Nephrosis as a paraneoplastic syndrome in the course of Hodgkin's lymphoma in a 13-year-old boy – case report

Nerczyca jako zespół paraneoplastyczny w przebiegu chłoniaka Hodgkina u 13-letniego chłopca – opis przypadku

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Summary
Idiopathic nephrotic syndrome is diagnosed in 16 out of 100,000 children, which makes it one of the most common childhood kidney diseases. The therapeutic process is based on the results of a series of tests, of which the most important in terms of diagnostics is the ratio of protein to creatinine in urine >2 and a decrease of albumin concentration in serum <2.5 g/l. The above symptoms are accompanied by edema and hyperlipidemia. Attention should be paid to careful assessment of the child's condition based on medical history and physical examination supplemented with ultrasound examination. It is not often the case that the clinical presentation typical for nephrotic syndrome with generalized lymph node enlargement (lymphadenopathy), liver and spleen enlargement may suggest the presence of lymphoma. Paraneoplastic syndrome is a condition of clinical presentation associated with tumors that are not a close implication of local neoplastic or metastatic infiltration. The purpose of the article is to draw attention to the possibility of concealing Hodgkin's disease by the symptoms of nephrotic syndrome by the case of a thirteen-year-old boy.

Keywords: nephrotic syndrome, Hodking's lymphoma, paraneoplastic syndrome, pediatrics

Case report

A 13-years-old boy with symptoms of nephrotic syndrome in the form of peripheral edema (eyelids and ankles) was assessed, proteinuria (6 g/l), elevated cholesterol level (403 mg/dl) triglycerides (157 mg/dl) hypoproteinemia (47 g/l), hypoalbuminemia (19 g/l), ESR (after the first and second hour >110 mm) and weight gain observed for several days. The boy was admitted to the Nephrology Department of the University Children's Hospital of Cracow (UCH) in October 2018.

The medical history showed that he had been weak for several days (no B type symptoms were found: fever, sweat and itching). The medical history for chronic diseases or allergies was negative. Positive medical history of cancer from mother's side. A few days before the incidence of symptoms typical for neurosis, the subject undertook physical effort - hiking.

When assessing the child's condition by a specialist in the nephrology department, physical examination revealed enlarged packages of supraclavicular lymph node and single lateral cervical ones, as well as tenderness in the left epigastrium. While, axillary and inguinal nodes unchanged. Ultrasound of the abdominal cavity was recommended, which showed enlargement of the spleen, there are several hypoechoegenic focal areas of the parenchyma with a diameter of up to 15 mm around it, enlarged kidneys (11.5 cm) with increased echogenicity with blurred corticomedullary differentiation, supraclavicular lymph nodes unevenly hypoechogenic, round with a diameter between 9 and 27 mm arranged in packages. Such an ultrasound image of lymphoid organs suggested that a proliferative disease was suspected [1]. In addition, an x-ray of the chest was done, which showed irregular widening of the mediastinal shadow (larger on the left side, joining in the lower part with enlarged lung cavities on both sides), arousing suspicion of proliferative disease in the area of mediastinum as well as the left diaphragmatic dome positioned higher, while the castophrenic angles free of fluid (Fig. 1). A biochemical blood test showed normal LDH and proper level of uric acid. Monitoring of diuresis was recommended, which did not require pharmacological boosting.

