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CASE REPORT

## Paraneoplastic Nephrotic Syndrome and Hodgkin's Lymphoma: A Case Report

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Nephrotic Syndrome,  
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### Abstract

**Introduction:** An association between nephrotic syndrome (NS) and malignant tumors was first described in 1922. This syndrome is more frequently associated with carcinomas and lymphoproliferative malignancies and is 10 times more common in Hodgkin's lymphoma (HL). The onset of NS can occur earlier or later than or simultaneously with HL. **Case Description:** A 4-year-old boy consulted due to an infection of the upper airways, followed by eyelid and scrotal edema. Laboratory tests confirmed the hypothesis of NS, and secondary causes were ruled out. Two years later, a biopsy of a cervical lymph node was performed, and histology and immunohistochemistry revealed mixed cellularity classical HL. Chemotherapy was initiated following the Adriamicin-Doxorubicin-Bleomicin-Vimblatin-Dacarbazine (ABVD) protocol. (ABVD) Protocol. **Comments:** we aim to highlight the importance of ruling out secondary causes of NS, such as infections and collagen, metabolic, genetic, and neoplastic diseases as well as maintaining a long-term follow-up of patients with high diagnostic suspicion, thereby aiming at early identification and treatment of these conditions.

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## INTRODUCTION

Nephrotic syndrome (NS) is a disorder characterized by massive and persistent proteinuria due to a pathologically exaggerated increase in the glomerular permeability to proteins. The consequences include hypercholesterolemia, hypoalbuminemia, and edema<sup>1,2</sup>. This disorder can be caused by primary glomerular disease or systemic diseases. Minimal-change disease is the main glomerulopathy found in children with idiopathic NS. The main secondary causes are collagen diseases, infections, and neoplasms<sup>1,3</sup>.

The association between NS and malignant neoplasms was first described in 1922, with few cases reported in the literature so far<sup>1,2-7</sup>. The incidence of NS is reported to be 0.4% in cases of Hodgkin's lymphoma (HL) in adults, but the incidence of this association in children is not yet established<sup>3,6,8</sup>. The onset of NS can occur earlier or later than or simultaneously with the manifestations of the lymphoproliferative disorder<sup>4,7</sup>.

This article presents a case of paraneoplastic NS approximately 24 months before the diagnosis of HL, highlighting the importance of follow-up for these patients and of this diagnostic hypothesis, thereby aiming at early identification and treatment of this neoplasia.

## CASE DESCRIPTION

A 4-year-old boy, previously healthy, presented with upper respiratory tract infection, followed by eyelid and scrotal edema, in addition to reduced urination. Upon arrival, the patient was in good general condition, with normal blood pressure, and showed the following: bilateral eyelid edema, crackles at the base of the lungs, presence of abdominal air-fluid sounds, and presence of scrotal and lower-limb edema. His abdomen was round, depressible, and painless, and the liver was palpable 3 cm from the right costal margin.

Laboratory tests showed the following results: protein/creatinine ratio in urine: 10, albumin: 2.1 g/dL, cholesterol: 436 mg/dL, serum electrolytes and renal function without changes (creatinine: 0.4 mg/dL, urea: 30 mg/dL, sodium: 139 mEq/L, and potassium: 4.7 mEq/L), and normal serum complement (C3 and C4) levels; qualitative examination of urine indicated the presence of albuminuria. The thoracic X-ray was normal (Figure 1). Renal and urinary tract ultrasound scans revealed kidneys of normal topography, contours, and dimensions, with preserved parenchymal thickness and corticomedullary ratio.

Using clinical and other data, the diagnosis of NS was defined. Initial tests ruled out secondary causes: initial blood count - hematocrit: 41.8%, hemoglobin (Hb): 14.5 g/dL, white blood cell count (WBC): 9,770/ $\mu$ L (basophils: 1.2%, eosinophils: 4.2%, segmented cells: 25.5%, lymphocytes: 59.5%, and monocytes: 9.6%), and platelets: 746,000/ $\mu$ L. The patient was negative for rheumatoid factor and ANA, and his serology was non-reactive for anti-HIV, HbsAg, total anti-HBc, and anti-HCV. Treatment was initiated with corticosteroids at

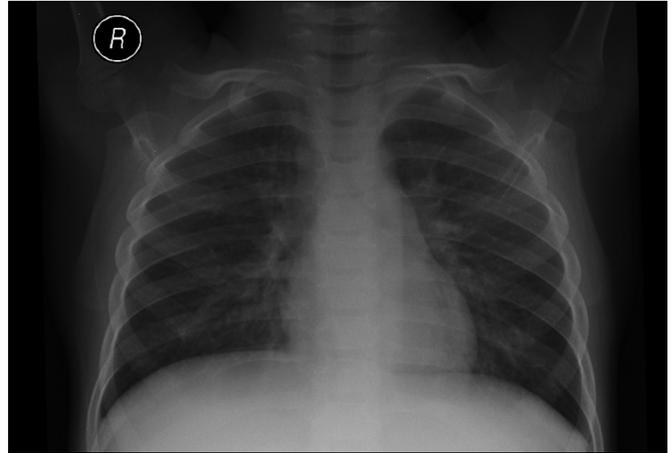


Figure 1. Normal thoracic X-ray.

a dose of 2 mg/kg/day, low sodium diet, and follow-up in the pediatric nephrology outpatient clinic, with good response to drug treatment and infrequent relapses.

