

Case Report

Fibrillary glomerulonephritis with prevalent IgA deposition associated with undifferentiated connective tissue disease: A case report

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Abstract

We described a 41-year-old female patient, who presented with proteinuria occurring 5 years after the onset of an undifferentiated connective tissue disease (UCTD). At renal biopsy, a pattern of focal necrotizing glomerulonephritis with mesangial and parietal deposition of the IgA, C3 and K chains was observed. Electron microscopy showed organized fibrillary deposits in mesangial, subendothelial, intramembranous and subepithelial sites. Fibrils were randomly arranged, had no hollow core and had a diameter ranging between 10 and 23 nm. This case showed a rare combination of fibrillary glomerulonephritis and prevalent IgA deposition, in the clinical context of UCTD.

Keywords: electron microscopy; fibrillary glomerulonephritis; IgA nephropathy; undifferentiated connective tissue disease

Background

Fibrillary and immunotactoid glomerulonephritis (GN) represent pathological entities, characterized by structured fibrillary/microtubular deposits, whose identification is possible only by electron microscopy. The fibrillary GN variant (FGN) exhibits morphological aspects of organized deposits, such as size, arrangement, eventual hollow core and location, which differentiates it from the immunotactoid GN (ITGN) [1]. FGN, unlike ITGN, is rarely associated with systemic disorders. The clinical difference is in favour of considering the two conditions as separate entities, although some authors disagree about this [2].

In this controversy, we introduce a stimulating contribution to this discussion in a case report where FGN was found to be associated with a peculiar deposition of IgAk, without paraproteinaemia but in the interesting context of an undifferentiated connective tissue disease (UCTD). UCTD is described as a systemic autoimmune disease not completely fulfilling the classificative criteria for a defined CTD [3]. To our knowledge, renal involvement and, in par-

ticular, IgA nephropathy (IgAN) have never been described in the course of UCTD, in spite of the well-known IgAN secondary to rheumatologic or gastroenteric autoimmune diseases. Rare cases of IgAN associated with Congo-red negative F/ITGN have been reported [4–6]. Some of these cases are suggestive of underlying paraproteinaemia and/or lymphoproliferative diseases [1].

In the current paper, we describe a case of UCTD with proteinuria and microscopic haematuria occurring 5 years after the apparent onset of the disease. Renal involvement was *'per se'* peculiar and worth being described, because of the pattern of focal necrotizing GN with IgA deposits connected with fibrillary glomerular deposition.

Case report

A 41-year-old white woman was referred to our unit in February 2008 with proteinuria and microscopic haematuria, which were found in 2006. In 2001, she started with swelling and stiffness at hand joints and bilateral conjunctival hyperaemia. In 2003, she complained of arthralgias that involved upper and lower extremities and left elbow. Ocular sicca syndrome was confirmed by the Schirmer test; antinuclear antibodies (ANA) with a speckled pattern, 1/320 titre, were detected. On the basis of persistent arthralgias, ocular syndrome and ANA positivity, a diagnosis of UCTD was made. The patient refused a salivary gland biopsy.

In February 2008, because of persistent proteinuria, the patient was hospitalized. On examination, she had right eye sicca syndrome, diffuse arthralgias, no hypertension. The prominent laboratory data were ANA 1/320 titre with speckled pattern positivity, proteinuria (280–300 mg/dl), slight microscopic haematuria, moderate anaemia and creatinine clearance 108 ml/min. Proteinuria was glomerular, non-selective, with 50% albumin. Of note, ANCA, ENA, anti-DNA antibodies and cryoglobulins were negative. Serum and urinary immunoelectrophoresis showed no monoclonal proteins. Serology for HCV Ab and HBsAg was negative. A bone marrow biopsy revealed no plasmocytosis