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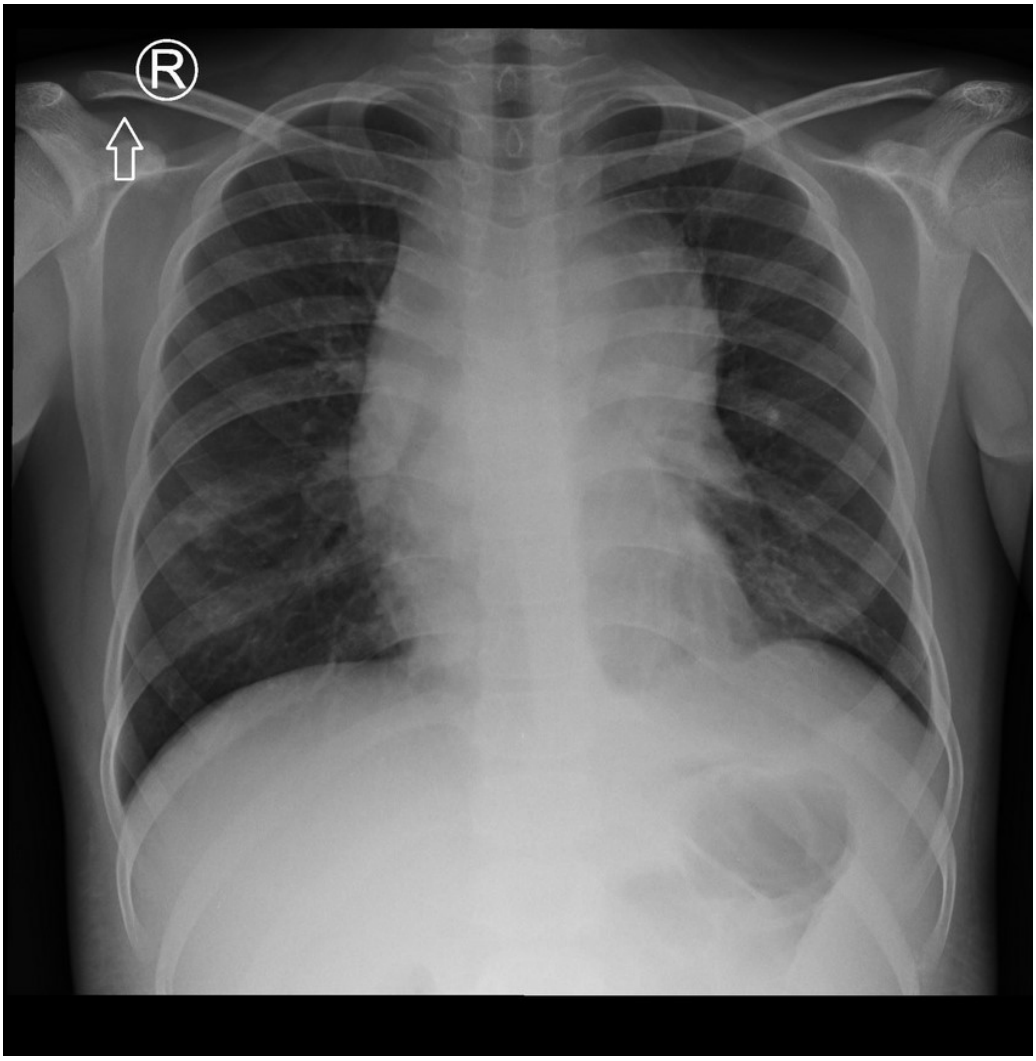

Figure 1. X-ray of the patient's chest

The next step in expanding the diagnosis was computed tomography after intravenous amplification with a contrast agent. The examination showed numerous bilateral lymph nodes in the upper and lower cervical levels and in the supraclavicular fossa (the largest single ones up to 30 mm in the mandibular angle, the remaining ones from a dozen to 25 mm in the length axis, and in the right infraclavicular and axillary region from a dozen to 20 mm, lungs with regular infiltrative lesions, fluid in both pleural cavities: in the left up to 45 mm, in the right up to 20 mm thick with an indentation into the interlobar fissure, nodal masses in the upper, middle and lower mediastinum present, with a slight impression on the tracheobronchial tree, with maintained patency. Enlarged lymph nodes along the *mammary artery* and within the lung cavities were also found.

On the fourth day of hospitalization, the child's condition worsened. Shortness of breath appeared, tachypnea, and there was a need for passive oxygen therapy. The bedside chest x-ray showed new fluid in the left pleural cavity obscuring the lower and partially middle parts of the left lung (Fig. 2). In the view of the symptoms of the superior mediastinal syndrome and the intensification of the symptoms of nephrotic syndrome, a decision was made to include steroid prophase. The patient's condition enabled PET examination only on 5th day of the prophase.

Under local anesthesia, a package of interior cervical and supraclavicular lymph nodes was collected on the right side from the boy. Based on the result of the examination, the classic form of Hodgkin's lymphoma was diagnosed, after full diagnostic imaging (including PET on the fifth day of the prophase), the stage was determined as 4 A (no symptoms of B).

After talking to the child's parent about the diagnosis and treatment, an informed consent was obtained to start the treatment. Treatment with OEPA chemotherapy, which the patient tolerated well, was started. A check-up x-ray image was taken at the Ward, based on which a reduction of the amount of fluid and the width of the mediastinal shadow was observed. The actions taken resulted in a rapid resolution of symptoms of nephrotic syndrome and complete regression of fluid in the pleural cavities. After 8 days of the OEPA cycle, the patient was discharged home before the next dose.

