

CASE REPORTS

Nephrotic Syndrome, Paraneoplastic Syndrome Associated to Hodgkin Lymphoma

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ABSTRACT

Background: There is enough literature data - case reports and case series - regarding the association between nephrotic syndrome (NS) and different neoplasia, but only a few of these data address the specific link between NS and Hodgkin lymphoma. It has been demonstrated that intrinsic renal lesions – glomerular injury – can be found as a complication in these malignancies.

Material and methods: This report presents the case of a 9 year-old child in whom the diagnosis of NS was established two months before the diagnosis of Hodgkin lymphoma. Once chemotherapy was initiated, proteinuria and the clinical manifestations of NS, mainly oedema, disappeared.

Conclusion: Considering that the NS can be a paraneoplastic manifestation of Hodgkin lymphoma, the careful clinical evaluation becomes mandatory in any child with NS and persistent proteinuria despite appropriate treatment protocol. The prognosis of these patients is good, the treatment of Hodgkin disease causing the disappearance of proteinuria.

Keywords: nephrotic syndrome, paraneoplastic syndrome, Hodgkin lymphoma, children

INTRODUCTION

Since 1922 the association between NS and extra renal neoplasia was described by Galloway et al. (1). To date, the literature addressing this relationship consists of only a limited number of case reports and case series in which NS, as paraneoplastic syndrome, is linked to different malignancies such as leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and different carcinomas (2). Particularly, it was observed the association between minimal change nephrop-

athy and Hodgkin's lymphoma, these two entities emerging either simultaneously or within several months one from the other (3-6). The accurate basis of this relationship rests unknown, even though there have been hypotheses regarding a T-cell dysfunction (7). □

DESCRIPTION OF CASE/MATERIAL AND METHODS

A 9 year-old boy was admitted in our clinic for calf and eyelid oedema, developed progressively over the last four days. His per-

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sonal pathologic background revealed an episode of acute pancreatitis with no detectable cause. The physical examination at admission was normal except eyelid, ankle, calf and scrotum oedema, and movable dullness at abdomen percussion - relevant for ascites. No liver, spleen or lymph node enlargement was noticed. Laboratory findings revealed nephrotic range proteinuria (8.76 g/24h), hypoproteinemia (4.1 g/dl), mixed dyslipidaemia (serum cholesterol 346 mg/dl, total lipids 1089 mg/dl) and mild elevation of the erythrocyte sedimentation rate (44 mm/h). Chest X-ray was normal. Renal biopsy was not performed. The diagnosis of NS was established on clinical and biological arguments and systemic corticosteroid treatment was started according to the ISKDC protocol. The patient was discharged after fourteen days, in remission. Fourteen days later, he was re-hospitalized for dipstick proteinuria and laterocervical adenopathy. Physical exam revealed left laterocervical enlarged lymph nodes, having 4/3 cm diameter, of increased consistency and adherent to deeper tissues, without any inflammatory signs. Soft tissue ultrasound was performed, revealing multiple other enlarged lymph nodes localised at cervical and supraclavicular level. A computed tomography (CT) scan of the thoracic segment confirmed the modifications seen on the ultrasound and also observed mediastinal adenopathy (Figure 1 a, b). Hodgkin lymphoma was suspected, so a lymph node biopsy was performed, sustaining this diagnosis based on histological and immunohistochemical criterias. The final diagnosis was of a classic Hodgkin lymphoma – nodular sclerosis stage II A Ann-Arbor. Chemotherapy was initiated according to Euronet PHL – C1 protocol: two OEPA (methylprednisolone, vincristine, doxorubicine and etoposidum) cures plus local radiotherapy. Disappearance of proteinuria was observed after the first cure of chemotherapy. At follow-up, five months after the ending of the Hodgkin lymphoma treatment, the patient was still in remission regarding both pathologies. □

DISCUSSION

The relationship between NS and Hodgkin lymphoma is well known. Consequently, attention must be paid to the presence of proteinuria as a sole element of a paraneoplastic syndrome. The careful examination, in order to

exclude malignancies, becomes mandatory when facing a patient with NS. Chemotherapy once initiated, will determine the remission of NS, the collaboration between the pediatric nephrologists and oncologists being of utmost importance (8).