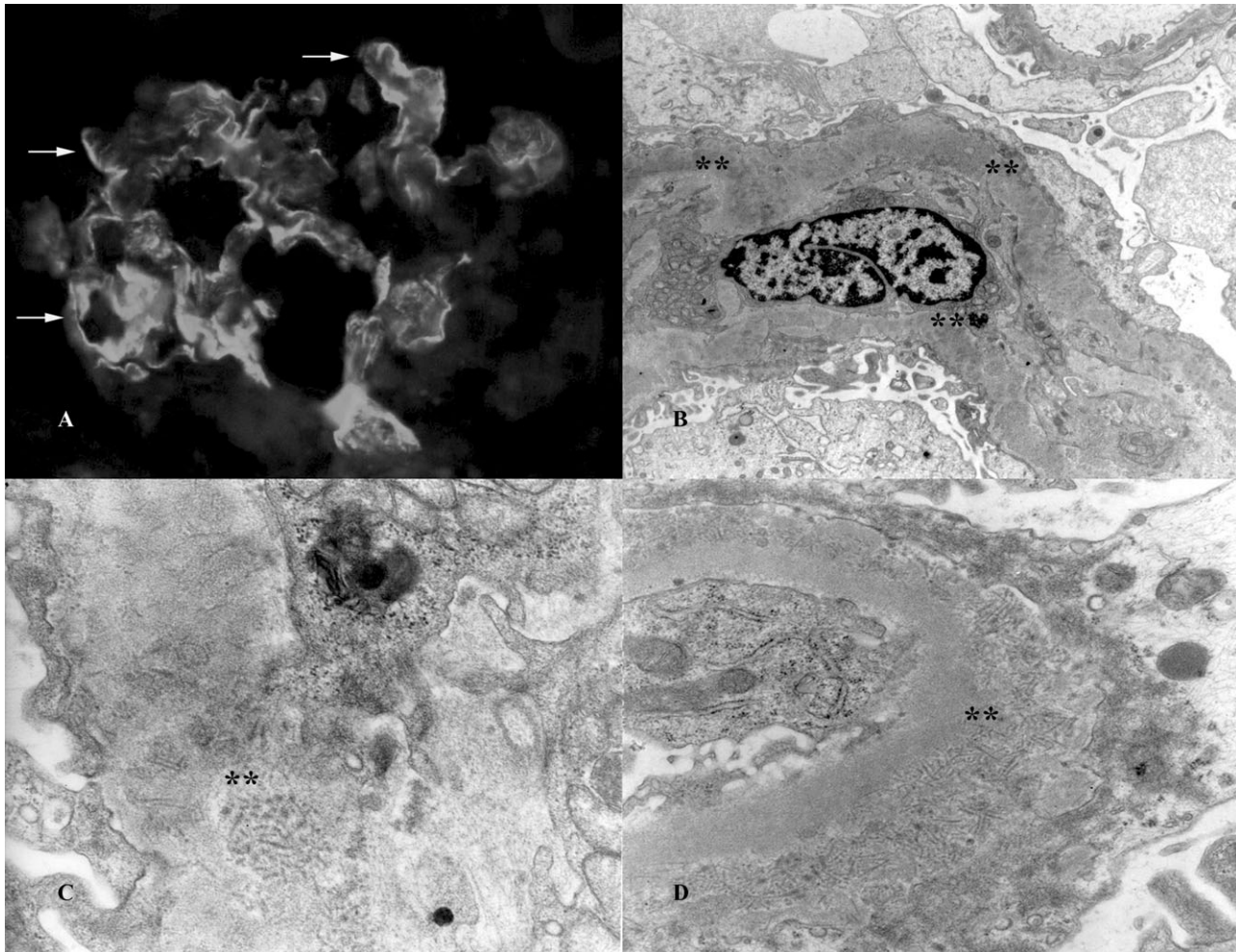


Fig. 1. Panel A: intense IgA deposition in the mesangium and in most of the capillary walls (white arrows). (Immunofluorescence, IgA antiserum FITC, OM 40 \times .) Panel B: electron-dense deposits located in the mesangium (**). (Electron microscopy, uranyl acetate lead citrate; OM 3000.) Panels C and D: mesangial (panel C) and subepithelial (panel D) deposits composed primarily of short and rigid fibrils without a hollow core, with a diameter ranging between 10 and 23 nm (**), contained in dense fine granular material. (Electron microscopy, uranyl acetate lead citrate; OM 20000 panel C and 12000 panel D.)

and, by immunophenotyping, no evidence of abnormal B cell clones was seen.