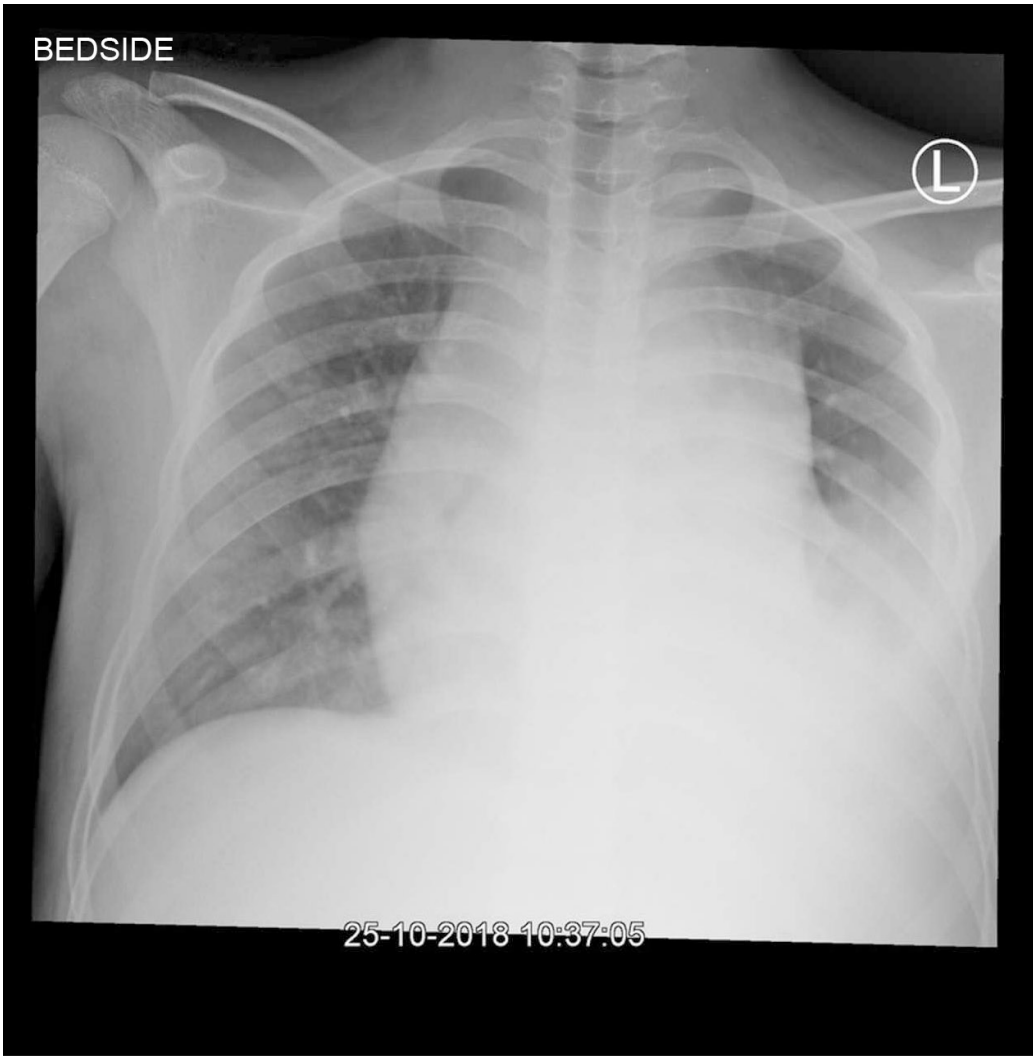

Figure 2. X-ray of the patient's chest

Overview

Nephrotic syndrome, which was paraneoplastic in this case, presented all the symptoms of the idiopathic form. The patient had: nephrotic proteinuria, hypoalbuminemia and hypoproteinemia, hypercholesterolemia, edema. The incidence of nephrosis is 2-7 cases per 100,000 children up to 16 years of age, boys are predominant, the typical age of incidence is 3-8 years [2].

The first-line treatment according to the recommendations of the Polish Society of Pediatric Nephrology is the use of prednisone in the morning dose for 6 months [3] (Table 1). The primary disease of the boy, however, was not nephrotic syndrome, but Hodgkin's lymphoma (HL) also referred to in the specialist literature as Hodgkin's disease. It is a malignant tumor of the lymphatic system, characterized by the presence of pathological Reed-Sternberg and Hodgkin cells in the affected tissue, with the presence of inflammation. In Poland, the incidence rate is estimated at 5/100,000 children up to the age of 15, boys are more often affected in the age group up to 10 years. The disease more often affects patients with both acquired and congenital immunodeficiencies. The causes of Hodgkin's Lymphoma have not been confirmed so far, early infection with Ebstein-Barr virus may play a role in the pathogenesis [4].

