Case Report

Thrombotic microangiopathy in a patient with Sezary syndrome treated with interferon-α

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Introduction

Sezary syndrome is a cutaneous T-cell lymphoma (CTCL), characterized by erythroderma and infiltration of the epidermis, the dermis and the bone marrow by monoclonal CD4+ T lymphocytes [1]. Renal complications of patients with CTCLs have rarely been reported [2–4]. In patients with other haematological malignancies, treated with interferon-α, renal complications have already been described [5]. We report here a rare case of Sezary syndrome, treated with interferon-α, who developed renal thrombotic microangiopathy (TMA).

Case

A 63-year old male, who had been diagnosed with Sezary syndrome 4 years before, was admitted to our department because of persistent microscopic haematuria. The patient had been treated with UVA/UVB radiation after his diagnosis. Ever since, he had been taking interferon-α (5 × 106 IU s.c., three times a week) which maintained his disease under control. Physical examination was unremarkable, except for a mild hypertension (160/95 mmHg) and a mild diffuse erythroderma. The laboratory values were as follows: Ht 43%, Hb 12 g/dl, platelets 72 000/μl, WBC 3900/μl with a normal differential count (neutrophils 67%, lymphocytes 27%, monocytes 6%), BUN 9.4 mmol/l, serum creatinine 150 μmol/l and, by serum protein electrophoresis, albumin 3.4 g/dl and diffuse hypergammaglobulinaemia 2.1 g/dl. Urinalysis revealed SG 1020, pH 5.5, protein 1(+), blood 3(+) with 100 red blood cells/high-power field (HPF) and three polymorphonuclear cells/HPF. The 24 h proteinuria was 3.5 g. Urine culture was negative and ultrasound of the urinary tract, including the prostate, was normal. The erythrocyte sedimentation rate was 20 mm/h and C-reactive protein 17 mg/dl (normal values <5 mg/dl). HBsAg and antibodies against hepatitis C, human immunodeficiency virus (HIV), herpes simplex virus, varicella zoster virus toxoplasma and Ebstein–Barr virus were negative. Autoimmune serology disclosed rheumatoid factor (RF) > 270 IU (normal values < 20) and IgG antiphospholipid antibodies 40 GPLU/ml (normal values IgG: <15 GPLU/ml). The relative sensitivity and relative specificity of the method used were 86.6 and 99%, respectively). ANA, ANCA and anti-Sl70 were not detected. All other laboratory tests were within normal limits. The light microscopic findings of a percutaneous renal biopsy disclosed changes of thrombotic microangiopathy, with glomeruli showing an increase in the number of endothelial and mononuclear cells, rare thrombi, reduplication of capillary basement membranes or aneurysms in rare glomeruli (Figure 1). Only one out of 24 glomeruli was sclerotic. The interstitium contained a moderate degree of fibrosis with atrophy of several tubules. Rare thrombi were found in the lumen of arterioles (Figure 2). Some arterioles demonstrated mucoid intimal hyperplasia. Immunofluorescence in all the three observed glomeruli demonstrated moderate positivity for IgM (++) and C3 (++) in a granular pattern along the glomerular capillary walls. This was interpreted as non-specific staining. Fibrin was detected in rare intracapillary thrombi. Electron microscopy was not performed. Skin biopsy did not reveal either infiltration by Sezary cells or immunoglobulin deposition.

Interferon-α was suspected to be the cause of renal TMA and was discontinued accordingly. The patient was lost to follow-up and he reportedly died in another hospital due to sepsicaemia.
Discussion

Our patient is the first case of Sezary syndrome on interferon-α complicated with renal TMA. TMA is a pathological process that may occur in several disorders, including thrombotic thrombocytopenic purpura, uraemic–haemolytic syndrome, scleroderma, antiphospholipid syndrome, diffuse malignancy, HIV infection and hypertension [6]. The above causes were excluded in our patient. There was no significant thrombocytopenia, no microangiopathic changes in the peripheral blood smear and no evidence of retinopathy in fundoscopy.

So far, eight cases of glomerular disease in patients with CTCL have been reported: four cases with IgA nephropathy (with circulating Sezary cells in urine), one with membranous nephropathy, one with minimal change nephropathy and another with immunonatoctoid nephropathy [2–4]. In the literature, there is only one case of mycosis fungoides with renal injury related to interferon-α therapy, but the renal biopsy revealed acute interstitial nephritis and minimal change glomerulonephritis [7].

In our case, we could not document a correlation of the glomerular disease with Sezary syndrome since neither bone marrow immunophenotype nor skin biopsy disclosed infiltration by Sezary cells at the time of glomerular disease.

It is known that the most common side effects of interferon-α include flu-like symptoms, leukopenia, anaemia, thrombocytopenia and elevation of serum transaminases [8]. Renal complications of interferon-α are rare and are present in patients with haematological and other malignancies [9]. Interferon-α-induced TMA has already been reported in 19 patients with chronic myelogenous leukaemia (CML), one patient with hairy cell leukaemia and two with hepatitis C [5,10–12]. It is not certain whether this reflects a predisposition of haematological malignancies to cause TMA or is related to duration and dose of interferon therapy. All the patients were receiving high doses of interferon-α (mean 4.6 MU/week) for a prolonged period of time (mean 34 months). In our case, renal TMA appeared after 46 months of treatment with interferon-α.

Although different mechanisms have been proposed, the causative mechanism of interferon-induced renal injury remains elusive [5]. It has been suggested that interferon-α could damage renal endothelial cells by interferon-α-induced antiphospholipid antibodies, but antiphospholipid antibodies were not present in all cases of interferon-α-induced TMA.

In conclusion, our case of Sezary syndrome shows that renal TMA can be a complication of interferon-α treatment in haematological malignancies, other than CML. Further studies are needed to clarify the mechanism of renal injury.

Conflict of interest statement. None declared.

References


Fig. 1. Glomerulus showing reduplication of the basement membrane (arrowhead) and a thrombus into a capillary lumen (arrow) (methenamine silver ×300).

Fig. 2. Arteriole occluded by fibrin-like material (PAS ×300).

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