

# Nephrotic Syndrome as An Unusual Presentation of Hodgkin Lymphoma in A 7-Year-Old Boy

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## ABSTRACT

Hodgkin lymphoma may present with nephrotic syndrome, but this coexistence is rare. Some hypotheses have been proposed, however, the reason of is not fully known. The patient was a 7-year-old boy who presented with the complaint of edema in the legs and around the eyes. Laboratory tests revealed hypoalbuminemia, hyperlipidemia, and nephrotic range proteinuria. Hodgkin lymphoma was found in the biopsy performed due to the detection of mediastinal enlargement and lymphadenopathy on X-ray and computed tomography. At the end of chemotherapy responding to Hodgkin lymphoma, nephrotic syndrome resolved without the need for other immunosuppressant treatment. Clinicians should keep in mind that the first evidence of Hodgkin lymphoma may be a nephrotic syndrome and the importance of the use of imaging methods.

**Keywords:** Hodgkin lymphoma, nephrotic syndrome, proteinuria, X-ray

## INTRODUCTION

Nephrotic syndrome (NS) is one of the important chronic diseases of childhood, characterized by edema, heavy proteinuria, hypoalbuminemia, and hypercholesterolemia.<sup>1</sup> NS, mostly idiopathic in childhood, may also occur secondarily due to some rare causes like malignancy as a paraneoplastic phenomenon.<sup>2</sup>

In rare cases, NS can be the first manifestation of Hodgkin lymphoma (HL) with an incidence of 0.5-1% reported in the literature.<sup>3</sup> Although the relationship between HL and NS is not fully clarified, hypotheses are accusing T-cell dysfunction.<sup>4</sup> Polyanions are important in maintaining glomerular permeability. Polyanions are damaged by decreased synthesis of cytokines because of dysfunction of T-cells. It has been stated that this may result in proteinuria because of disruption of the glomerular barrier.<sup>1</sup>

However, strong evidence derived from extensive studies on this relationship is lacking since the current data are mainly from limited case series or individual reports.

Here, we describe a seven-year-old male patient who presented with clinical and laboratory features of NS and was eventually diagnosed with HL.

## CASE REPORT

A seven-year-old, previously healthy boy presented with bilateral periorbital and pretibial edema. He had no history of weight loss, night sweats, or persistent fever. On physical examination, body temperature was 36.4 °C, respiratory rate 20/minute, oxygen saturation in room air was 98% and blood pressure was 102/61 mmHg, which was within normal limits for his age. No lymphadenopathy (LAP) or hepatosplenomegaly was observed.

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Laboratory tests were leukocytes;  $6.83 \times 10^3/\mu\text{L}$ ; hemoglobin g/dL; platelet count:  $350 \times 10^3/\mu\text{L}$ ; albumin: 2.0 g/dL; total cholesterol: 424.9 mg/dL; erythrocyte sedimentation rate: 91 mm/hour; lactate dehydrogenase: 367 U/L; uric acid: 3.2 mg/dL; creatinine; 0.51 mg/dL. Serum electrolytes were within normal limits, while serology for hepatitis B and hepatitis C were negative. Spot urinalysis showed proteinuria (+3) and the protein/creatinine ratio was 4.0 mg/mg. Mediastinal lymph node enlargement was found on a chest X-ray which was performed to identify a pleural effusion without symptoms. Based on these findings, along with conglomerated LAPs in the chest tomography compressing the superior vena cava, pushing the trachea to the left posterior, and compressing the right main bronchus lymph node biopsy was performed, eventually diagnosing nodular-sclerosing HL. On the initial F-18-fluorodeoxyglucose (18 F-FDG) positron emission tomography/computed tomography (PET/CT) scan, multiple LAPs showed increased FDG uptake in both supra-infraclavicular lymph nodes and the spleen, indicating stage IIIA HL. He was given ABVD chemotherapy (Adriamycin 25 mg/m<sup>2</sup>, bleomycin 15 mg/m<sup>2</sup>, Vinblastine 6 mg/m<sup>2</sup>, Dacarbazine 375 mg/m<sup>2</sup>, on days 0 and 14). At the end of the first course of ABVD, we observed no pathological findings on physical examination, renal function tests, albumin, and cholesterol levels were normal, and proteinuria disappeared. In term 18 F-FDG PET/CT scan after three cycles of ABVD chemotherapy showed a complete metabolic response (Figure 1). During the follow-up, NS findings disappeared after ABVD treatment without the use of corticosteroids. The patient's NS was still in complete remission after four cycles of chemotherapy.