According to the World Health Organization (WHO) classification, histological subtypes are distinguished. Clinically, the most common symptom is asymmetrical enlargement of the cervical and supraclavicular lymph nodes, much less frequently of the mediastinum ones. In the early stages of the disease, enlarged lymph nodes do not differ from lymphadenopathy associated with viral infection. It should also be noted that a small mediastinal tumor does not give any symptoms, only significant lesions can cause compression symptoms, in extreme cases superior vena cava syndrome (2% of diagnoses). During the development of the disease, further node packages and postnodal organs are getting affected - the spleen, liver, lungs, bone marrow, CNS. In this case, the cervical lymph nodes, mediastinum and, prognosticly important, the spleen were enlarged. Immunohistochemical and pathomorphological examination of the entire lymph node or non-lymphatic organ material is decisive for the diagnosis of **HL**.

Table 1.

Recommendations of the Polish Society of Pediatric Nephrology regarding the use of prednisone

For the first-line treatment of nephrotic syndrome, it is recommended to use prednisone 60 mg/m2/day or 2 mg/kg/day (max. 60 mg/day) for 4 weeks:
• It is suggested to extend the treatment with 60 mg/m2/day or 2 mg/kg/day (max. 60 mg/ day) to 6 weeks if NS remission is not achieved within 14 days of starting treatment
• The following method of reducing prednisone doses is recommended: – prednisone 40 mg/m2/48 hours or 1.5 mg/kg/day [1B] for 4-6 weeks; – further gradual reduction of prednisone to complete withdrawal from taking it within 4 months (total treatment duration 6 months)
• It is recommended to administer prednisone in one morning dose
• It is suggested to determine the dose of prednisone based on body area

The basis of Hodgkin's Lymphoma treatment is multi-drug chemotherapy with steroids (OEPA – short for chemotherapeutic agents used to treat Hodgkin's Lymphoma in children Vincristine (**O**ncovin), **E**toposide, **P**rednisone, Doxorubicin (**A**driamycin)) [5]. Steroid therapy is designed to reduce the volume of tumor mass. In some children, low-dose radiation therapy is also added to the region affected by tumor growth. In pediatric patients with Hodgkin's Disease, radiation therapy is not used as an isolated treatment. The intensity of the therapy is individually adjusted to the stage of the disease and co-existing risk factors [6].

Inclusion of treatment of choice in nephrotic syndrome (steroids only) too quickly would most likely reduce mediastinal tumor mass, which would delay the boy's HL diagnosis by several months. Such a significant delay in diagnosis has a negative effect on the prognosis for patients with Hodgkin's Lymphoma.

Literature/References

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Streszczenie

Idiopatyczny zespół nerczycowy diagnozowany jest u 16 na 100 000 dzieci, co pozwala określić go jako jedną z najczęstszych chorób nerek wieku dziecięcego. Postępowanie lecznicze opiera się na wynikach serii badań, z których diagnostycznie najistotniejszy jest stosunek białka do kreatyniny w moczu wynoszący >2 oraz obniżenie stężenia albumin w surowicy wynoszące <2,5 g/l. Powyższym objawom towarzyszy wystąpienie obrzęków oraz hiperlipidemii. Należy zwrócić uwagę na staranną ocenę stanu dziecka na podstawie wywiadu i badania przedmiotowego uzupełnionego o badanie ultrasonograficzne. Nie często zdarza się, że obraz kliniczny charakterystyczny dla zespołu nerczycowego z uogólnionym powiększeniem węzłów chłonnych, powiększeniem wątroby i śledziony może sugerować występowanie chłoniaka. Zespół paraneoplastyczny to stan klinicznych objawów związanych z nowotworami, nie będącymi ścisłą implikacją miejscowego nacieku nowotworowego lub przerzutowego. Celem artykułu jest zwrócenie uwagi na możliwość zatajenia choroby Hodgkina przez objawy zespołu nerczycowego na przykładzie trzynastoletniego chłopca.

Słowa kluczowe: zespół nerczycowy, chłoniak Hodkinga, zespół paraneoplastyczny, pediatria