Correlation of Chemotherapy-Induced Kidney Disorder and Antimyosin Antibody Uptake in Kidneys

TO THE EDITOR: Indium-111-labeled antimyosin antibodies have been introduced for the detection of myocardial necrosis (1-10). Myocardial enhancement also has been found to occur in cases of myocarditis, cardiomyopathy, and rejection of heart transplants (11-15). Since 1987, we have used a commercially available kit, Myoscin® (Centocor, Leiden, The Netherlands) for diagnosing embryonal tumors (16,17). Intravenous injection was performed after labeling of 0.2-0.5 mg Fab-DTPA with 40-80 MBq 111InCl (age-dependent). We found, like Estorch et al. (18), that myocardial damage by chemotherapy results in increased myocardial enhancement (2/35 children). However, because of other chemotherapeutic regimes, we found the kidneys to be more frequently affected than the myocardium.

Scans were performed 1 wk up to 1 yr after chemotherapy (VAJA regime, consisting of adriamycin, vincristin, and isophosphamide). While we found high antimyosin uptake in normal kidneys (Fig. 1), enhancement was decreased in the kidneys of 5/35 children, in accordance to raised creatinine blood levels. In order to find the reason for the strong enhancement of the kidneys on immunoscan, we performed immunohistochemical staining in acetone-fixed freezecut sections of human kidneys. After 1:400 dilution of the primary antibody solution immunostaining was performed according to the avidin-biotin complex technique (19). Incubation times were 20 hr for the primary antibody (at 4°C) and 30 min (at room temperature) for the secondary antibody (DAKO, Glostrup, Denmark). 3,3'-diaminobenzidine (Sigma München, FRG) was used as the chromogen. The result is shown in Figure 2. The tubular cells are homogenously demarcated; no other cell structures are stained. For negative controls, the primary antibody was replaced by normal mouse serum at the appropriate dilution. Control stains were performed with the mouse Mab BW250/183 (Behringwerke/Hoechst, Frankfurt, FRG), which is directed against epitopes (CEA, NCA-95) in granulocytes. No staining of the tubular cells is visualized in Figure 3, but several granulocytes dispersed in kidney tissue are demarcated.

In order to quantitate antimyosin uptake in the kidneys, we determined the antibody deposition per pixel in the left kidney and the liver (without the right kidney) with an ROI technique and calculated the ratio of kidney/liver uptake. The greatest difference between normal kidneys and kidneys with tubulopathy was found at 24 hr postinjection (Fig. 4). For this reason, we used the liver/kidney ratios at 24 hr postinjection for comparison with creatininé blood levels. The uptake ratio discriminates well between creatininé levels in normal and pathological ranges (Fig. 5). No correlation was calculated, as the normal range of creatinine varies with the children’s age. On the other hand, creatininé is known to depend on metabolism, so that creatininé values as a single prognostic parameter for induced renal failure is problematic, especially in patients undergoing chemotherapy. The results support our findings on scintigrams in that kidneys with tubulopathy show diminished antimyosin uptake with a relative stronger uptake in the liver (Figs. 6 and 7).

We conclude that the application of a radiolabeled antimyosin antibody offers the possibility to simultaneously control patients undergoing chemotherapy for both heart and kidney disorders. We propose further investigation of cardiac and renal deposition of antimyosin in well-designed prospecitive studies, which take into consideration the type of chemotherapy applied and the time after chemotherapy as proposed by Jain and Zaret (20).

REFERENCES


FIGURE 1. Immunoscintigraphy with an antimyosin Mab labeled with 111In on a child 2 yr after operation and irradiation of a rhabdomyosarcoma. Normal antibody distribution 24 hr postinjection with strong uptake in the kidneys, and lesser in the liver.

FIGURE 2. Tissue section of a human kidney after immunostaining with an antimyosin Mab. Tubulus cells are shown to present the site of antibody enrichment.

FIGURE 3. Tissue section of a human kidney after immunostaining with a Mab directed against granulocytes. Renal tubular epithelial cells remain unstained, while granulocytes in the renal interstitium are stained (arrow).
FIGURE 4. Ratio of tracer uptake in the left kidney and the liver after intravenous injection of an antimyosin Mab labeled with $^{111}$In. Calculations at 3, 24, and 48 hr postinjection show best discrimination between normal renal function and renal failure after 24 hr. (For clarity only seven patients with normal creatinine levels and representative uptake ratios are included beside five patients with creatinine levels in the pathological range).

FIGURE 5. Distribution of uptake ratios of left kidney/liver in dependence of serum creatinine levels. Uptake ratios were calculated for the deposition of the antimyosin Mab 24 hr postinjection. No correlation was calculated because of age-variant normal ranges of creatinine.

FIGURE 6. Immunoscans with antimyosin Mab on a child with a moderately raised creatinine blood level. Comparable enhancement of the kidneys and the liver is demonstrated 24 hr postinjection.

FIGURE 7. Reversed kidney/liver ratio of tracer uptake in a child suffering from chronic kidney failure (scan with antimyosin Mab 24 hr postinjection).

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