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Case Report

Pediatric Hodgkin's lymphoma presenting with nephrotic syndrome: a case report

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ABSTRACT

Hodgkin's lymphoma (HL) is a common type of lymphoma in children and adolescents, and it typically presents with lymphadenopathy, fever, and weight loss. Nephrotic syndrome is a rare but reported complication of HL, and it is associated with a poor prognosis. We report a case of a 12-year-old boy who presented with nephrotic syndrome as the initial manifestation of HL. The diagnosis was confirmed by a biopsy of the lymph node, which showed the characteristic Reed-Sternberg cells. The patient was treated with chemotherapy and he achieved complete remission of both HL and nephrotic syndrome. This report aims to raise awareness of the potential association between HL and nephrotic syndrome in pediatric patients, which can aid in early detection and prompt management.

Keywords: Hodgkin's lymphoma, Nephrotic syndrome, Minimal change disease, ABVD regimen

INTRODUCTION

Nephrotic syndrome is a known para-neoplastic syndrome of Hodgkin's lymphoma; although rare, the incidence of nephrotic syndrome associated with Hodgkin's lymphoma is 0.6–11%.[1] The association between nephrotic syndrome and extrarenal neoplasia was first reported in 1922.[2] The first case of Hodgkin's lymphoma associated with nephrotic syndrome was first reported by Corning in 1939.[3] The pathogenesis involving immunological abnormalities or T-cell dysfunction has been postulated, though definitive mechanisms have not been described.[4,5] Nephrotic syndrome can occur simultaneously or within 12 months with Hodgkin's lymphoma; minimal change disease appears to be the most commonly associated variant among focal segmental.[6]

RESULTS

Written informed consent for the publication of the clinical details and clinical images was obtained from the parents. A 12-year-old male child presented with complaints of facial swelling for the past year, gradually progressing to involve both lower limbs and decreased urine output for the past 2 days. There have been no complaints of the passage of blood in the urine or similar complaints in the past.

At presentation, the patient was vitally stable (HR 96/min, RR 22/min, BP 98/72 mmHg), and on examination, mild pallor was present with periorbital oedema along with pitting oedema in bilateral lower limbs and a palpable lymph node present in the right upper neck of size about 1×2 cm, firm, fixed, matted, and non-tender. On abdominal examination, the liver was palpable 2 cm below the right costal margin at the midclavicular line, and the spleen was non-palpable. Examination of other systems was within normal limits.

Routine investigations were done. Hb was 13 g/dl, TLC counts were 8.7×10^9/l (polymorphs 68%, lymphocytes 30%), platelets 326×10^9/l, S. urea 23 mg/dl, creatinine 0.3/dl, and total bilirubin 0.9 mg/dl. Urine routine microscopy was suggestive of protein 4+, serum protein, and albumin, which were 4.2 and 1.1 g/dl, respectively, suggesting hypoalbuminemia. A chest x-ray was done,

suggesting mediastinal widening. The Mantoux test was 6×4 mm. A further investigation targeting nephrotic syndrome was done; the 24-hour urinary protein was 2.2 gram, and the spot urinary protein and creatinine ratio was 6.8. Ultrasonography of the abdomen and KUB was suggestive of hepatomegaly; urine and blood cultures were sterile; and other investigations such as C3, C4 levels and antinuclear antibody were within normal limits.

The child underwent ultrasonography of the neck because of the palpable lymph node in the right upper neck, which is suggesting multiple enlarged lymph nodes present in the bilateral submental, jugular, and submandibular regions. Fine needle aspiration cytology was planned and was suggesting reactive lymphadenitis. Later, the patient was taken up for an excisional biopsy, which was suggestive of the presence of Reed-Sternberg cells, which stained positive for CD15 and CD30, with the presence of inflammatory cells in the background favouring mixed cellularity Hodgkin lymphoma (Figure 2). Contrast enhanced computed tomography of the neck, thorax, abdomen, and pelvis was suggenting of stage 2 hodgkins lymphoma.

The patient was undergoing for renal biopsy and was suggesting of minimal change disease (Figures 3a and b); hence, the patient was diagnosed as a case of mixed cellularity Hodgkin's lymphoma stage 3A with secondary nephrotic syndrome.

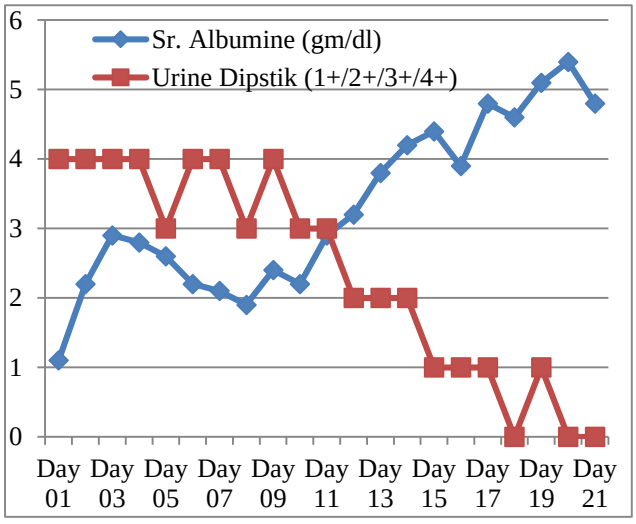

Figure 1: Levels of serum albumin and urine dipstik.

