Case Report

Castleman’s disease with renal amyloidosis and nephrotic syndrome

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Introduction

Castleman’s disease (CD) is known as a giant lymph node hyperplasia which was first described in 1956 by Castleman. CD is a rare clinicopathologic entity classified among atypical lymphoproliferative disorders [1]. Asymptomatic mediastinal lymph node mass and variants are the main clinical feature of the localized form and generally has a good prognosis. On the other hand the systemic form of the disease has an aggressive clinical course and is frequently fatal [2]. The two histologic subtypes of the disease may overlap a hyaline vascular variant that accounts for 80–90% of cases and a plasma cell variant that constitutes the remaining 10–20% of cases. Also intermediate (mixed) histologic appearance was described. Systemic symptoms such as fever, weight loss and signs of inflammatory activity (increased C reactive protein, erythrocyte sedimentation rate, anaemia, polyclonal hypergammaglobulinaemia) occur in many patients with plasma cell variant [2]. These systemic symptoms usually disappeared after resection of the mass [3]. Renal alterations, such as proteinuria, mild haematuria, decreased GFR may be seen in CD; however a true nephrotic syndrome due to amyloidosis has rarely been reported [6]. In the present report we describe a patient with retroperitoneal CD and a nephrotic syndrome secondary to amyloidosis.

Case report

A 17-year-old woman was admitted to the nephrology unit with pretibial oedema. Apart from 4+ pretibial oedema, physical examination was normal. Laboratory findings were as follows: haemoglobin 11 g/dl, serum total protein 5 g/dl, albumin 2.9 g/dl, total cholesterol 257 mg/dl. Other biochemical findings were in the normal ranges. ESR 110 mm/h, CRP 12 mg/dl, daily urinary protein excretion 6 g/d, ANA(+), dsDNA antibody (−), creatinine clearance 94 ml/min. Peripheral blood smear showed hypochromia and microcytosis. Serum ferritin level was 29.94 ng/ml (normal 20–220 ng/ml), serum iron level was 50 mg/dl (70–140 mg/dl), serum iron binding capacity was 280 mmol/(200–400 mmol/l), serum immunoglobulin levels were normal except increased IgG; serum C3 and C4 levels were normal. Protein electrophoresis showed polyclonal gammopathy. Tests for hepatitis B surface (HBs) antigen, HBs antibody, HIV antibody, hepatitis C virus antibody were negative. EBV early antigen was positive but other antigens and antibodies were negative. She had no history of chronic inflammatory diseases, recurrent infections, neoplasms or hereditary amyloidosis. Abdominal ultrasonography showed 6×5 cm solid mass and abdominal CT demonstrated 6×6×5 cm retroperitoneal mass which compressed the vena cava inferior. Intravenous pyelography showed a 7.5×4.5 cm mass which was located in the right area of L4–5 vertebrae. Celiac, superior, inferior mesenteric and right renal artery angiography was normal. Thorax CT was normal. Renal biopsy showed extensive amyloid deposits. An ultrasonography-guided mass aspiration biopsy showed a soft tissue tumour characterized by borderline or malign behaviour. A laparatomy was performed and excision biopsy showed CD with mixed type (Figs 1 and 2). The gross view of the specimen was a lobulated white coloured 4×6 cm mass. The cross-section of the specimen was granular in appearance and there were also areas of haemorrhage. Multiple samples from the specimen were examined. The microscopic examination of the specimens revealed a lymph node structure with numerous lymphoid follicles. Some of these follicles showed vascular structures in their germinal centres and a hyaline-like change was prominent in these vascular structures. In the parafollicular areas, there were numerous plasma cells. The specimen also contained eosinophilic material which was proved to be amyloid with congo red stain. The final histological diagnosis was Castleman’s disease of transitional (mixed hyaline vascular and plasma cell) type. The histopathological examination of the renal biopsy revealed hyaline like material deposition in the
glomeruli which was proved to be amyloid with the congo red stain and it was concluded that the patient had also renal amyloidosis (Fig. 3).

One year after the mass was removed, the patient’s clinical and laboratory findings were as follows: daily urinary protein excretion 8.3 g/day, serum albumin 2.3 g/dl with pretibial and sacral 3+ oedema, serum BUN and creatinine levels were normal. ESR was 70 mm/h, ANA was still (+).

**Discussion**

Castleman’s disease is a rare clinicopathologic entity among atypical lymphoproliferative disorders. The
disease is mainly located in the mediastinum in 80% of cases, and the remaining 20% occur in superficial nodal groups (cervical, axillar, inguinal etc.). Occasionally CD is found in intraperitoneal or retroperitoneal locations. In a review of 315 cases of CD 21 (7%) retroperitoneal tumours were described, with six (2%) having a pararenal location [7]. CD with renal amyloidosis has been rarely described. In the literature, 12 cases of CD associated with amyloidosis, and only three with retroperitoneal mass were found. Most of the cases were located in mesenteric region. Histologically one patient had plasma cell type, two patients had hyaline vascular type and three patients had mixed type [7]. Our patient had a retroperitoneal mass which was of histologically mixed type. The most common form of CD is the hyalin vascular type, followed by plasma cell type. The transitional or mixed type of CD is rarely seen with areas of hyaline vascular structures in the follicles and focal plasmosytosis [8]. Though renal alterations are common in patients with CD, nephrotic syndrome with secondary renal amyloidosis has rarely been reported. Most authors showed that abdominal and especially mesenteric cases of CD are proven to be associated with systemic amyloidosis AA type [6]. An elevated plasma level of acute phase proteins are common laboratory findings in CD. This increase could be a reaction to the production of interleukin-6 in the germinal centres of the affected lymph nodes in CD. IL-6 is a cytokine which is a major regulator of the acute phase response in tumours [4,5]. C reactive protein and serum amyloid A protein (SAA) increase during acute phase response. Serum AA is the precursor of amyloid AA protein in the reactive inflammatory type of amyloid [6]. Increased immunoglobulin levels, immune complex and some autoantibodies (ANA, RF) have been reported in some patients with CD. In our patient ANA was positive and also she had increased levels of gammaglobulin, ESR and CRP. Most of the investigators have shown that the regression of systemic symptoms and nephrotic syndrome occurs after removal of the lymphoid mass [6]. The absence of progression of amyloid deposition after removal of the tumour, emphasizes the role of the lymphoid mass in the development of amyloidosis, but in the present study, after the tumour was removed, nephrotic syndrome did not regress [3]. This type of progression of the disease is unusual.

CD with renal amyloidosis has been reported rarely. Although the resection of lymphatic mass corrected most abnormalities, including the nephrotic syndrome, in some cases nephrotic syndrome and amyloidosis may be persistent. We consider that more advanced investigations must be performed concerning the pathogenesis of CD with amyloidosis.

References
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