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Mediastinal tumor: thymoma or lymphoma?

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Lymphomas account for c.10–15% of childhood cancers. Lymphoblastic lymphoma (LBL) is the second most common type of lymphoma in the non-Hodgkin lymphoma (NHL) group. The T-cell subtype of lymphoma (T-LBL) is located in 85–90% of cases in the antero-superior mediastinum. The average age at onset is 9 years, and it is 2.5 times more common in boys than girls. Most patients with T-LBL have disseminated disease (stages III and IV), with bone marrow involvement in 15–20% and central nervous system involvement in <5% [1, 2].

In the differential diagnosis of an anterior mediastinal tumor in a child, the following should be taken into account: simple hyperplasia of the thymus, hyperplasia from the lymphoid tissue of the mediastinal lymph nodes or the thymus, tumor of the thymus originating from epithelial tissue (thymoma), and germ cell tumors. A pathological mass in the mediastinum can cause life-threatening symptoms in the form of airway compression and superior vena cava syndrome, and diagnostic procedures carry the risk of respiratory failure [3, 4]. Making this diagnosis requires a biopsy of the tumor or nodes, and extending the histopathological examination to include immunohistochemical, molecular and genetic tests [5, 6].

We present the case of a 14-month-old boy diagnosed with a mediastinal tumor with symptoms of dyspnea at rest and obstructive bronchitis. Chest X-ray revealed a very wide mediastinal shadow of up to 13 cm, blurring the silhouette of the heart. A lateral projection image confirmed the presence of a pathological mass in the anterior mediastinum (Figures 1A, B). His neonatal history was normal (first pregnancy and delivery, birth weight 3,530 g, Apgar score 10). Psychomotor development had been normal so far. On admission, no hepatosplenomegaly or peripheral lymphadenopathy were observed. Respiratory syncytial virus (RSV) infection was confirmed. In laboratory tests: leukocytosis 21.75 G/L, neutrocytosis 18.5 G/L, presence of 6% of atypical lymphocytes, elevated uric acid, and lactate dehydrogenase (LDH) = 2,073 U/L. In a lymphocyte subpopulation study, an increase in the percentage of CD19+ and a decrease in the percentage of CD3+CD4+ with normal absolute values and normal lymphocyte immunophenotype was observed. Ultrasound examination showed a small amount of fluid in the right pleural cavity and pericardium, hepatomegaly, and lymph nodes up to 9 mm in the abdominal cavity. Ultrasound of the lymph nodes in the right supraclavicular fossa showed a single, hypoechoic, suspicious lymph node, with a diameter of 7 mm. A pathological mass of the thymus ranging from the sternal notch to the diaphragm was seen in ultrasound of the anterior mediastinum.

Due to emerging mediastinal symptoms, glucocorticoid salvage therapy was applied according to the lymphoma treatment program with simultaneous prophylaxis of the tumor lysis syndrome. Clinical improvement and normalization of biochemical parameters were achieved. Computed tomography showed the presence of an enlarged thymus with hypodense areas, suggesting differentiation with thymoma, without enlargement of mediastinal, pulmonary hilar and abdominal lymph nodes (Figure 1C, D). Histopathological verification (UCK, Medical University, Warsaw) showed hyperplasia from T lymphoblastic cells.

However, due to subsequent progression of the disease, a second biopsy of the tumor was performed. The postoperative course was complicated by respiratory failure and arterial hypertension. Histopathology result from the second biopsy revealed thymoma, type B2. Verification of the preparation in Warsaw confirmed the diagnostic difficulties resulting from the possible coexistence of T lymphoblastic lymphoma and thymoma. The performed myelogram showed few cells morphologically suggestive of lymphoma cells in the lymphoid tissue of the bone marrow. The diagnosis of clinical stage IV T-cell lymphoma with involvement of the mediastinum, bone marrow and kidneys, but without involvement

