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Evaluation of the Banff Criteria for the Histological Diagnosis of Rejection in Renal Allograft Biopsies

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A HISTOLOGICAL diagnosis of renal allograft rejection can be made readily if the clearcut picture is present (ie, considerable interstitial infiltrate, tubular invasion, and intimal arteritis¹). In many cases, however, the histological changes are less characteristic and the differential diagnosis—especially with regard to cyclosporine (CyA) toxicity, borderline changes, and innocent interstitial infiltrates—may be difficult and subject to variable interpretation.²⁻⁶ Recently, the Banff working classification of kidney transplant pathology was proposed as an attempt to devise a schema for interpretation and gradation of the histological findings in renal graft biopsies that can be used as an indication for therapeutic consequences and expected graft survival.⁷ In the Banff schema, apart from interstitial infiltration, tubulitis and intimal arteritis are important lesions indicative of acute rejection (AR). As stated by the authors, the usefulness of the Banff schema with regard to standardization of histological criteria for rejection and clinical implications must be assessed by clinicopathological studies in larger series.⁷ We tested the value of the Banff criteria by comparing the retrospectively and blindly scored histological diagnosis according to the Banff classification with the eventual clinical diagnosis.

MATERIALS AND METHODS

The clinical analysis was done in a series of 246 consecutive renal allograft biopsies over a period of 3 years (1988-1990). Indications for biopsy were graft dysfunction with an increase of creatinine >25% and/or proteinuria >2.5 g/24 h. The immunosuppressive regimen consisted of CyA and prednisone (P). CyA was started at a dose of 12 mg/kg and was tapered down to 5 mg/kg in the 12 weeks following transplantation, with conversion to azathioprine in a dose of 3 mg/kg at 12 weeks after transplantation. P was started at a dose of 100 mg daily, with a gradual decrease to 25 mg daily during the first month, 20 mg during the second and third month, and then 10 mg. Core biopsies were performed using a 14-gauge Tru-cut needle. Histological examination was performed retrospectively, without knowledge of clinical data, on 2- μ m paraffin sections of Bouin's fixed renal tissue stained with haematoxylin and eosin, periodic acid-Schiff, silver methenamine, and chrome aniline blue. Biopsies with insufficient cortical tissue were excluded as inadequate. The histological findings were, according to the Banff schema, grouped in six categories: (1) normal; (2) hyperacute rejection; (3) borderline changes ("very mild AR"); (4) AR, divided into grade I—mild AR, grade II—moderate AR, and grade III—severe AR; (5) chronic allograft nephropathy (CR), grades I to III; and (6) other changes including CyA toxicity and acute tubular necrosis (ATN).⁷ The final clinical diagnoses were made retrospectively by three nephrologists based on clinical signs, original histological diagnosis, response to therapy, and eventual outcome. These clinical diagnoses were coded as (1) AR; (2) probable AR; (3) equivocal, or uncertain rejection combined with

Table 1. Comparison of the Final Clinical Diagnosis and the Banff Histological Diagnosis in 210 Renal Graft Biopsies

BANFF Diagnosis	No of Bx	Clinical Diagnosis				
		AR	Prob AR	Equivocal	CR	No R
Borderline changes	38	8	6	0	8	16
AR Grade I	30	14	2	2	2	10
Grade II/III	118	85	13	7	5	8
CR/CyA/ATN/other	24	1	1	0	9	13
Total	210	108	22	9	24	47

Abbreviations: Bx, biopsies; Prob AR, probable acute rejection; ATN, acute tubular necrosis.

other causes of graft dysfunction; (4) chronic rejection (CR); and (5) no rejection (no R).

RESULTS AND DISCUSSION

Of a total of 246 consecutive renal allograft biopsies, 210 (originating from 145 patients) were adequate and available for analysis. The time interval between biopsy and transplantation varied from 1 to 308 weeks (mean 24 weeks). The clinical diagnoses in each Banff category are summarized in Table 1. There were no biopsies with normal histology or with signs of hyperacute rejection.

Borderline Changes (n = 38)

Fourteen cases had a clinical diagnosis of AR or probable AR, with a favorable response to antirejection therapy in 11 cases and stabilization of moderately impaired graft function in three. Thus, the advice in the Banff classification that borderline changes are insufficient to justify antirejection treatment must be regarded with caution.

AR Grades I Through III (n = 148)

The Banff diagnosis correctly identified the eventual clinical diagnosis in 114 cases (77%). A combination of Banff diagnosis AR and a clinical diagnosis CR or no R was seen in 25 cases (17%). This group consisted of 12 of the 30 cases with grade I AR (40%) and 13 of the 118 cases with grades II and III AR (11%). This difference was significant ($P < .0005$; Fisher exact test). Therefore, the Banff classification

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has a tendency to overdiagnosis of AR, especially in grade I. In nine cases (6%) with a Banff diagnosis of AR, the clinical diagnosis was uncertain (equivocal). In seven of these, antirejection therapy was given with a favorable response in four cases, stabilization of renal function in two, and a rise of serum creatinine in one case. Of the two patients who did not receive antirejection therapy, one patient showed spontaneous recovery of graft function, whereas the other lost the graft after surgery for renal artery stenosis.

Other Histological Changes (n = 24)

A Banff diagnosis of CR/CyA/ATN/ or other was clinically correct in 22 of these cases (92%). Of the two remaining cases, one patient had a suspected posttransplant lymphoma in his graft biopsy leading to excision of the graft (clinical diagnosis of AR at biopsy). The other patient had a histological diagnosis of combined AR and CyA toxicity. He died of myocardial infarction 1 day after installment of antirejection treatment with a lowering of the CyA dose (clinical diagnosis probable AR).

The data in this series suggest that the Banff schema can serve as an acceptable guideline for a standardized histo-

logical evaluation of renal graft biopsies. A major problem in the histological diagnosis is the relative weighting of the respective criteria of AR, such as interstitial infiltrate and tubulitis. For validation of the semiquantitative grading of these symptoms, as suggested by Solez et al,⁷ it will be necessary to study the relative importance of the different qualitative and quantitative changes in large series. In addition, the diagnostic problems in cases with a complex of changes suggesting AR and CyA toxicity and/or CR remain unsolved.

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