Case Report

Minimal change nephrotic syndrome in a 74-year-old patient following parenteral administration of sheep cells

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Key words: corticosteroids; immunization; minimal change disease; nephrotic syndrome

Introduction

Minimal change nephrotic syndrome (MCNS) is the most common cause of idiopathic nephrotic syndrome in children and young adults, but is relatively uncommon in elderly patients. The disease has been associated with a variety of conditions, including malignancies, in particular Hodgkin's disease, viral infections, allergies, various drugs, and immunizations [1–5]. Given the evidence that MCNS is a disorder mediated by T-lymphocytes and/or their secretory products [reviewed in 6], such associations may help to better understand the pathogenesis of the disease.

We report a case of MCNS following the intramuscular injection of so-called 'fresh cells'. In 'fresh cell' therapy, cells isolated from a variety of organs of unborn or newborn animals, usually sheep, are injected into patients. Depending on the mixture of organs from which the cells have been derived, they are postulated to harbour at certain sites in the human body and to thereby 're-vitalize' the target organs. Despite the lack of controlled trials showing that 'fresh cell' therapy exerts more than placebo effects, and despite reports of adverse reactions such as anaphylaxis, infections, and various neurologic complications [7], this type of therapy is still legal in Germany.

Case report

The 74-year-old woman had a relatively unremarkable medical history until 1993. No history of allergic diseases or malignoma was present. From 1979 to May of 1993 the patient had received intramuscular injections of 6.3 mg ribonucleic acid sodium (isolated from bovine intervertebral discs, synovia and placenta as well as from yeast) every 3 months for low back pain. This is another 'paramedical' yet still legal therapy in Germany. Since March 1993 increased blood pressure values were recorded and treated with lisinopril and hydrochlorothiazide. No other regular medication was taken. Renal function had been documented to be normal in March and November 1993, and no proteinuria had been noted upon dipstick examination.

In 1981 and again in late November 1993 the patient had entered a private clinic and received an intramuscular injection of freshly isolated sheep cells (derived from various organs, including brain, kidney, heart, spleen, thymus, lymph nodes, and bone marrow of foetal or young sheep) for lower back pain. During February of 1994 the patient noted an 11 kg weight gain and increasing oedema of the lower extremities as well as anasarca. No preceding viral infection had been noted. In late February 1994 she was admitted to our hospital.

Upon admission, nephrotic range proteinuria (8.9 g/day), hypoproteinaemia (48 g/l) and hypercholesterolaemia (12.5 mmol/l) were present. Microhaematuria (48 x 10^6 erythrocytes/day), as well as few hyaline and granulated cylinders were noted in the urinary sediment. Serum creatinine was 200 µmol/l. Immunological findings showed low serum IgG (4.1 g/l) and low titre antinuclear antibodies (titre 1:40, speckled staining pattern; no anti-DNA antibodies; absent antinuclear antibodies upon re-determination in May 1994). Normal or negative values were obtained for IgA, IgM, CH50, C3, C4, rheumatoid factors, extractable antinuclear antibodies, anti-streptolysin titre, cryoglobulins, p- and c-ANCAs, and anti-GBM antibodies. An indirect Coombs test revealed the presence of anti-sheep erythrocyte antibodies in the patient's serum (titre 1:40, speckled staining pattern; no anti-DNA antibodies; absent antinuclear antibodies upon re-determination in May 1994). Normal or negative values were obtained for IgA, IgM, CH50, C3, C4, rheumatoid factors, extractable antinuclear antibodies, anti-streptolysin titre, cryoglobulins, p- and c-ANCAs, and anti-GBM antibodies. An indirect Coombs test revealed the presence of anti-sheep erythrocyte antibodies in the patient's serum (titre 1:128) and an Ouchterlony test showed circulating antibodies against sheep serum (titre 1:64). Renal size determined by ultrasound was normal. Work up showed no evidence of a malignoma.

Renal biopsy (performed by U. Helmchen, University of Hamburg, Germany) revealed a typical minimal change lesion without evidence of focal and segmental glomerulosclerosis upon examination of
serial sections of the whole biopsy cylinder. Immunohistology showed sparse mesangial IgM and C1q deposits but no glomerular IgG, IgA, C3, or fibrin/fibrinogen deposition.

Therapy with prednisolone (1 mg/kg body weight/day) was instituted and followed by complete remission of the nephrotic syndrome and normalization of serum creatinine concentrations (Figure 1). Steroids were tapered and finally stopped in April 1995. Complete remission of the nephrotic syndrome has been maintained until August 1997 (Figure 1). However, arterial hypertension has persisted and is currently treated with captopril and hydrochlorothiazide.

Discussion

The case described exhibits all features of a typical case of MCNS as far as clinical presentation, histological findings, and the response to corticosteroids are concerned. In support of our observation, several studies on MCNS in the elderly have demonstrated that the clinical findings in this group of patients did not differ from those in younger adults [8,9]. Microhaematuria and acute renal failure are also a well recognized potential feature of MCNS in adults [8].

Was the MCNS in our patient causally related to the preceding 'fresh cell' therapy? Three points merit consideration in this respect:

(i) MCNS is a very rare disease in the elderly: In British persons aged 14 years and older, the incidence of MCNS has been estimated ~3 cases per million population per year [10]. In one of the largest series published, Cameron et al. [11] observed that only 2.8% of 212 patients with MCNS were older than 70 years. In another series, 5.9% out of 334 patients aged >65 years who underwent renal biopsy for various reasons showed MCNS [12]. In unselected patients undergoing renal biopsy, the combination of MCNS and age >60 years was also rare: 0.8% of 1100 biopsies in the series of Moorthy and Zimmerman [9] and 0.2% of 1136 biopsies in the series of Kingswood et al. [13].

(ii) A strong immunologic response to the injected sheep cells could be demonstrated in the patient. This may relate to the previous administration of sheep cells in 1981, i.e. the second administration of sheep cells may have boosted a pre-existing immune response. An association of MCNS with immunizations has repeatedly been proposed [6,14]. The role of the repeated injections of bovine and yeast RNA in the immune response remains unknown.

(iii) The patient did not exhibit any other condition known to be associated with minimal change nephrotic syndrome at the time of presentation nor has she manifested any such condition during follow-up.

Although circumstantial, the above points suggest that a causal relationship between the ‘fresh cell’ therapy and the subsequent MCNS may have existed. Our case therefore illustrates another potential way in which stimulation of the immune system may relate to the manifestation of MCNS. Another interesting feature of the present case is that despite high titre anti-sheep antibodies no immunohistochemical evidence of an immune complex mediated nephritis was present.

References


Received for publication: 22.8.97
Accepted: 3.9.97