Characterization of Inflammatory Cells in Drug-Induced Tubulointerstitial Nephritis

A.		Giménez
F.		Mampaso

Immunopathology Section, Department of Pathology, Centro Especial Ramón y Cajal, Madrid, Spain

Dr. Antonio Giménez, Departamento de Anatomía Patológica, Centro Especial Ramón y Cajal, Carretera de Colmenar Km 9.100, E-28035 Madrid (Spain)

Dear Sir,

Tubulointerstitial nephritis comprises a heterogeneous group of diseases with a characteristic set of clinical symptoms, producing occasionally acute or chronic renal failure [1]. Besides infection, the most important type of acute tubulointerstitial nephropathy is that induced by drugs [2, 3]. We have had the opportunity of studying a group of 8 patients with a recent history of drug exposure and acute renal failure; 6 were male and 2 female, with ages ranging from 8 to 75 years. Percutaneous renal biopsy specimens were obtained from all patients and tubulointerstitial damage confirmed on routine light microscopy examination. Interstitial cell infiltrates were further characterized in frozen tissue sections by the avidin-biotin-peroxidase complex (ABC) technique, using monoclonal antibodies to recognize T cells (leu-1, Becton-Dickinson, Monoclonal Center Inc., Mtn. View, Calif, USA), helper T cells (Leu-3a, Becton-Dickinson Monoclonal Center, Inc., Mtn. View), cytotoxic suppressor T cells (OKT8, Ortho Diagnostic Systems Inc., Raritan, N.J., USA), B cells (Dako-Pan-B, Dakopatts a/s, Denmark), monocytes and null cells (OK-Ia, Ortho Diagnostic Systems Inc., Raritan) and dendritic reticular cells (Dako-Drc-1, Dakopatts a/s, Denmark). The specificity of these monoclonal reagents was assessed using normal mouse serum, normal mouse IgG and hybridoma-induced ascitic fluids containing unrelated antibodies as described previously [4]. Evaluation of the inflammatory interstitial cell infiltrates was done by determining the percentage of positive labeled cells in 15 randomly chosen areas of interstitial infiltration. The ratio of per-oxidase-positive cells to the total number of infiltrating cells was obtained using a conventional light microscopy objective ($\times 60$). We observed that Leu-1 + cells (total T cells) were, in all cases, the most numerous interstitial cell population (table I). Analysis of T cell subsets showed, in 50% of the

Table I. Characterization of interstitial cell infiltrates

77

M

Streptomycin

49.0 ± 4

25.5 ± 2

74.5 ± 8

12.0 ± 2
 3.0 ± 3.0 9.0 ±
 240
 Giménez/Mampaso

f_{1/8}Δ^{5/8}
 i'mi > ilKB < 1/8 1 # * ä_{1/8}» i

Fig. 1. Immunoperoxidase stain showing OMT+ interstitial cells infiltrate. × 600.

cases, a OMT8 + cell predominance, indicating a prevalence of the suppressor cytotoxic T cell population over that of helper T cells. This predominant phenotypic OMT8 + cell subset was found in those patients with a history of antibiotic ingestion (fig. 1). Similar results have been previously observed by Bender et al. [5] in a group of 9 patients with tubulointerstitial nephritis and exposure to nonsteroidal anti-inflammatory agents. In the remaining 50% of our cases receiving a heterogeneous treatment (diuretics, anticholinergics, antipyretics, etc.), the predominant T cell subset consisted preferentially of Leu-3a + cells.

In summary, the results we present here support the idea that cell-mediated immunity may be implicated in

drug-induced tubulointerstitial inflammatory reaction. Additionally, a prevalence of OMT8 + cells in those cases with tubulointerstitial nephritis induced by antibiotics and nonsteroidal anti-inflammatory agents [5] also indicates that cytotoxic T cells may play an important role in this renal kind of tissue damage.

References

- Laberke, H.G.; Bohle, A.: Acute interstitial nephritis: correlations between clinical and morphological findings. Clin. Nephrol. 74:263–273(1980).
- Bennett, W.M.; Plamp, C; Porter, G.A.: Drug-related syndromes in clinical nephrology. Am. intern. Med. 87: 582–590 (1977).
- Symposium on drug effects on the kidney. Kidney int. 18: 539–711 (1980).
- Mampaso, F.; Wilson, C.B.: Characterization of inflammatory cells in autoimmune tubulointerstitial nephritis in rats. Kidney int. 25:448–457(1983).
- Bender, W.L.; Whelton, A.; Beschoner, W.E.; Darwish, M.O.; Hall-Craggs, M.; Solez, K: Interstitial nephritis, proteinuria and renal failure caused by nonsteroidal anti-inflammatory drugs. Immunologic characterization of the inflammatory infiltrate. Am. J. Med. 76:1006–1012 (1984).