Immunotactoid glomerulopathy associated with mycosis fungoides

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Summary: A patient with mycosis fungoides developed a nephrotic syndrome. Renal biopsy revealed deposits of a highly organized fibrillar material which did not stain with the typical amyloid stains; this picture was consistent with the diagnosis of non-amyloidotic fibrillary glomerulopathy or immunotactoid glomerulopathy. We believe this is the first case reported of immunotactoid glomerulopathy associated with mycosis fungoides. Possible pathogenetic implications are discussed with reference to previous publications.

Introduction

In 1977, Rosenmann and Eliakim¹ described a patient with a nephrotic syndrome associated with deposits of an amyloid-like material in the glomeruli, which consisted of highly organized fibrillar structures composed of immunoglobulins or immune complexes. This material did not stain with typical stains for amyloid (Congo red and thioflavin). The terms non-amyloidotic fibrillary glomerulopathy or immunotactoid glomerulopathy were later accepted in order to differentiate this entity from other lesions associated with glomerular fibrillar deposits such as amyloidosis, cryoglobulinaemia, monoclonal gammopathy, light chain glomerulopathy and systemic lupus erythematosus. This new clinico-pathological syndrome is characterized clinically by proteinuria (100%) sometimes in the nephrotic range (70%), microscopic haematuria (70%), chronic renal insufficiency (50%), and acute renal failure (20%).² Diagnosis is made by finding microtubules 10–20 nm in diameter located in mesangium and glomerular basement membrane, which do not stain with amyloid stains. High blood pressure, nephrotic syndrome, male sex, and extensive fibrillar deposits are associated with poor prognosis, with progressive deterioration in renal function, leading to end-stage renal failure.³

There is only one previous published case of immunotactoid glomerulopathy (IG) associated with a lymphoproliferative disease (chronic lymphocytic leukaemia),³ although similar microfibrils

have been described in a patient with membranous nephropathy and lymphoma.⁴ Thus, we believe this is the first case of immunotactoid glomerulopathy in a patient with mycosis fungoides (MF).

Case report

A 49 year old white female was admitted to our hospital for re-staging and treatment of MF stage IB (T2N0M0B0). Her initial lesions had first appeared 5 years earlier. She had a history of mild hypertension which was controlled by thiazides, and intermittent oedema in lower limbs. A non-quantified proteinuria was present at her last admission 5 months before. The patient had been treated with PUVA-therapy 4 months before admission. On clinical examination blood pressure was 160/100 mmHg. She had poikilodermatous lesions in her back and proximal limbs, and erythematous and brown, finely scaling, mildly infiltrated plaques which affected her trunk and limbs. Two lymph nodes were palpable in her right axilla and one in the left; no other enlarged lymph nodes were present. Clinical examination was otherwise unremarkable.

Investigations revealed serum creatinine 124 µmol/l (normal 26.5–106), urea 27.7 mmol/l (3.05–16.8), creatinine clearance 69.9 ml/min (82–142), triglycerides 4.19 mmol/l (0.33–1.70), cholesterol 8.34 mmol/l (3.62–6.72), and total serum proteins 53 g/l (60–80). Urinalysis showed proteinuria in a nephrotic range (80 mg/kg/day; weight 55 kg), 12–15 red blood cells per field (Addis 23750 erythrocytes per minute), and hyaline, granular and fatty casts. A serum electro-

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phoresis showed albumin 49.7% (53–62). IgG was 5.9 g/l (6.4–13.5). ANA were positive at low titre (1/20). Other studies were normal or negative: blood cell count, clotting, IgA and IgM levels, complement studies, cryoglobulins, intradermal tests with PPD and candidine, urine culture, urine electrophoresis, and serum and urine immunoelectrophoresis. Circulating Sézary cells were not present. Renal ultrasonography showed both kidneys of normal size and morphology. Chest and abdomen roentgenograms and abdominal tomographies were normal.

A skin biopsy specimen obtained from the trunk showed a diffuse lymphohistiocytic infiltrate, including atypical lymphocytes with hyperchromatic, irregularly-shaped nuclei which eventually invaded epidermis. Immunophenotype of the atypical cells was that of mature T helper cells. A lymph node biopsy from the right axilla showed dermatopathic changes; infiltration of atypical cells was not evident. A bone marrow biopsy revealed non-specific reactive changes. A renal biopsy specimen showed by light microscopy a variable increase in the mesangial matrix and the presence of a material deposited in the mesangial area showing a brown colour staining with silver methenamine stain and was negative after Congo red and T thioflavin staining. By direct immunofluorescence, peripheral capillary wall deposits of IgG and C3 were demonstrated. Ultrastructural studies revealed the presence of coarse fibrils with a diameter ranging from 10 to 20 nm, located in the mesangium and glomerular basement membranes (Figures 1 and 2).

Treatment with topical mechlorethamine (10 mg in 50 ml of water; corporal application once a day) and nifedipine 30 mg/day was started. Ten months after discharge, skin lesions are quiescent and renal function is stable.

Discussion

Mycosis fungoides is a malignancy of T lymphocytes which initially involves skin, with eventual dissemination to lymph nodes and internal organs. Our patient developed an immunotactoid glomerulopathy in the context of a MF stage IIA (T2N1M0) without haematic dissemination. Other causes of fibrillary glomerulopathy were excluded.

Invasion of the kidneys by atypical cells in MF is common,⁵ but primary glomerulonephritis in patients with MF has only been described in three cases with advanced disease.^{6,7} In one patient,⁷ renal invasion by atypical cells coexisted with glomerulopathy.

Very little is known about the pathogenesis of immunotactoid glomerulopathy.³ An abnormal production of monoclonal immunoglobulins, even

Figure 1 Microfibrillar mesangial deposits sized 10–20 nm ($\times 5586$).

Figure 2 A detail showing immunotactoid microtubules within electrondense deposits (arrows) ($\times 16758$).

in the absence of a clinical paraproteinaemia or plasmocytosis, or immune complexes of uniform structure could account for the deposits. It is not known why these deposits only appear in renal glomeruli.⁸

Atypical cells in MF usually show immunophenotype of mature helper/inducer T lymphocytes,⁹ capable of promoting B lymphocyte response, leading to formation of diverse types of autoantibodies and immunoglobulins (mono- or polyclonal). It is well known that MF can coexist with monoclonal gammopathy or multiple myeloma.¹⁰ In our patient there was no hypergammaglobulinaemia, but diminished IgG, as may be seen in nephrotic syndrome. Likewise, none of the cases of primary immunotactoid glomerulopathy previously described showed elevated levels of immunoglobulins.

A case of immunotactoid glomerulopathy in a patient with a chronic lymphatic leukaemia has

been reported,³ and it has also been reported in association with diseases of the immune system.^{2,8,11,12} In our patient, the appearance of immunotactoid glomerulopathy at an early stage of MF, when most of the atypical cells preserve a T

helper/inducer immunophenotype with possible functional expression supports the hypothesis that immunotactoid glomerulopathy could be a secondary feature of MF.

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