Management

The patient had started chemotherapy with an ABVD regimen (adriamycin, bleomycin, vinblastine, and dacarbazine), and six cycles were given for stage 3A Hodgkin lymphoma. He tolerated the chemotherapy well. Though he had symptomatic oedema, he was managed conservatively with an albumin infusion once the urine output was adequate. On follow-up, he attained spontaneous remission of the nephrotic syndrome.

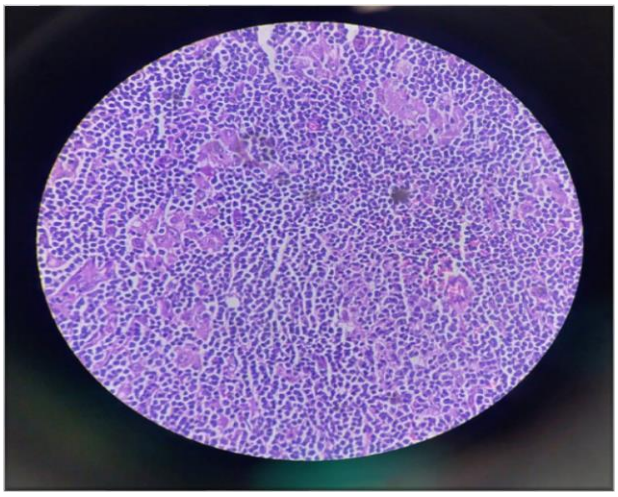

Figure 2: Lymph node biopsy specimen showing Reed Sternberg cells and mixed cellularity Hodgkin lymphoma.

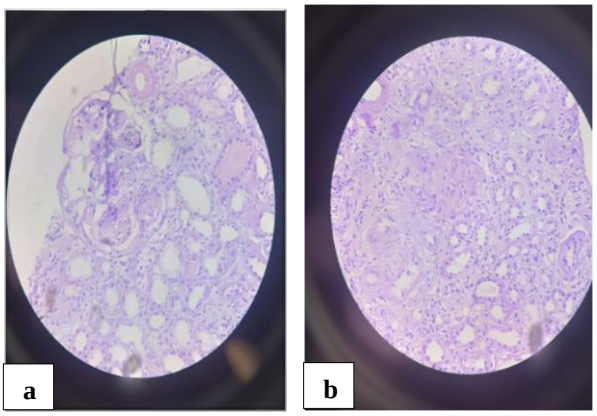

Figure 3: (a) Renal biopsy specimens suggestive of minimal change nephropathy, and (b) renal biopsy specimens suggestive of minimal change nephropathy.

Table 1: Sequential CECT Scan at baseline, after 2 cycles and after 6 cycles of chemotherapy.

Size of the largest lymph node	Baseline (cm)	After 2 cycle (cm)	After 6 cycle (cm)
Neck	4×3.6	2.6×1.5	0.5×0.1
Chest	0.9	0.7×0.5	0.1
Abdomen	1.2×1	0.9	0.3×0.2
Pelvis	1.6×1.2	0.8×0.6	0.4×0.2

Outcome and follow-up

The patient underwent six cycles of chemotherapy and was followed up with serial contrast-enhanced computed tomography of the neck, thorax, abdomen, and pelvis every two cycles of ABVD. Baseline CECT at the start of chemotherapy and the end of cycle 6B of ABVD were compared and were suggestive of radiological remission of

the disease (reduction in lymph node size by >80% of the baseline). He was monitored closely for the development of late effects of chemotherapy, including secondary malignancies and cardiac toxicity, and was found to be free of any complications during his follow-up visits.