A renal biopsy obtained cortical tissue containing around 20 glomeruli, among which 3 were scarred. Nine glomeruli showed segmental sclerotic lesions with flocculo-capsular adhesions and fibrous or fibroepithelial crescents; three glomeruli had segmental necrosis with small epithelial crescents. Tubuli, interstitium, and vessels were normal.

At immunofluorescence, all glomeruli showed an intense deposition of IgA (Figure 1-A), C3 and kappa chain localized in mesangium as well as along most of the capillary walls. The aspect of parietal deposits was coarse granular and focally pseudolinear. Fibrinogen had a focal and segmental parietal positivity, whereas IgG, IgM, lambda chains and C1q were negative.

Ultrastructural examination of four glomeruli disclosed a large amount of electron-dense deposits located in mesangial, subepithelial, intramembranous and subendothelial sites, containing numerous short and rigid fibrils without a hollow core. The maximum length of the fibrils was about

200 nm and their diameter ranged between 10 and 23 nm; they were unbranched, randomly arranged and, occasionally, coupled in parallel arrays (Figure 1-B-D).

After diagnosis, she was treated with high-dose steroids and cyclophosphamide (quarterly 500 mg i.v. pulses) for 6 months; then, steroids were tapered. At 1-year of follow-up, proteinuria decreased to 0.5 g/day. ANA 1/160 titre and scleritis persisted. Renal function remained normal.

Discussion

This case report describes a very rare association between UCTD and renal involvement. This event is defined by some authors as virtually absent [3]. The patient's signs and symptoms were classified as UCTD. Most of the patients with UCTD exhibit a stable undifferentiated clinical course for years. In our patient, arthritis and arthralgias, ocular sicca syndrome, ANA antibodies and proteinuria were the only clinical manifestations. The association between

FGN and rheumatologic disease, in particular SLE, has been published, both in anecdotal reports [7] and within large series [1]. Rosenstock *et al.* [1] referred, out of 61 FGNs, 1 patient with SLE and 4 other cases with underlying rheumatological disorders. Therefore, unlike the above-mentioned associations, FGN and underlying UCTD represent a novel event. Moreover, one-third of the patients affected by UCTD evolve towards a definitive CTD, mainly in SLE [3], within 5 years of follow-up. Nevertheless, in our patient clinical data at biopsy, immunofluorescence pattern and follow-up excluded such evolution. The association of FGN/ITGN with IgA deposition, as observed in our case, has been previously published, but it is a rare event [4–6,8]. They were all single case reports, where no associated plasma cell dyscrasia was seen.

FGN is reported to contain predominantly IgG, K chain and C3 deposits [9]. Some of these cases are associated with an underlying lymphoproliferative disease. In our patient, an MIDD was excluded for no evidence of plasma cell dyscrasia at serum/urine and bone marrow examination.

In our patient, the size of fibrils, their random organization and the absence of a hollow core clearly allow a morphological classification as an FGN. Occasionally, fibrils were coupled in parallel arrays; this pattern is more suggestive of intraglomerular cryoglobulins; nevertheless, the morphology of fibrils and the clinical features, including the repeatedly negative serum cryoglobulins, excluded this hypothesis.

As already mentioned, FGN, unlike ITGN, is an entity in which most patients have no underlying systemic disorders, in particular, haematopoietic diseases, dysproteinaemia or viral infections [1,10].

In conclusion, the reported case confirms the possible spectrum of clinical syndromes where prevalent IgA deposition can be observed. Moreover, new information is given

on clinicopathological conditions that can favour the development of FGN, whose precise pathogenetic mechanisms are still obscure.

Conflict of interest statement. None declared.

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