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Renal diseases associated with malignancies

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Introduction

The kidney may be involved in patients with malignancy for a variety of reasons. It may be the site of a primary tumour or less commonly a secondary tumour. Furthermore, tumours may exert an effect by pressure at the hilum compressing the renal artery or vein or to the renal outflow tract by compression of the ureter. Rarely, tumours may infiltrate the kidney and these are usually lymphomatous or leukaemic.

Malignancies may also have an indirect effect on the kidney through electrolyte disorders such as hypokalaemia and/or hyponatraemia from prolonged vomiting, hypercalcaemia from marrow infiltration, prolonged immobilization, or the secretion of PTH substances, and hyponatraemia from inappropriate ADH secretion.

Therapy may also have an adverse effect on renal function by drug nephrotoxicity, particularly with cisplatin and analgesic therapy and rarely a result of the adverse effects of radiation.

Malignancy-associated nephropathy

Malignancy-associated nephropathy has been recognized for many years [1] and the most common association is of solid tumours and nephrotic syndrome due to membranous nephropathy [2] and Hodgkin's disease and nephrotic syndrome due to minimal change nephropathy. The pathogenesis is immunological [3] due to the involvement of tumour associated antigen, re-expressed fetal antigens, and/or viral antigens. In some cases the pathogenesis is by intravascular coagulation or amyloidosis.

The most common presentation is as a nephrotic syndrome and in approximately 40% of patients the nephrotic syndrome presents prior to the diagnosis of malignancy. The true incidence of glomerulopathy in malignancy is not known as many patients with malignant disease have minor urinary abnormalities [4] and are seldom referred for invasive investigation that would establish the presence of an underlying nephropathy. Clinical studies have revealed haematuria and/or proteinuria in a significant number of patients with tumours and autopsy studies have revealed glomerular immune deposits in 17–30% of patients with malignancy although usually the glomerular histological changes are minor.

Malignancy-associated glomerular disease has only rarely been reported in children [5].

It is difficult to establish a causal relationship between the malignancy and the glomerular changes and frequently a causal link can only be inferred. In some patients it is possible to detect tumour antigens with glomerular deposits. A causal relationship, however, is suggested if nephrotic range proteinuria develops either 6 months before or after the diagnosis of a malignancy. There are a number of anecdotal reports that document the resolution of nephropathy with effective surgical excision of the underlying tumour [6].

Types of malignancy

A wide variety of both malignant and benign tumours have been associated with nephropathy. The most common are solid tumours particularly adenocarcinomas of the lung and gastrointestinal tract (stomach, colon, rectum). Many other tumours have been involved, usually on the basis of anecdotal reports. It is interesting to note, however, that nephropathy is rarely associated with carcinoma of the breast despite the high incidence of this tumour. There are only rare reports of benign tumours being associated with a nephropathy, but angiomyolipoma occurs in patients with tuberous sclerosis and there is frequently renal involvement.

Glomerular pathology

The most common nephropathy identified is that of membranous glomerulonephritis. This occurs in approximately 70% of patients reported to have

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malignancy associated nephrotic syndrome. The microscopic and ultra structural appearances are similar to those of idiopathic membranous nephropathy. A wide variety of other appearances have been described particularly mesangiocapillary glomerulonephritis, crescentic nephritis, and IgA nephropathy. There appears to be an interesting association between renal cell carcinoma and the development of glomerular amyloidosis.

There is no association between the nature, site, and size of malignancy, and any particular glomerular appearance. It would appear, therefore, that the glomerular response relates more to the immunological events than to the nature of the provoking tumour.

Management

The management of patients with malignancy-associated renal disease centres around:

(i) Symptomatic treatment of the nephrotic syndrome by appropriate diuretic therapy.
(ii) Detailed investigation of any electrolyte abnormalities with subsequent appropriate treatment.
(iii) Evaluation of the extent of the malignancy to determine whether tumour removal can be performed.
(iv) Regular review of all drug therapy to avoid potential nephrotoxicity.

In the majority of patients a satisfactory control of the nephrotic syndrome can be achieved by the use of a distal diuretic such as bendrofluazide or metolazone. Loop diuretics are seldom required, but may be needed in patients with profound nephrotic syndrome. The most common electrolyte disorders are hypokalaemia and hyponatraemia and effective correction involves the use of supplements as well as the control of vomiting. In patients with hypercalcaemia greater than 3 mmol/l control with bisphosphonates such as pamidronate or clodronate may be effective and relieve the frequently associated thirst. In many patients with hypercalcaemia there may be associated magnesium depletion requiring appropriate therapy.

It is important to regularly review the medication chart to avoid any potential nephrotoxicity either from therapy directed specifically at the tumour or from analgesic therapy to control pain.

Conclusion

There are many ways in which the kidney may be involved in patients with malignancy. Electrolyte abnormalities involving sodium potassium and calcium are common and respond satisfactorily to effective therapy. The incidence and prevalence of nephropathy is unknown due to the lack of any large-scale prospective studies in patients with malignancy. The association of malignant disease and nephrotic syndrome is well recognized and is immunologically mediated. The prognosis in patients with malignancy-associated nephrotic syndrome is determined more by the malignancy than by the underlying glomerulopathy. Although the most common histological appearance is membranous nephropathy a wide variety of glomerular appearances are recognized. There is no association between the site, size, or type of malignancy and the associated glomerular disease.

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