Clinical case

Type 1 diabetes and idiopathic retroperitoneal fibrosis: Case report

Diabète de type 1 associé à une fibrose rétropéritonéale idiopathique : à propos d’un cas

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Résumé

La fibrose rétropéritonéale est caractérisée par le développement d’une fibrose inflammatoire autour des structures rétropéritonéales. La fibrose rétropéritonéale est idiopathique dans deux tiers des cas. Nous rapportons une observation clinique d’association de fibrose péritéonéale idiopathique et de diabète de type 1. Il s’agit d’une patiente âgée de 61 ans présentant un diabète insulinoprive découvert sur un coma acidocétosique associé à une fibrose rétropéritonéale révélée par une hydronéphrose bilatérale. Le dosage des anticorps anti-GAD est positif alors que les anticorps anti-IA2 sont négatifs. Il n’y a pas d’arguments en faveur d’une pancréatite chronique auto-immune : pas de stéatorrhée, taux d’IgG4 normal, l’image scanographique du pancréas est sans particularité. L’association d’un diabète insulinoprive à une fibrose rétropéritonéale en l’absence de pancréatite chronique auto-immune suggère l’existence d’un diabète de type 1.
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Abstract

Retroperitoneal fibrosis is a rare disease characterized by the presence of a retroperitoneal tissue, consisting of chronic inflammation and marked fibrosis, which entraps the retroperitoneal organs. In two-thirds of cases, the retroperitoneal fibrosis is idiopathic. The pathogenic mechanism is not clearly identified. We report a case of idiopathic retroperitoneal fibrosis associated with type 1 diabetes mellitus. A 61-year-old woman with C peptide negative insulin-dependent diabetes developed retroperitoneal fibrosis revealed by bilateral hydronephrosis. Anti-GAD 65 antibodies were positive. There were no signs of autoimmune pancreatitis: no steatorrhea, normal IgG4 isotype levels, and absence of pancreas morphological abnormalities.
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Mots clés : Fibrose rétropéritonéale idiopathique ; Diabète de type 1

Keywords: Idiopathic retroperitoneal fibrosis; Type 1 diabetes

1. Introduction

Retroperitoneal fibrosis (RPF) is a rare disease characterized by the presence of fibro-inflammatory tissue, which entraps the vascular structures (abdominal aorta, common iliac arteries) and ureters. Common symptoms are diffuse abdominal pain, end-stage renal disease and anemia. Erythrocyte sedimentation is accelerated. RPF is considered a systemic inflammatory disease, which may present other symptoms including mediastinitis, chronic thyroiditis or slerosing cholangitis. Two-thirds of RPF cases are idiopathic [1]. Pathogenesis remains unclear. In the literature, this disorder has been reported as associated with different autoimmune diseases such as Hashimoto’s thyroiditis, systemic lupus erythematosus, ankylosing spondylitis, and pol-

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yarteritis nodosa [1–6]. We report here a case of idiopathic RPF associated with type 1 diabetes.

2. Case report

The patient was a 61-year-old non-smoking woman with type 1 diabetes known since the age of 43. Hyperglycemic coma had led to the diagnosis of diabetes. There is no family history of diabetes. The patient’s diabetes is very unstable in spite of intensive insulin therapy with multiple daily injections. Under insulin glargine 10 IU/day and insulin aspart 6 IU in the morning, 7 IU at lunch and 16 IU in the evening, the HbA1C level reached 8.5%. The patient experienced two to three minor hypoglycemic events per week. Plasma C peptide level was negative, anti-GAD antibodies positive at 6.6 kU/L (N < 1) and anti-IA2 antibodies negative.

The patient’s lipid profile showed 2.45 g/L cholesterol (<2 g/L), 1.34 g/L LDL-CT (<1.6 g/L), 0.9 HDL-CT (>0.4 g/L). Complications of diabetes were numerous:

- lower limb arteriopathy;
- stroke;
- stenosis of the right renal artery;
- peripheral polyneuropathy;
- nephropathy with macroproteinuria;
- proliferative retinopathy.

When questioned specifically, the patient confirmed that she had not taken any medication known to trigger RPF (methysergide, bromocriptine, ergotamine, methyldopa, analgesics...).

At the age of 56, the diagnosis of bilateral hydronephrosis caused by extrinsic compression of the ureter was established. The patient complained of abdominal pain and developed renal deficiency. Exploration with a double J probe ruled out hydronephrosis. At that time, the patient weighed 66 kg and measured 162 cm; the BMI was 25. Physical examination showed no particular anomaly except for a loss of reflex in the lower limb. Computed tomography of the abdomen showed no changes in the aspect of the pancreas: no enlargement, pancreatic ducts with regular walls and free of narrowing, no cyst formation. However, bilateral ureterohydronephrosis was noted (Fig. 1).