The exact incidence of NS in patients with Hodgkin lymphoma remains unknown. Incidence of 1% and 0.6% respectively was reported in two large series from France and Turkey – 9 out of 1144 children with Hodgkin lymphoma in both studies (6,9). Between 1984 and 2015, 136 patients with Hodgkin lymphoma were treated in our clinic, the case present-

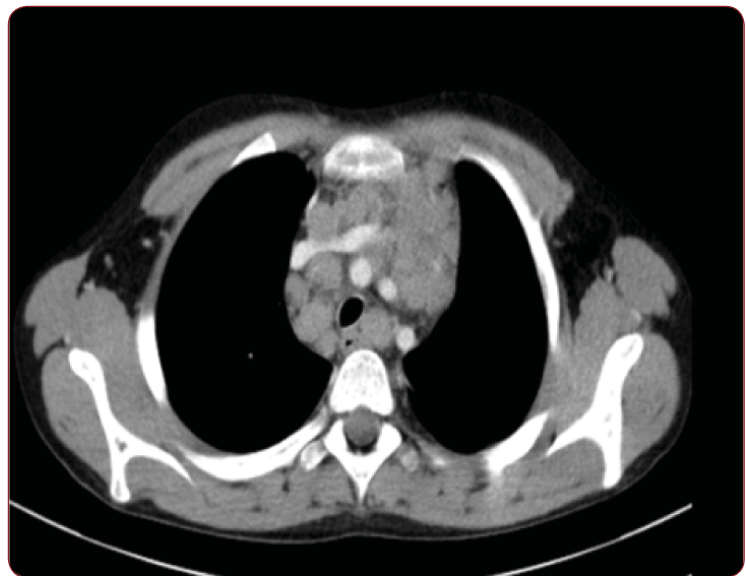


FIGURE 1A. Computed tomography scan showing mediastinal adenopathy.



FIGURE 1B. Computed tomography scan showing mediastinal adenopathy.

ed here being the second in which these two pathologies co-exist. To the best of our knowledge, these two cases (1.6%) are the only ones presented in Romanian paediatric population, the first case being published by Scurtu C. et al in 1998 (10).

Stephan et al. analysed the prevalence of NS in patients diagnosed with Hodgkin's lymphoma and found that 5 out of 483 children suffering from Hodgkin lymphoma, followed for a period of 13 years, developed nephrotic range proteinuria. This group of research concluded on the basis of their case series that thorough evaluation of patients with Hodgkin lymphoma is mandatory because, even though rare, glomerular dysfunction can be present (6).

In 2010, Farruggia et al. published two case reports where they analysed patients who had the association Hodgkin lymphoma - nodular sclerosis and NS - minimal changes nephropathy. Both patients received chemotherapy which consisted in the administration of 6 COPP/ABV cures plus radiotherapy, observing that 4 years after the end of the treatment patients maintained remission of both diseases (11). These results are in accordance with the literature data where in patients with this unusual association, the most prevalent subtype of Hodgkin's lymphoma, in both adults and children, was nodular sclerosis (6,9) and the predominant form of nephrotic syndrome was the minimal change nephropathy (4,5). Nonetheless, it is to be mentioned that 0.4% of patients with Hodgkin lymphoma present this histological feature of NS (12).

Geeta Gathwala et al. published in 1994 a case similar to ours, in which a 6 year-old boy was admitted in the hospital for right laterocervical tumefaction evolving for about 9 months, and generalised oedema developed progressively over the past 10 days. Laboratory data revealed nephrotic range proteinuria and severe hypoalbuminemia, sustaining the diagnosis of nephrotic syndrome. Biopsies of the

lymph node concluded on Hodgkin lymphoma – nodular sclerosis and chemotherapy was initiated with very good response and remission of proteinuria after the first two cures (13).

In 2002, Raphael et al. published two case reports with Hodgkin's lymphoma and secondary NS, underlining the fact that chemotherapy determined the remission of the NS. They also observed that recrudescence of proteinuria was associated to Hodgkin's lymphoma relapse (14).

Nephrotic syndrome can develop before or after the diagnosis of Hodgkin lymphoma. In one of his studies, Audard et al. found that 38% of patients developed NS before the diagnosis of lymphoma, 43% after, and 19% developed the two diseases simultaneously (15). Also, Stephan et al. presented two patients in whom NS preceded with 6 months and 12 months respectively the diagnosis of lymphoma and other 3 patients where the two diagnosis were made at the same time (6). In our reports, the diagnosis of NS preceded the one of Hodgkin lymphoma by 2 and 36 months, respectively. To date, the longest interval reported between these two entities was 42 months (4). □

CONCLUSION

Given the fact that NS can be a paraneoplastic syndrome in Hodgkin lymphoma, it is mandatory to perform a thorough physical examination in any patient with persistent proteinuria, proteinuria that is found in the absence of the known complications associated to NS and after applying the right treatment protocol. The prognosis of these patients is good, lymphoma treatment determining the consecutive disappearance of proteinuria. Furthermore, very often it was observed that a relapse of the Hodgkin lymphoma causes consecutively the relaps of the NS.

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