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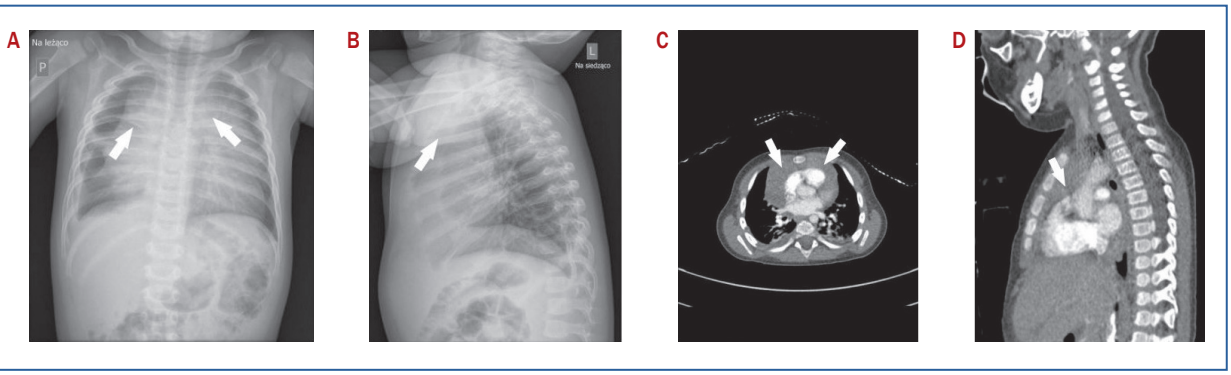

Figure 1A. Chest X-ray posterior-anterior (P-A); huge central shadow, up to 13 cm wide, blurred heart silhouette (arrow); **B.** Lateral chest X-ray; greatly widened shadow anterior mediastinum (arrow); **C, D.** Chest computed tomography (CT); thymus changed without calcifications, heterogeneously reinforced; dimensions 66 × 26 × 78 mm, does not show features od mediastinal and tracheobronchial tree modeling (arrow)

Table I. Histopathological results

Histopathological results	Biopsy 1	Biopsy 2
Local diagnosis	Ambiguous picture — to differentiate T-ALL (acute lymphoblastic leukemia) and thymocyte-rich thymoma	Thymoma, type B2
Central verification (Warsaw)	The image supports proliferation from T lymphoblastic cells	No unequivocal diagnosis: thymoma type B1 and T-lymphoblastic lymphoma need to be differentiated
International verification (*Institut für Pathologie*, Germany)	Slides from both biopsies: T-cell lymphoblastic lymphoma involving the thymus issue Molecular analysis: clonality analysis according to BIOMED-2 protocols-monoclonal rearrangements of T-cell receptor (274 bp fragments for beta-chain in reaction 'd', 245 bp for gamma-chain in reaction 'va'), a small fragment of 267 bp in reaction 'a' for beta-chain	

of the central nervous system, was confirmed. Due to the diagnostic uncertainty, the material was sent abroad for verification (*Institut für Pathologie Universitatsklinikum Schleswig-Holstein*, Germany). The presence of epithelial structures suggested a thymoma, and the immunophenotypic features indicated the presence of lymphoblastic cells. Finally, the diagnosis was made on the basis of genetic tests of DNA isolated from the tumor: T-lymphoblastic lymphoma occupying the thymus tissue (Table I). The applied treatment brought complete remission of the disease, with 20 months follow-up.

Lymphomas are the most common cause of a pathological mass in the anterior mediastinum in children, with NHL accounting for 15–25%. Among lymphoblastic lymphomas, the T-cell subtype is the most frequently diagnosed in this location, especially in younger children. Lymphoma often infiltrates the pleura and pericardium, causing symptoms of superior vena cava syndrome and airway obstruction. Gene rearrangements of the T-cell receptor in the gamma or beta chain are present in most cases. Differential diagnosis should include thymic hyperplasia (simple hyperplasia or epithelial tumors) and germ cell tumors [7, 8]. Radiological examinations will narrow the range of differential diagnosis, but the final diagnosis always requires histopathological examination.

In the rare case of T-cell lymphoma originating primarily in the thymus, diagnosis can be challenging and genetic testing may be required. Lymphoblastic lymphomas are characterized by an aggressive clinical course, but with the use of ALL-like chemotherapy [treatment protocols from the Berlin-Frankfurt-Münster (BFM) group acute lymphoblastic leukemia (ALL) strategy], better results are achieved in 75–90% of patients [9]. Genetic analysis may be essential, not only to confirm the diagnosis in some T-cell lymphomas, but also to evaluate the prognostic factors for favorable or unfavorable progress. Patient stratification based on immunogenetic analysis reveals the possibility of using novel strategies including immunotherapies. Individualized treatment is crucial for patients with relapsed and refractory T-cell malignancies [10].

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Authors' contributions

BT — design of the study, writing manuscript. Both authors — clinical data, critical revision of manuscript, final approval of manuscript.

Conflict of interest

The authors declare no conflict of interest.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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