sciendo

J Biomed Clin Res Volume 16 Number 1, 2023

DOI:10.2478/jbcr-2023-0008

Case Report

A CASE OF HEPATOSPLENIC γ/δ T-CELL LYMPHOMA DEBUTING WITH MASSIVE HEMOPTYSIS

Antonio I. Antonov

Department of Clinical Hematology, Medical University – Varna, St. Marina University Hospital, Varna, Bulgaria, St. Marina, University Hospital, Pleven, Bulgaria, Department of Clinical Hematology

Corresponding author:
Antonio I. Antonov
St. Marina, University Hospital, Pleven, Bulgaria,
Department of Clinical Hematology
e-mail: aantov@abv.bg

Received: October 26, 2022
Revision received: December 8, 2022
Accepted: December 22, 2022

Summary

Hepatosplenic γ/δ T-cell lymphoma (HSTL) is a very rare, aggressive extranodal lymphoma affecting mainly young adults. Clinically, presents with a symptomatic hepatosplenomegaly and systemic symptoms but without lymphadenopathy. The diagnosis is confirmed after careful evaluation of bone marrow and liver biopsies or, in some cases, after diagnostic splenectomy. Overall, survival is short regardless of chemotherapy regimens applied, including autologous stem cell transplantation. We present a case of γ/δ HSTL with massive pulmonary hemoptysis requiring bronchial artery embolization.
Keywords: Hepatosplenic γ/δ (gamma/delta) T-cell lymphoma, hemoptysis, bronchial arteriography, embolization

Introduction

Hepatosplenic T-cell lymphoma (HSTL) is a rare, aggressive subtype of extranodal lymphoma. It originates from non-activated cytotoxic T lymphocytes, usually expressing the γ/δ (gamma/delta) T cell receptor (TCR) [1]. In 80% of cases, the etiology is unclear, and in the rest, it develops against the background of chronic immune suppression [2]. Apart from massive hepatosplenomegaly without lymphadenopathy, the typical clinical presentation includes constitutional symptoms (fever, sweating, and weight loss) and peripheral cytopenia due to the early bone marrow involvement. Histologically, sinusoidal infiltration of medium-sized CD3+, CD4-, CD8-, CD5- γ/δ T lymphocytes in the liver and the bone marrow is found. Splenomegaly develops due to the diffuse infiltration of the red pulp cords and sinusoids, with atrophy or even absence of white pulp [3].

The disease takes a very aggressive course with a short remission and development of chemoresistance [4]. The prognosis is poor with a median overall survival (OS) of 12 months (3 - 34 months) [5-8]. There is no standard therapeutic guideline worldwide, and the role

of consolidating autologous or allogeneic bone marrow transplantation is controversial.

We present a case of γ/δ HSTL in an 18-year-old patient with hepatosplenomegaly and massive life-threatening hemoptysis. After a successful bronchial arteriography with embolization, the condition was controlled [9]. The diagnosis was confirmed after trepan biopsy, flow cytometry, TCR PCR and splenectomy. Chemotherapy was started.

Clinical case

An 18-year-old patient with fever up to 39.2°C for 3 days and severe fatigue was accepted in the Emergency Department. On the clinical examination the patient was with a poor performance status, febrile, with massive hepatosplenomegaly. The peripheral blood count showed severe anemia (Hg=55g/l), with thrombocytopenia (PLT=71 g/l), and normal leukocyte count (WBC=10.59g/l), the differential blood count revealed reactive changes, C-reactive protein was 48.25mg/l (No 0 – 5.0), and LDH was 1120 U/l (No 208 – 378 U/l). The abdominal ultrasound examination confirmed the enlarged liver and objectified the splenomegaly (189/70 mm).

Routine X-ray examination revealed oval shadowing with central brightening in the left hilus associated with striated hilus. In differential diagnostic (DD) plan: specific process or non-specific inflammation were considered (Fig. 1).

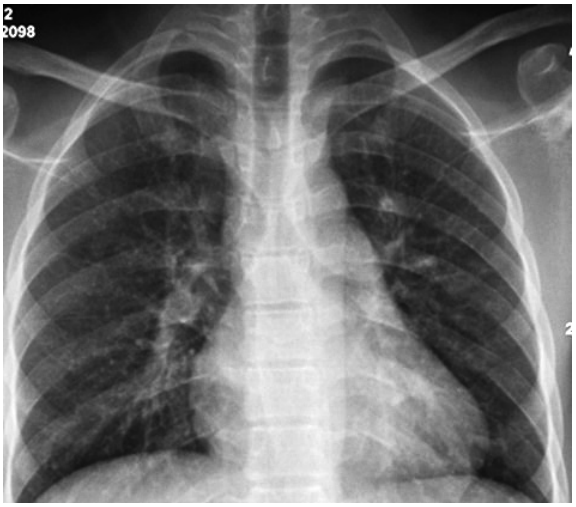

Figure 1. Initial Ro graphia

A consultation with a pulmonologist ruled out a typical lung inflammation and a septic condition was suspected. There was no past or family history of such diseases.