Histological examination of the paraureteral biopsies obtained during the laparotomy showed a vascular connective tissue modified by a dense fibrosis separated by a chronic moderately profuse inflammatory lymphocyte plasma cell infiltrate. No malign cells were detected and the histological examination suggested inflammatory fibrosis (Fig. 2). RPF was therefore retrained as the diagnosis.

The patient’s class II HLA antigens are not known to predispose to type 1 diabetes but are often found in patients presenting...
idiopathic RPF (allele DRB1*03). Serum protein electrophoresis and immunoglobulin gravimetry were not in favor of autoimmune pancreatitis: IgG4: 0.275 g/L (0.13–1.03 g/L) and IgG: 13.1 g/L (12.2–14.7 g/L). There was no steatorrhea. Thyroid function was normal when anti-TPO antibodies were absent. Anti-DNA and antinuclear antibodies were negative ruling out a lupus. Considering the absence of an identified cause, the diagnosis of idiopathic RPF was made. The patient was treated with steroids (1 mg/kg for one year then doses were gradually reduced the following year). The clinical course was marked by partial regression of infiltrate images observed in the various abdominal scans. This suggested a slight improvement of the RPF.

3. Discussion

Idiopathic RPF is a rare disease. It was first described by Albarran in 1905 then by Ormond in 1948 [1]. In a Finnish study, the annual incidence of idiopathic RPF was 0.1 cases per 100,000 persons and the prevalence 1.38 out of 100,000 people [1]. It mainly affects men in the fourth to sixth decade but in our case, it was observed in a female patient. Our patient exhibited clinical and histological signs strongly in favor of RPF. In addition, she had class II HLA antigens, which are often found in idiopathic RPF. Indeed, RPF is significantly associated with the HLA-DRB1*03 [7,8] allele, which was also found in our patient. The pathogenesis of RPF fibrosis is very hypothetical.

Atherosclerotic plaques might be involved in triggering the immunologic reaction [9]. Elements incriminated in this inflammatory process are ceroids (protein complex) and oxidized LDL, IgG and interleukins (IL1, IL2, IL4 . . .) found on the edges of the plaques [9,10].

The release of ceroids and oxidized LDL when atherosclerotic plaques break up and their migration into the adventitia tissue would trigger a strong inflammatory reaction due to the release of cytokines and profibrotic factors (TGF-β; transforming growth factor). This reaction would lead to an inflammation of the arterial walls, which would then lead to the RPF and its propagation to the ureters (Fig. 3). In our case, the patient showed marked atherosclerosis with macrovascular lesions and a history of stroke. However, the abdominal computed tomography shows a predominant fibrous reaction around the ureters and not around vessels. Atherosclerosis alone cannot account for all cases of RPF and its frequent association with autoimmune diseases suggests a different pathogenesis. Even though idiopathic RPF can be associated with various autoimmune diseases (Hashimoto’s thyroiditis, systemic lupus erythematosus, ankylosing spondylitis, polyarteritis nodosa), its association with an autoimmune type 1 diabetes has never been reported. Our patient did not present any clinical sign nor any immunological disorder in favor of the autoimmune diseases classically found in RPF patients. Different types of diabetes have been associated with RPF. Steroid-induced diabetes after starting treatment for RPF is the most common, resulting in this situation from insulin resistance. In 11% of patients, RPF is associated with chronic autoimmune pancreatitis. Clinical signs are steatorrhea with abdominal pain suggesting exocrine pancreatic failure associated with pancreas hypertrophy, an irregular narrowing of the pancreatic ducts with cysts and an increase in IgG4 [11–13]. In this latter case, the patients have no endogenous insulin production due to the autoimmune pancreatitis affecting both the exocrine and endocrine pancreas. Even though an increased IgG4 is essential for the diagnosis of autoimmune pancreatitis, it is nonetheless not specific since such an increase has also been reported in certain inflammatory articular and renal diseases as well as in hypophysitis [11,14]. However, our patient was free of pancreas exocrine deficiency and developed diabetes with no endogenous insulin secretion associated with increased anti-GAD 65 antibodies.

In our patient who did not present any biological elements or imaging evidence supporting the diagnosis of chronic autoimmune pancreatitis, the metabolic data favored an association of RPF with type 1 diabetes. It is very difficult to identify the pathological mechanisms linking the type 1 diabetes to RPF. However, given that the diabetes was immediately characterized by particularly wide glycemic variability and that the RPF was diagnosed 13 years after the diabetes, we can suggest that the glycemic instability caused proinflammatory and oxidative phenomena potentially favoring RPF.

4. Conclusion

The association of C peptide negative diabetes with RPF in absence of autoimmune pancreatitis is in favor of type 1 diabetes.

References


Fig. 3. Pathogenic hypothesis of the retroperitoneal fibrosis according to Meier et al. [10].

Hypothèse pathogénique de la fibrose rétropéritonéale selon Meier et al [10].