

Original article

The relationship between pancreatic atrophy after steroid therapy and diabetes mellitus in patients with autoimmune pancreatitis



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ABSTRACT

Background/objectives: Many patients with autoimmune pancreatitis (AIP) have an association with diabetes mellitus. It has not been clarified whether steroid therapy for AIP improves or worsens the condition of diabetes mellitus. The aim of this study was thus to investigate the relationship between pancreatic atrophy after steroid therapy and the clinical course of diabetes.

Methods: Thirty-one AIP patients, who were treated by steroid therapy, were included in this study during December 2005 to March 2013. Pancreatic atrophy 6 months after the beginning of steroid therapy was defined to be present when the width of the pancreatic body was less than 10 mm. The relationships between pancreatic atrophy and patient characteristics as well as the course of diabetes were examined.

Results: Steroid therapy was effective in all treated patients. Pancreatic atrophy was observed in 12 patients and not in 19 patients after the steroid therapy. AIP patients with pancreatic atrophy showed higher incidences of diabetes mellitus ($p = 0.001$, 9/12 vs. 2/19), diabetes control worsening ($p = 0.007$, 7/12 vs. 2/17), and new onset of diabetes ($p = 0.02$, 5/7 vs. 1/18) than those without atrophy. It was not associated with gender, other organ involvement, pattern of pancreas swelling (diffuse/focal), serum IgG4 level, alcohol intake, and pancreatic calcification on CT. Patients with new onset of diabetes needed insulin therapy, even in the maintenance therapy of AIP.

Conclusions: AIP patients with pancreatic atrophy after steroid therapy have a high incidence of diabetes mellitus. New onset of diabetes is closely associated with pancreatic atrophy after steroid therapy.

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Introduction

The pathogenesis of autoimmune pancreatitis (AIP) is suspected to involve autoimmune mechanisms. International Consensus Diagnostic Criteria for AIP and Japanese Clinical Guidelines for AIP recommend steroid therapy as a first-line therapy, to which most cases of AIP have an effective response [1,2]. It was reported that many AIP patients with type 2 diabetes mellitus before AIP onset showed worsening of diabetes mellitus control after steroid

therapy [2,3]. However, some reports showed that the improvement of diabetes mellitus control after steroid therapy was observed in 25%–45% of AIP patients [4,5]. It has thus been controversial whether steroid therapy for AIP can improve or worsen the condition of diabetes mellitus.

We have sometimes experienced that pancreatic atrophy suddenly progressed after steroid therapy in AIP patients, who did not have pancreatic atrophy beforehand. In several studies, pancreatic atrophy was observed in 17%–61% of AIP patients [5–8]. Pancreatic atrophy is usually considered as a marker of advanced disease associated with an increased incidence of diabetes mellitus [9,10]. Therefore, in this study, we hypothesized that pancreatic atrophy after steroid therapy might be associated with the clinical course of diabetes mellitus.

Abbreviations: AIP, autoimmune pancreatitis; CT, computed tomography; DM, diabetes mellitus.

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Methods

Patients

From December 2005 to March 2013, 43 consecutive patients were diagnosed with AIP in our hospital. The diagnosis of AIP was based on the Japanese Clinical Guidelines for AIP [2]. All patients were categorized with type 1 AIP. Among the 43 patients, 31 patients who were treated by steroid therapy were enrolled in this study. The median follow-up duration of this study is 50.4 months (range, 7–115). Prednisolone at an initial dosage of 30 mg/day was administered for 2–4 weeks. The dose was then tapered by 5 mg every 2–4 weeks until the dosage of maintenance therapy. Maintenance therapy at a dosage of 2.5–7.5 mg/d was continued thereafter.

In this study, pancreatic atrophy after steroid therapy was defined as being present when the width of the pancreatic body was less than 10 mm (Fig. 1), according to the previous report [8]. Pancreatic atrophy was evaluated by computed tomography (CT) before and after steroid therapy. Pattern of pancreas swelling (diffuse or focal) and pancreatic calcification were also examined by CT.

Medical records were examined and information was collected about the patients' demographics (age and gender), alcohol intake (>50 g/day), serum IgG4, and diabetes.