The patient was admitted to the Department of Hematology. A working diagnosis of sepsis was accepted. Blood and urine cultures were taken, empiric antibiotic therapy and hemotransfusions were administered.

On the 36th hour of hospitalization, massive hemoptysis began with a clinical deterioration. The emergency laboratory tests showed a persistent low platelet count with a normal coagulation status results. The CT showed involvement of the lung parenchyma bilaterally, from the apex to the bases of extensive "ground-glass" type areas involving the subpleura, and a consolidation in the hilar region in the air bronchogram. The first DD we considered was massive pulmonary hemorrhage due to vasculitis, the second was a superimposed inflammatory process. (Fig. 2)

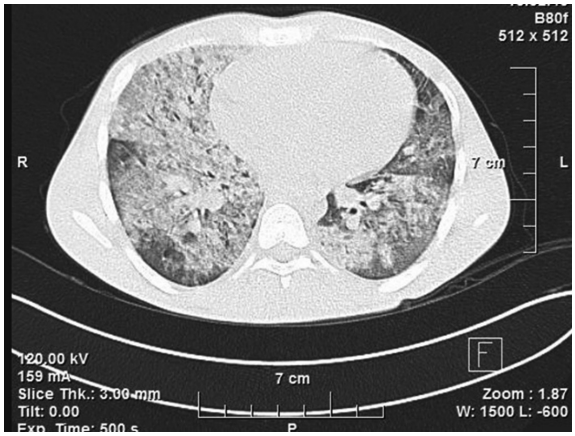

Figure 2. Computerized tomography during the hemorrhage

Due to deteriorating vital signs and the development of hypoxia and arterial hypotension, the patient was admitted in the ICU and intubated with the initiation of IVF REEL12. Regardless of the complex treatment and a change a change of the ventilation regimes, the pulmonary hemorrhage continued. Selective angiography was performed. It visualized parenchymal contrast accumulation in the late arterial phase around the trachea. At the second stage, embolization of the bronchial arteries was performed. After the pulmonary bleeding ceased, the patients's condition quickly stabilized. We started high-dose corticosteroid

therapy. Multiple tests were performed to rule out sepsis, vasculitis, connective tissue diseases, antiphospholipid syndrome, local infection, or coagulopathy. The follow-up CT on day 8 from the onset of the bleeding showed no pathological lesions in the lung parenchyma bilaterally. There were no pathologically enlarged LNs in the mediastinum and hili. No evidence of AV malformations or abnormal placement of pulmonary vessels was found (Fig. 3).

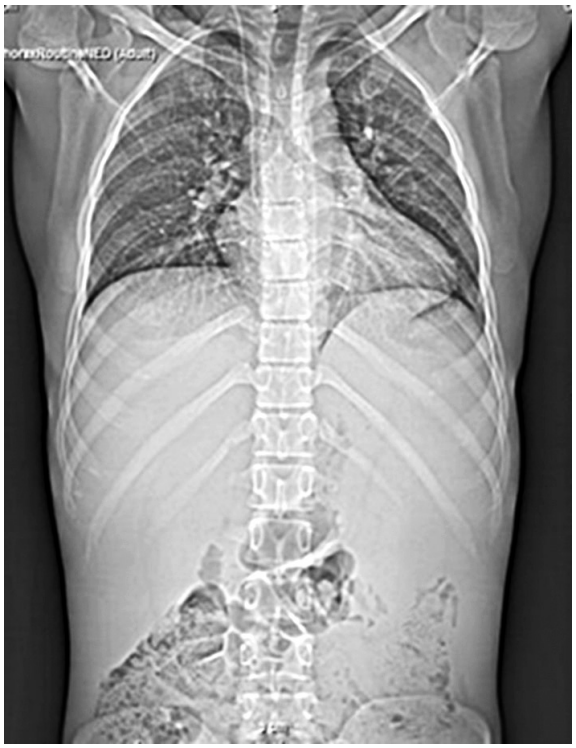

Figure 3. CT on Day 8

The diagnostic process continued with a bone marrow examination.

Trepan biopsy revealed hypercellularity up to 100% of the bone marrow parenchyma showing all three lines of hematopoiesis. Erythrophagocytosis was present. There was evident infiltration of the interstitium and in the dilated sinusoids by small groups of monomorphic, atypical lymphoid cells of small and medium size, light cytoplasm and nuclei with dispersed chromatin expressing intense cytoplasmic CD 3+. We concluded that this was a morphological picture of reactive changes in the bone marow and infiltration by T cell Non Hodgkin Lymphoma (Fig. 4).