DISCUSSION

Nephrotic syndrome is characterised by heavy proteinuria manifesting as periorbital swelling and pitting oedema of the lower limbs, hypoalbuminemia (serum albumin <3 g/dl), and hyperlipidaemia (total serum cholesterol >200 mg/dl). Heavy proteinuria is indicated by urine protein levels of 3+/4+ or a spot urine protein/creatinine ratio of >2.[7] The association between secondary nephrotic syndrome and classical Hodgkin lymphoma is 0.6–1%.[1]

A study done by Audard et al on the incidence of nephrotic syndrome and classical Hodgkin lymphoma suggested nephrotic syndrome can occur simultaneously in 19% of patients with Hodgkin lymphoma; 38% and 43% of patients developed nephrotic syndrome before and after the diagnosis of Hodgkin lymphoma, respectively.[8] The longest reported interval between these two events is 42 months.[8] Moreover, several cases of recurrent nephrotic syndrome have been reported with the recurrence of Hodgkin lymphoma.[10] Minimal change nephropathy is the most common variant of nephrotic syndrome associated with Hodgkin lymphoma, although membranous nephropathy, focal segmental nephrosclerosis, membranous-proliferative lesions, and IgA nephropathy are also said to occur concomitantly.[6,11,12] Involvement of the kidneys in patients with malignancies can be due to various reasons, such as direct infiltration of tumour cells, renal artery stenosis, tumour lysis syndrome, acute kidney injury, adverse effects of chemotherapeutic agents, and various paraneoplastic syndromes.[13]

Nodular sclerosis is the most common histological subtype of Hodgkin lymphoma to be associated with nephrotic syndrome and usually manifests as severe hypoalbuminemia with normal renal function tests. Usual therapy of nephrotic syndrome with a 12-week course of oral steroids with tapering (prednisolone) appears to be ineffective in cases of nephrotic syndrome associated with Hodgkin lymphoma.[7] Remission, as a reversal of renal disease and hypoalbuminemia, is attained spontaneously via the administration of chemotherapy or radiation for lymphoma, and generally, a good response is seen.[14]

CONCLUSION

Clinical examination and planned investigations should be performed in children presenting with nephrotic syndrome and severe hypoalbuminemia, as this can be the only clinical presentation in patients with underlying malignancy. Moreover, a clinician should suspect the possibility of malignancy in patients with nephrotic syndrome who have a poor response to oral steroid therapy.

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REFERENCES

1. Stéphan JL, Deschênes G, Pérel Y, Bader-Meunier B, Brunat-Mentigny M, Lejars O, Lamagnères JP. Nephrotic syndrome and Hodgkin disease in children: a report of five cases. Eur J Pediatr. 1997;156(3):239-42.
2. Gagliano RG, Costanzi JJ, Beathard GA, Sarles HE, Bell JD. The nephrotic syndrome associated with neoplasia: an unusual paraneoplastic syndrome. Report of a case and review of the literature. Am J Med. 1976;60(7):1026-31.
3. Cornig HJ. Une forme nouvelle de la maladie de Hodgkin: lymphogranulomatosemaligne à type de nephroselipoi-dique. These de Paris. 1939;517.
4. Shalhoub R. Pathogenesis of lipoid nephrosis: A disorder of t-cell function. Lancet. 1974;304(7880):556-60.
5. Alpers CE, Cotran RS. Neoplasia and glomerular injury. Kidney Int. 1986;30(4):465-73.
6. Mallouk A, Pham PT, Pham PC. Concurrent FSGS and Hodgkin's lymphoma: case report and literature review on the link between nephrotic glomerulopathies and hematological malignancies. Clin Exp Nephrol. 2006;10(4):284-9.
7. Audard V, Larousserie F, Grimbert P, Abtahi M, Sotto JJ, Delmer A, et al. Minimal change nephrotic syndrome and classical Hodgkin's lymphoma: report of 21 cases and review of the literature. Kidney Int. 2006;69(12):2251-6.
8. Levi I, Dinour D, Ben-Bassat I, Raanani P. Acute myeloid leukemia associated with nephrotic syndrome: case re¬port and literature review. Leuk Lymphoma. 2002;43(5):1133-6.
9. Peces R, Sánchez L, Gorostidi M, Alvarez J. Minimal change nephrotic syndrome associated with Hodgkin's lymphoma. Nephrol Dial Transplant. 1991;6(3):155-8.
10. Mori T, Yabuhara A, Nakayama J. Frequently relapsingminimal change nephrotic syndrome with natural killer celldeficiency prior to the overt relapse of Hodgkin's disease. Pediatric Nephrol. 1995;9(5):619-20.
11. Fer MF, McKinney TD, Richardson RL, Hande KR, Oldham RK, Greco FA. Cancer and the kidney: complications of neoplasms. Am J Med. 1981;71(4):704-18.
12. Mallouk A, Pham P-TT, Pham P-CT. Concurrent FSGS and Hodgkin's lymphoma: case report and literature review on the link between nephrotic glomerulopathies and hematological malignancies. Clin Exp Nephrol. 2006;10(4):284-9.
13. Nada A, Jetton JG. Pediatric onco-nephrology: time tospread the word: Part I: early kidney involvement in childrenwith malignancy. Pediatric Nephrol. 2021;36(8):2227-55.

14. Huisman RM, de Jong PE, de Zeeuw D, van Imhoff GW, van derHem GK. Nephrotic syndrome preceding Hodgkin's disease by42 months. Clin Nephrol. 1986;26(6):311- 3.

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