Liver Cell Adenoma Associated with Membranous Nephropathy

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Dear Sir,

Membranous glomerulonephritis is a renal injury caused by immune complexes, among which different antigens associated with tumors have been implicated; most of them are carcinomas. Another, less numerous group corresponds to malignant hematologic diseases [1–3]. Very rarely, benign neoplasms have been reported to be associated with this condition. There are also cases of liver carcinoma with or without HBsAg [4, 5], but up to now, we have not found associations between liver cell adenoma and nephropathy.

The membranous nephropathy is characterized by discontinuous deposits of immunoglobulins and complement exclusively in subepithelial distribution along the outer surface of the glomerular capillary wall.

A 62-year-old man who was admitted to hospital with dyspneic cough, blood-stained sputum and pain in the right hemithorax. He had malaise, anorexia and weight loss for 1 month. On examination, there were diminished breath sounds in the lower and posterior right thorax; the liver edge was palpable 4 cm below the costal margin; the patient also had malleolar swelling. X-ray of the chest showed right pleural effusion. The laboratory findings were as follows: serum protein 5.6 g/dl, albumin 1.69 g/dl and α_2 globulin 1.145 g/dl (20.44%). Immunoglobulins: IgG 1,250 mg/dl, IgA 419 mg/dl and IgM 145 mg/dl. CEA, α -fetoprotein, HBsAg and HBsAc were all negative. The results of the urine test were: proteins 12.4 g/24 h. No other abnormal substance was found. Urinary sediment was normal. As a secondary nephropathy was suspected, an echography was carried out; which revealed a solid growth in the right hepatic lobe; the tumor was hyperechogenic, irregular in shape with hypodense areas inside and arterial supply coming from the hepatic artery. These findings were confirmed by laparoscopy. In view of the relatively good general condition of the patient, the precise diagnosis made, the antecedents of pulmonary embolism and the possibility to resect the mass, a laparotomy was indicated. A few hours before surgery was due to take place, the patient began to suffer from another dyspneic crisis and hypertension, followed by loss of consciousness, cyanosis and cardiorespiratory arrest, which could not be overcome. At autopsy, a massive pulmonary embolism and renal vein thrombosis

contiguous to the vena cava inferior was found. Apart from the massive embolism, which was the cause of death, there were peripheral infarctions of long standing in the lungs.

Fig. 1. Liver cell tumor: there is a resemblance to normal liver tissue, except for the absence of portal tracts. Some cells contain fat vacuoles. HE. $\times 80$.

The hepatic neoplasm, situated below the right hepatic lobe, measured $10 \times 10 \times 8$ cm, and could easily be distinguished from the rest of the normal liver tissue. Microscopically (fig. 1) it was a neoplasm formed by well-differentiated hepatocytes, without nuclear pleomorphism and mitosis. There were neither biliary ducts nor portal spaces, but some areas of ischemic necrosis and fibrosis were apparent. Therefore, the tumour was an adenoma.

The kidneys showed diffuse glomerulonephritis with uniform and homogeneous thickening of the glomerular capillary walls and minimal cellular proliferation. By immunofluorescence, granular deposits of IgG and complement were seen in the basal capillary membranes.

Ultrastructurally (fig. 2), moderate electron-dense deposits were seen on the subepithelial side of the basal capillary membrane. There was also extensive pedicelular fusion and hyperplasia of the foot processes of the podocytes.

No other tumor, amyloid deposits or other alteration was found.

The incidence of nephrotic syndrome associated with neoplasm varies depending on the author:

Papper [2] considers that an average of 10% of the adults with the

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Fig. 2. Electron micrograph of a glomerulus showing obliteration of epithelial foot processes and epimembranous deposits. $\times 3,450$. The inset shows a detail of deposits. $\times 9,100$.

nephrotic syndrome have a concomitant neoplasm and that this percentage is even higher, if one considers only the cases of membranous nephropathy. Membranous glomerulonephritis is the most common glomerular lesion seen in association with carcinomas [7]. Circulating immune complexes in the serum of patients with different neoplasms have been demonstrated [8] in up to 82% of the cases [9]. Among the rare studies reporting the association of nephropathy and benign tumors are: basal cell carcinoma [3], dermoid cyst, uterine leiomyoma [10], neurofibroma and hemangioma [11]. There are also a variety of entities, not yet well defined, such as Kimura's disease [12] and systemic mastocytosis [13].

With reference to the liver, Pascal et al. [4] reported a case of a patient with liver cell carcinoma and glomerular deposits of IgG, IgM, B-I-C, and ultrastructurally confirmed the mesangial and subendothelial immune complexes. Zolinger and Mihatsch [5] report of two further cases of nephropathy associated to liver cell carcinoma, one of them corresponding to mesangiocapillary glomerulonephritis and the other with a positive HBAg corresponding to membranous glomerulonephritis. A primary sclerosing cholangitis has also been described [14]. But we have not found any case of nephropathy associated with liver cell adenoma in our survey of the literature. In different studies about coagulation in patients with nephropathy, it is said that renal vein thrombosis, the ultimate cause of death of our patient, is an alteration caused by the nephrotic syndrome [15]. Because of the patient's quick death, it was not possible to evaluate the evolution of the nephrotic syndrome after the extirpation of the benign tumor.

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