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Limitations and Practice of Current Nephropathology

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Description

The investigation of renal disease relies on biochemical and immunological analysis of blood, urine and histopathological examination of biopsy specimens. Non-invasive diagnostics can yield important information, and in some cases, obviate the necessity for invasive tissue sampling. However, specific circulating biomarkers of disease are available for only a small subset of pathologies, for example, the presence of anti-phospholipase A2 receptor antibodies in membranous nephropathy [1], the presence of anti-myeloperoxidase or anti-proteinase antibodies in anti-neutrophil cytoplasmic antibody associated vasculitis, or circulating anti-Glomerular Basement Membrane (GBM) antibodies in good pasture's disease [1,2]. Thus, renal biopsy remains an important investigation in nephrology, providing both diagnostic and prognostic information. Biopsies consist principally of cortical tissue that is subsequently evaluated using a combination of light microscopy, immunofluorescence, and electron microscopy. Typically, the acquisition of a biopsy is prompted by biochemical analysis of blood demonstrating impaired excretory function of the native kidneys or allograft, often within the context of abnormal urinalysis. In native kidney biopsies, underlying pathologies include autoimmunity, viral or bacterial infection, metabolic disease such as diabetes mellitus, or genetic disorders. Each are characterized by typical morphological changes within the glomerular, vascular, interstitial, and tubular compartments that allow a diagnostic category to be assigned. For example, a thickened glomerular basement membrane is consistent with a diagnosis of membranous glomerulonephritis. At the ultrastructural level, electron microscopy can identify disease-associated morphological changes, including podocyte foot-process effacement and aberrant deposition of immune complexes or fibrils. Immunostaining supplements these data, providing information on the presence and site of specific molecular features. In transplantation, renal biopsies have a central diagnostic role within the context of allograft dysfunction. The consensus arrangement for allograft biopsies is that the Banff criteria [3]. Biopsy appearances are categorized according to the pattern of renal injury and diagnostic subsets include Antibody-Mediated Rejection (ABMR), T-cell–Mediated Rejection (TCMR) interstitial fibrosis and tubular atrophy. Immunostaining allows the detection of C4d, indicative of complement fixation by donor-specific antibodies, supporting a diagnosis of ABMR. However, although valuable in classifying appearances into historically defined diagnostic categories, these approaches don't provide insights into the cell-specific molecular processes that drive disease pathogenesis.

Conclusion

Malignant diseases of the kidney also are classified consistent with histological appearance. Renal cell carcinomas are the principal neoplasm to affect the kidney parenchyma, and there is considerable heterogeneity within this diagnostic category. RCCs are classified into clear cell RCC, papillary RCC, and chromophobe RCC, with ccRCC being the most prevalent [4]. This classification system is based on histology and characteristic chromosomal alterations [5]. In addition, there is heterogeneity within tumors types in terms of oncogene and tumors suppressor gene mutational status. A small proportion of RCCs (2%-3%) arise in the context of a hereditary genetic syndrome, for example Von Hippel-Lindau (VHL) disease [6]. Aside from diagnosis, histological evaluation of cancer biopsies also can provide prognostic information and guide treatment. There is an increasing appreciation that the presence of immune cells within tumors may have prognostic value; for instance, infiltration of the tumors with exhausted CD8+ T cells and tregs identifies patients with poor prognosis [7].

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