractory chronic pancreatitis to relieve severe abdominal pain and preserve endocrine function.⁴ Here, we present a patient who was clinically diagnosed with AIP, was resistant to steroid therapy, and underwent TP-IAT.

CASE REPORT

A 26-year-old woman was referred to our clinic for retractable abdominal pain. She had no history of smoking or drinking. Autoimmune pancreatitis was diagnosed based on her elevated serum IgG4 level (231 mg/dL) and image findings of endoscopic ultrasonography 4 years ago, although fine-needle aspiration did not provide a sufficient quality for evaluation. Steroid therapy with 30 mg/d of prednisone relieved her pain for only 2 months, and an adjustment to 40 mg/d of prednisone with the addition of 75 mg/d of 6-mercaptopurine resolved her pain for several years.

On hospital admission, she had a 120-mg morphine-equivalent dose per day for abdominal pain, even receiving prednisone and 6-mercaptopurine. Her endocrine test demonstrated a fasting serum C-peptide level of 3.9 ng/mL and Hb_{A1c} of 8.0% without any diabetic medication. Patent portal vein flow was confirmed with Doppler ultrasonography. Liver needle biopsy revealed no remarkable cholangitis.

The patient underwent TP-IAT in April 2011. The pancreas preservation and islet isolation were performed as previously reported.^{5,6} The islet isolation yielded 3459 islet equivalents

per kg of body weight, with 50% purity. The final tissue volume was 9.0 mL. The isolated islets were infused into the portal vein.

Her recent laboratory data on day 102 after TP-IAT have the following values: fasting C-peptide, 0.5 ng/mL; Hb_{A1c}, 6.8%; and serum IgG4, 208 mg/dL. No hypoglycemic unawareness has been reported. She has successfully reduced her narcotic medications with 4 mg/d of morphine-equivalent dose. Steroid administration was slowly tapered off.

Macrographically, the removed pancreas had a moderately fibrotic, fatty appearance. A cystic lesion was found in the pancreas body to the tail and an odorless, yellowish, pus-like fluid was evacuated from the cyst. No bacteria were detected from the fluid.

The cyst wall had severe fibrosis, with mild inflammation adjacent to the adipose tissue (Fig. 1A). Coexpression of CD138, which was used for the marker of plasma cells,⁷ and IgG4 was observed in the cyst wall (Fig. 1B–C). A dense lymphocyte infiltration was also seen in the wall (Fig. 1D), and several IgG4-positive plasma cells were present (Fig. 1E–F). The pancreas body showed moderate to severe fibrosis (Fig. 1G) and CD138 expression (Fig. 1I), but no IgG4 stain (Fig. 1H). Of note, CD138 is widely known as a plasma cell marker; however, pancreatic acinar cells in chronic pancreatitis also express CD138.⁸ Islet structures were observed in the pancreas body specimen (Fig. 1J), and no IgG4 or CD138 expression was seen in the islet area (Fig. 1K–L). CD138-positive plasma cells (Fig. 1M and O) were present in the pancreas parenchyma but were not stained by IgG4 immunostaining (Fig. 1N). The section from the pancreas head also showed severe fibrosis with mild inflammation (Fig. 1R).

DISCUSSION

In the case presented here, some distinctive findings were found; macrographical finding of pseudocyst is an irregular lesion of AIP,⁹ and the histologic finding was also atypical, as no IgG4 stains were seen in the pancreas body specimen, in contrast to the cyst wall. These findings suggest that the main lesion of autoimmune reaction was located in the pseudocyst, because an autoimmune mechanism could stimulate IgG4 secretion.² Ten cases with AIP plus pancreatic pseudocyst have been published, although no case with an IgG4-positive pseudocyst and IgG4-negative chronic pancreatitis were reported.⁹ Similar cases to this patient might be missed because steroids or other immunosuppressants are standard treatment of AIP, and opportunities to perform histological evaluation are limited.

Total pancreatectomy with islet autotransplantation was chosen for this patient because of her poor response to steroids and retained endocrine function before the operation. Further administration of immunosuppressants might be another treatment option, but long-term use of immunosuppressants would increase the risks of adverse events.

Even after TP-IAT and discontinuation of steroids, the patient's serum IgG4 levels have remained above the reference range. A possible reason for her high serum IgG4 might be autoimmune response in the portal vein caused by infused islets. It is unlikely that this patient had an autoimmune reaction in the portal vein because no liver symptoms and no

elevated liver enzymes have been observed after IAT. Long-term follow-up of serum IgG4 levels and liver investigation should be considered.

In summary, our patient had AIP clinically diagnosed, with an IgG4-positive pancreatic pseudocyst and underwent TP-IAT. An advanced surgical procedure of TP-IAT could be a treatment option for the refractory case.

Acknowledgments

The authors thank Dr Luis F. Lara and Ms Mary Beth Ryabik for patient care, Ms Cynthia Orticio for professional editing, and Ms Rahman M. Ana, Mr Kanak Mazhar, and Mr Abdul-Rehman Syed for technical support.

This study a grant from the National Institute of Diabetes and Digestive and Kidney Disease (1R21DK090513-01) (to MFL), Roche Diagnostic Corporation (to BN) and Baylor Health Care Foundation.

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FIGURE 1.

Histological sections from the pseudocyst (A–F), pancreas body (G–O), and pancreas head (R). Sections in A, D, G, J, M, and R were stained by hematoxylin and eosin; in B, E, H, K, and N, by IgG4 immunohistochemistry; and in C, F, I, L, and O, by CD138 immunohistochemistry. The top 5 rows (ie, A–C, D–F, G–I, J–L, and M–O) were from an individual tissue sample. Also shown are the positive controls of IgG4 staining on a human tonsil specimen (P) and the negative control of CD138 staining without the primary antibody

(Q). Scale bars indicate 100 μm in A–C, G–I, Q, and R; 50 μm in P; 20 μm in D–F and J–L; and 10 μm in M–O.