Evaluation of diabetic status

Diabetes mellitus was diagnosed according to the diagnostic criteria of the Japan Diabetes Society [11].

The values of HbA1c are expressed as NGSP values [12]. With a decrease of HbA1c by more than 0.5% in patients treated with diet therapy, with the same dose or a decreased dose of oral anti-diabetic agents, insulin therapy was judged to produce an improvement after steroid therapy. An increased dose or initial use

of insulin/anti-diabetic agents, an increase in the HbA1c level by more than 0.5%, or new onset of diabetes was considered as worsening. The other patterns were judged as no change.

Statistical analysis

Statistical analyses were conducted using Stata/SE 12.1 for Macintosh (StataCorp, College Station, TX, USA). The distribution of data was evaluated with χ^2 test or Fisher's exact test, when expected cells were found to number fewer than five. Normally distributed variables were compared by Student's *t* test and non-normally distributed variables were compared by the Wilcoxon rank sum test. Values of $p < 0.05$ were considered significant.

Ethical considerations

This study was conducted in accordance with the ethical guidelines of Kobe University Hospital.

Results

Relationship between pancreatic atrophy and patients' characteristics

Steroid therapy was effective in all treated patients ($n = 31$). Pancreatic atrophy was observed in 12 patients and not in 19 patients 6 months after the beginning of the steroid therapy. The mean width of the pancreas was 7.95 ± 1.17 mm in patients with pancreatic atrophy and 14.85 ± 2.85 mm in those without atrophy 6 months after the beginning of the steroid therapy (Fig. 2). And, that was 8.36 ± 0.90 mm in patients with atrophy and 14.44 ± 3.44 mm in those without atrophy 12 months after the steroid therapy. There were no patients in whom pancreatic atrophy was newly observed over 6 months. AIP patients with pancreatic atrophy showed higher incidences of diabetes mellitus ($p = 0.001$, 9/12 vs. 2/19), diabetes

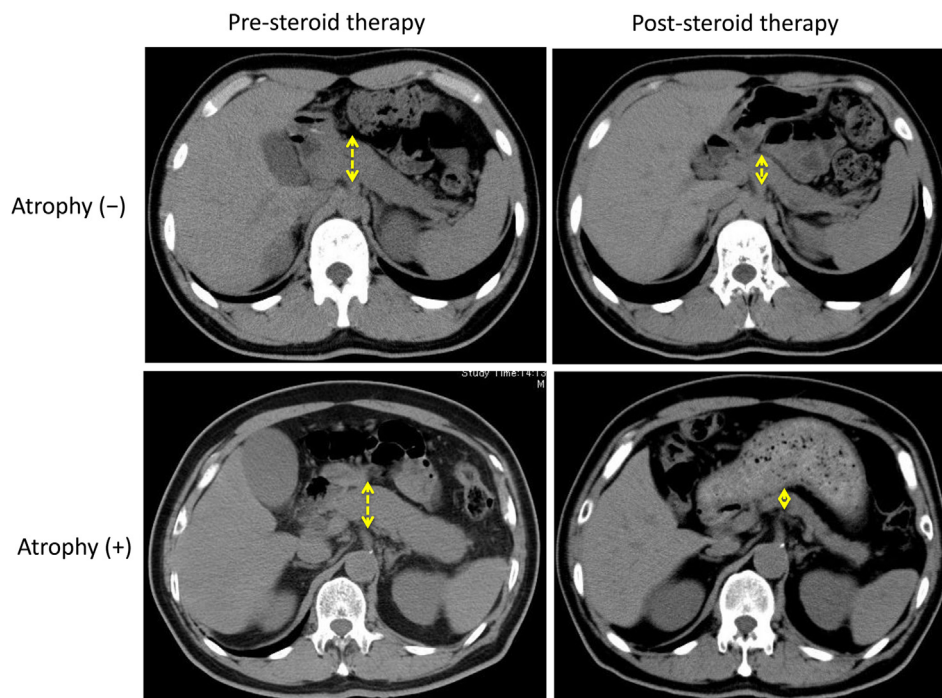


Fig. 1. Typical image of the pancreas on CT with or without pancreatic atrophy after steroid therapy. Pancreatic atrophy after steroid therapy was defined to be present when the width of the pancreatic body was less than 10 mm.

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