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15. Diagnostic Challenges of Coexisting AIHA and Hodgkin Lymphoma in an 11-Year-Old Boy

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Introduction and Aim

Hodgkin lymphoma (HL) stands as a predominant lymphoproliferative malignancy in the pediatric and adolescent population, representing approximately 6.5% of all childhood cancers. Timely diagnosis of Hodgkin lymphoma (HL) in children plays a critical role, as early detection of the disease allows for the rapid initiation of treatment and significantly increases the chances of a complete recovery. The interaction between HL and the immune system is a complex "two-way street": preexisting autoimmune dysregulation may contribute to oncogenesis, while the malignancy itself can disrupt immune tolerance, leading to paraneoplastic syndromes.

The Aim: This study analyzes diagnostic challenges, immunopathogenic mechanisms, and therapeutic strategies by presenting a detailed clinical report of an 11-year-old patient with autoimmune hemolytic anemia (AIHA), which masked the underlying HL.

Case report

An 11-year-old boy presented with severe constitutional symptoms, including progressive weakness, nausea, vomiting, significant skin pallor, and icteric sclerae. Physical Examination: Clinical findings included jaundice, enlarged left cervical lymph nodes (1.0 x 1.5 cm), hepatomegaly (+4 cm), and splenomegaly (+2 cm). Anamnesis: The history revealed that cervical lymph node enlargement was first noted two years prior (at age 9) but was managed as reactive lymphadenopathy associated with chronic nasopharyngitis. Laboratory Findings: Initial tests showed severe hyperregenerative anemia (Hb 43–57 g/L, reticulocytes: 22%), leukopenia ($2.4 \times 10^9/L$), accelerated ESR (85 mm/h), and hyperbilirubinemia (67 $\mu\text{mol/L}$, indirect 52 $\mu\text{mol/L}$). Immunological Confirmation: A direct Coombs test was strongly positive (4+), confirming the diagnosis of autoimmune hemolytic anemia (AIHA). First-line treatment failed. Initial management with pulse therapy (Solu-Medrol 500 mg/day) and then maintenance prednisolone (2 mg/kg) did not lead to remission. Also, four weekly cycles of Rituximab (375 mg/m²) did not result in a sustained response. Due to the persistence of hemolysis and progressive enlargement of the left cervical lymph node conglomerate (up to 30x18 mm), a biopsy was performed. Pathological Diagnosis: Histological and immunohistochemical examination established a diagnosis of Hodgkin lymphoma, mixed-cellularity variant. Tumor Profile: markers showed diagnostic expression of CD30, CD15, MUM-1, and PAX-5. Bone marrow involvement was excluded via myelogram. CT and PET-CT imaging identified pathological lymph node

conglomerates (54x38 mm) in the jugular, posterior cervical, and subclavian regions on the left, leading to a diagnosis of Stage IIB HL with associated AIHA. Definitive resolution of the hemolytic process was achieved only after initiating the EuroNet-PHL (OEPA/COPDAC) chemotherapy protocol. The Coombs test turned negative after the second OEPA block. PET-CT confirmed a partial/good metabolic response (90% reduction in lymph node size).

Discussion

Autoimmune hemolytic anemia (AIHA) is a well-documented complication in adult lymphoproliferative disorders, seen in 5–10% of CLL cases and 2–3% of non-Hodgkin lymphomas. However, in pediatric HL, the association with AIHA is exceptionally rare, with a reported frequency of only 0.2% in large-scale retrospective studies. The association of AIHA and HL in children is atypical, and reliable data regarding its frequency are lacking, making this clinical case unique and diagnostically challenging. The association of HL and AIHA was first described by Bowdler and Glick in 1966, yet pediatric cases remain underrepresented in the global literature compared to adult cohorts. In the studied case AIHA served as a paraneoplastic syndrome, in which neoplastic cells likely induced immune reactions that cross-reacted with erythrocyte antigens. While corticosteroids are the standard for idiopathic AIHA, they are notably less effective when the anemia is secondary to HL.

Conclusions

AIHA may precede the diagnosis of HL in children, complicating both the diagnosis and the selection of a treatment strategy. The mechanisms underlying AIHA in HL remain poorly understood. Further research is needed to improve treatment outcomes and prognosis. The management of secondary AIHA in this context must prioritize the treatment of the underlying malignancy. This case underscores the necessity of a multidisciplinary diagnostic approach and long-term longitudinal assessment to improve survival and quality of life for pediatric patients with complex onco-hematological presentations.