## DISCUSSION

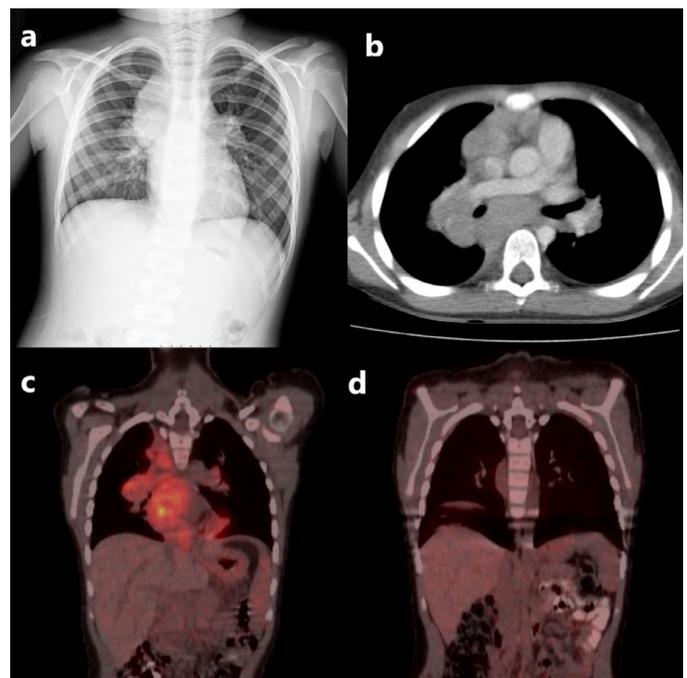
This case initially presented only with edema attributed to NS with no other specific complaints or symptoms suggesting HL. In a French study, it was shown that HL patients with NS mostly had LAP on physical examination at their first admission.<sup>5</sup> They also emphasized that if NS developed before the diagnosis of HL, resistance to steroids and other immunosuppressants may develop due to the glomerular permeability factor produced by Hodgkin cells. A chest X-ray was obtained to detect possible pleural effusion. Although there was no sign of pleural effusion on the chest X-ray, this led to the simultaneous diagnosis of HL and NS. Therefore, we believe that essential imaging methods such as X-rays can be an important part of diagnostic studies in children with NS.

In studies, it has been reported that systemic symptoms in HL patients with NS are higher than in those without NS.<sup>5,6</sup> The diagnosis of HL may be delayed if there are no systemic symptoms. In fact, our case was diagnosed with HL without systemic symptoms. Especially, kidney biopsy can be performed in patients whose NS is not cured because of unable to receive specific treatment for HL. We think that it is important to consider HL in patients presenting with NS clinical features without systemic symptoms to conserve patients from unnecessary invasive procedures and complications.

In this study, NS and HL were diagnosed simultaneously. However, NS may occur before or after HL.<sup>7</sup> There have been reports of cases with HL occurring years after the diagnosis of NS and a link between them.<sup>8</sup> It has also been reported that HL occurs when NS relapses in these patients and is completely cured after chemotherapy.<sup>5</sup> Therefore, we think that it is important to keep in consider that HL may occur in cases such as frequent relapses and resistance to treatment in the follow-up of patients with known NS.

The histopathological subtype of our case was found to be nodular sclerosing. Different results were found as the relationships between the histological subtypes of HL and NS were examined. In a study, NS was more frequently associated with nodular sclerosing histology, while in another study, the mixed cellular subtype was most common in NS.<sup>9</sup> It is thought that further studies in terms of histopathological frequency may be valuable in terms of determining the prognostic features of this association.

Investigation of HL as a possible etiologic cause in patients diagnosed with NS may also be beneficial in terms of response to treatment. If patients presenting with NS have underlying HL as a predisposing disease and cannot be diagnosed simultaneously, patients may unnecessarily receive long-term corticosteroid therapy. Furthermore, delayed diagnosis may complicate NS with resistance and frequent relapses.



**Figure 1.** (a) Mediastinal enlargement on a chest X-ray at diagnosis. (b) Conglomerate LAPs and compression of the trachea on chest tomography. (c) PET/CT with increased FDG uptake before treatment. (d) PET/CT with the complete metabolic response after treatment

LAP: Lymphadenopathy, PET/CT: Positron emission tomography/computed tomography, FDG: Fluorodeoxyglucose

HL may rarely present with NS. Therefore, lymphoma should be considered in the etiology of children NS, and early diagnostic steps should include appropriate imaging techniques to identify HL.

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#### Ethics

**Informed Consent:** A written informed consent was obtained from the patient's family.

**Peer-reviewed:** Externally peer-reviewed.

#### Authorship Contributions

Concept: K.D., F.K., Design: K.D., F.K., Data Collection or Processing: K.D., F.K., U.D., Analysis or Interpretation: K.D., F.K., U.D., Literature Search: K.D., F.K., U.D., Writing: K.D., F.K., U.D.

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