Phenytoin-Induced Nephrotic Syndrome

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Dear Sir,

An 83-year-old woman was admitted to our ward with nephrotic syndrome. Five years before, the patient had undergone surgery for a colonic adenocarcinoma (Duke classification stage B). 40 days before admission, therapy with phenytoin (100 mg u.i.d.) was started to control seizures (grand mal), occurring with increasing frequency, which were supposed to be caused by cerebrovascular disease. The patient appeared anasarctous. Massive proteinuria was present (about 10 g/day). Serum electrophoresis showed a polyclonal γ -peak (40.4%). Complement fractions (C3 and C4) and the total hemo-lytic complement were within the normal range. All the possible causes of nephrotic syndrome were excluded step by step, although we did not perform a renal biopsy on account of the patient's age and clinical condition. However, the presence of some hyaline and granular casts without hematuria suggested minimal-change disease or membranous glomerulonephritis. 15 days after admission, we decided to withdraw phenytoin in relation to a single case report [1] of low-dosage phenytoin-in-duced nephrotic syndrome.

The clinical picture improved dramatically in a few days, and the serum electrophoretic pattern returned to normal. Proteinuria was still absent after 15, 30 and 60 days. The chronic circulation of an antigen in low dosages (as in this case at a subtherapeutic concentration of $< 10 \mu\text{mol/l}$) could have induced the formation of immune complexes [2] or allowed their local formation in the subepithelial space [3]. Interactions of phenytoin with the immune response are also suggested by the evidence that the drug can modify the immunological alterations (although not the clinical course) occurring in IgA nephropathy [4].

We believe that the risk of developing nephrotic syndrome should be clearly indicated in the product information sheet in consideration of the therapeutic importance and widespread use of this drug.

References

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