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Paraneoplastic glomerular diseases and malignancies

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Abstract

Paraneoplastic glomerulopathies are rare manifestations of neoplastic disease to be distinguished from iatrogenic renal damage. Solid tumors are preferentially associated with membranous nephropathy, whereas Hodgkin's lymphomas are associated with minimal change disease. The most common neoplasia associated with paraneoplastic glomerular disease are carcinomas of the lung and of the gastrointestinal tract. Nephrotic syndrome is the most frequent presentation of paraneoplastic glomerulopathy and the most critical glomerular disease regarding prognosis and patient care.

Renal biopsy is recommended in patients with glomerular proteinuria or nephrotic syndrome and cancer, depending on life expectancy and therapeutic options. The primary treatment must be directed at the cancer in all cases. Symptomatic treatment of the nephrotic syndrome with diuretics and ACE inhibitors is justified. Prevention of nephrotic syndrome complications, i.e. thromboses and infections, should also be addressed and systematic regular renal follow-up is warranted. All treatments should be regularly reviewed to avoid toxicity, associated renal function loss or low albumin levels for patients receiving albumin-binding drugs.

Epidemiologic studies have low evidence-based value. There is no widely accepted experimental model of the association of glomerulopathy and cancer. Thus, epidemiologic and mechanistic studies are needed to determine the true prevalence of paraneoplastic glomerulopathies and investigate new pathophysiologic approaches.

Keywords: Paraneoplastic glomerular disease; Nephrotic syndrome; Cancer; Membranous nephropathy; Carcinoma

1. Introduction

Paraneoplastic syndromes are manifestations of neoplastic disease. The term 'paraneoplastic syndrome' refers to clinical manifestations not directly related to tumor burden, invasion or metastasis, but caused by the secretion of tumor cell products (such as hormones, cytokines, growth factors and tumor antigens) [1]. Among paraneoplastic syndromes, the concept of paraneoplastic glomerulopathy was first suggested by Galloway in 1922, with the description of a nephrotic syndrome associated with Hodgkin's disease [2]. After Galloway, many authors have also reported cases of patients with both cancer and glomerular disease, but the causal link remains unclear.

'Glomerulopathy' is a general term for glomerular damage. A nephrotic syndrome is a massive urinary protein loss resulting in hypoalbuminemia and edema. It is one of the most common clinical presentations of glomerulopathy. Since the most frequent glomerular disease associated with solid tumors is membranous nephropathy, and since it is usually manifested by a nephrotic syndrome, we will particularly focus on these two issues [1,3–5].

The diagnosis of paraneoplastic syndrome may be suspected in the presence of the following criteria: (i) no obvious alternative etiology for the associated syndrome; (ii) existence of a time relationship between the diagnosis of the syndrome and cancer; (iii) clinical (and histological) remission after complete surgical removal of the tumor or full remission achieved by chemotherapy; (iv) recurrence of the tumor associated with an increase of associated symptoms [1,6].

Different glomerular diseases are associated with different neoplasms: whereas the nephrotic syndrome is generally due to membranous nephropathy (MN) in patients with solid tumors, cases of minimal change disease (MCD), IgA nephropathy (IgA-N), focal and segmental glomerulosclerosis (FSGS), mesangiocapillary glomerulonephritis, crescentic glomerulonephritis, amyloidosis and thrombotic microangiopathies have also been reported. The most common neoplasias associated with paraneoplastic glomerular disease are carcinomas of the lung and of the gastrointestinal tract [5]; MCD is strongly associated with Hodgkin's lymphoma [7].

The purpose of this review is to analyze the characteristics and occurrence of both the glomerular disease and cancer, and to identify their major interactions. The following description is the result of a systematic search of the Pubmed database using the following items: 'cancer AND glomerulopathy', 'cancer AND glomerular disease', 'cancer AND