Two years later, the patient presented with poor appetite and prostration. Laboratory findings evidenced microcytic anemia: Hb: 8 g/dL; mean corpuscular volume (MCV): 71 fL, WBC: 13,470/ $\mu$ L (neutrophils: 73%, lymphocytes: 23%), and platelets: 920,000/ $\mu$ L. The patient was referred to the hematology outpatient clinic, which empirically decided to initiate oral iron replacement and proceed with an etiological investigation.

The patient returned 2 months later with the following tests: Hb: 6.4 g/dL, MCV: 72 fL, WBC: 10,250/ $\mu$ L, platelets: 651,000/ $\mu$ L, reticulocytes: 0.9%, and ferritin: 674 ng/mL. A diagnosis of iron deficiency anemia was suspected, with reactionary oral iron malabsorption, high platelet count, and increased ferritin. The treatment plan comprised intravenous iron administration. A bone marrow biopsy was planned after clinical stabilization.

The patient progressed with worsening of the general condition, shortness of breath, fever peaks up to 38°C, and cervical adenomegaly as well as oliguria and generalized edema. Additional tests were suggestive of relapsed NS: Hb: 3.7 g/dL, WBC: 12,910/ $\mu$ L (band cells: 2%, segmented cells: 83%, and lymphocytes: 12%), platelets: 124,000/ $\mu$ L. The thoracic X-ray evidenced the presence of a mediastinal mass (Figure 2), confirmed by a chest CT scan, which revealed large mediastinal and hilar masses, mainly to the right, with the largest one measuring 6.9 × 6.1 cm (right upper paratracheal area), compatible with lymph node conglomerates, as well as a right supraclavicular lymph node mass measuring 2.9 × 2.1 cm.

A cervical lymph node biopsy was performed; the histopathology was compatible with HL, and immunohistochemistry results indicated CD30-positive mixed cellularity classical HL. The bone marrow biopsy was negative for neoplasms. After staging, chemotherapy was initiated following the Adriamycin-Doxorubicin-Bleomycin-Vimblatin-Dacarbazine (ABVD) protocol, alongside treatment management of NS.



**Figure 2.** Thoracic X-ray showing a mediastinal mass.

## DISCUSSION

Paraneoplastic glomerulopathies are well established in the medical literature; however, their incidence remains rare<sup>4,6,7</sup>. NS is more often associated with carcinomas and lymphoproliferative malignancies and is 10 times more common in HL<sup>4</sup>. Minimal-change disease is the most often described glomerulopathy, and mixed cellularity and nodular sclerosis are the most associated histological varieties<sup>1,2,4,7</sup>. In the case described herein, renal biopsy was not performed because the behavior of the disease was compatible with minimal-change disease and the mixed cellularity subtype.

NS may appear either early in the course of HL or during its recurrences, constituting the first symptom of the disease with a variable temporal relationship of 1-42 months<sup>4,6,7</sup>. The patient described herein presented NS 24 months before the diagnosis of HL, which occurred during a relapse of the kidney disease.

The pathogenesis of glomerular disease associated with HL remains unknown, but it seems to be related to changes in T cells, which produce cytokines and alter glomerular basement membrane permeability<sup>1,4-7</sup>.

In most cases with this association, the kidney function is preserved, as observed in the present case, which is

consistent with the theory that albuminuria results from the production of inflammatory cytokines by malignant cells that alter the glomerular permeability without compromising filtration<sup>5</sup>.

The prognosis of NS is related to the underlying disease and its specific treatment. The clinical improvement associated with the treatment of the neoplasm supports the association with minimal-change disease, and renal biopsy is often restricted to refractory cases<sup>3,4-7</sup>.

## CONCLUSION

NS associated with HL, although rare, is well established in the medical literature. Persistent proteinuria can correspond to paraneoplastic syndrome; however, this relationship is not always present, as in this case. We aim to emphasize the importance of ruling out secondary causes of NS (such as infections and collagen, metabolic, neoplastic, and genetic diseases) as well as maintaining a long-term follow-up of these patients with high diagnostic suspicion, thereby aiming at early identification and treatment of these conditions.

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