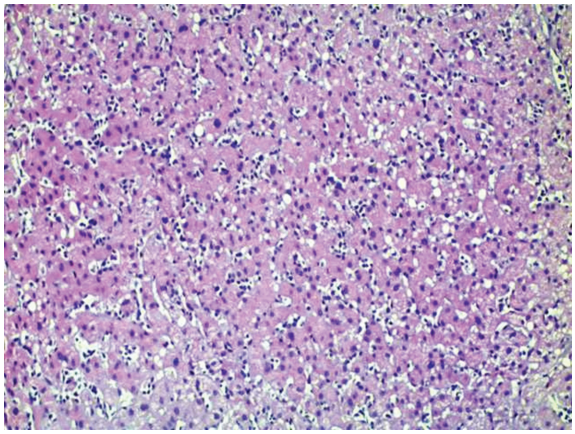

Figure 4. Hepatosplenic T-cell lymphoma – spleen infiltration

A PCR revealed TCRg rearrangement (+) and the presence of a clonal rearrangement of the T-cell receptor gamma genes (most likely Vgl-8+Jgl .3/2.3). The finding is consistent with clonal lymphocyte proliferation.

Due to contraindications for diagnostic liver biopsy, splenectomy with liver biopsy was performed. Histological and immunohistochemical studies confirmed the clinical diagnosis of hepatosplenic γ/δ T cell lymphoma (Fig. 4). Intensive chemotherapy was started.

Discussion

Perhaps somewhat speculatively, we believe that this life-threatening complication is due to the pathological γ/δ T lymphoma population. Normally, γ/δ T lymphocytes are composed of multiple subpopulations with different functions at different stages of the pathogen-induced immune response [10].These functions also depend on their tissue distribution, specific antigen-receptor structure, and local micro environment [11, 12].

In summary, we could outline some important characteristics of the situation. First: the process is local and affects only the lungs. Second: there is no additional coagulation disorder and the thrombocytopenia has no pathogenetic role either. Third: the only pathophysiological cause that could explain the clinical situation is a massive damage of the alveocapillary membrane leading to pulmonary hemorrhage. Fourth: there is a change in the behaviour of the malignant cytotoxic γ/δ T lymphoma population,

suggesting a local activation on contact with the pulmonary capillary structures. What changes in the pulmonary capillary structures might induce such an activation of the γ/δ T cell population and whether there is tropism in this process remains an open question.

References

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th ed. Lyon: IARS;2008.
2. Marques-Piubelli ML, Ferrufino_Schmidt MC, Miranda RN. Hepatosplenic T cell lymphoma: Limphoma & related disorders. 2022 May 2 [cited 2022 Oct 20]. Available from: https://www.pathologyoutlines.com/topic/lymphomanonBhepatosplenic.html
3. Ferreri AJM, Govi S, Pileri SA. Hepatosplenic gamma-delta T-cell lymphoma. Crit Rev Oncol Hematol. 2012;83(2):283-92.
4. Falchook GS, Vega F, Dang NH, Samaniego F, Rodriguez MA, Champlin RE, et al. Hepatosplenic gamma-delta T-cell lymphoma: clinicopathological features and treatment. Ann Oncol. 2009;20(6):1080-5
5. Pro B, Allen P, Behdad A. Hepatosplenic T-cell lymphoma: a rare but challenging entity. Blood. 2020;136(18):2018-26.
6. Krishnan M, Lunning M. Hepatosplenic γ-δ T-Cell lymphoma: who is on your speed dial? J Oncol Pract. 2019;15(6):307-12.
7. Madabhavi I, Modi G, Panchal H, Patel A, Revannasiddaiah S, Anand A, et al. Hepatosplenic Gamma Delta T-Cell Lymphoma (HSGDTCL): Two Rare Case Reports from Western India. Int J Hematol Oncol Stem Cell Res. 2017;11(4):296-300.
8. Aguilera NS, Auerbach A. T-cell lymphoproliferative processes in the spleen. Semin Diagn Pathol. 2020;37(1):47-56.
9. Todorov G, Bachvarov C, Valchev G, Popova R, Antonov A, Sirakov S, et al. Embolization of bronchial arteries in cases of life-threatening bleeding. Heart - Lung (Varna). 2015;21(1-2):45-9.
10. Carding SR, Egan PJ. γδ T cells: functional plasticity and heterogeneity. Nat Rev Immunol. Nature Publishing Group 2002;2(5):336-45.
11. Cano RLE, Lopera HDE. Introduction to T and B lymphocytes. In: Anaya J-M, Shoenfeld Y, Rojas-Villarraga A, Levy RA, Cervera R editors. From Bench to Bedside. Bogota (Colombia): El Rosario University Press; 2013. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459471/
12. Vantourout P, Hayday A. Six-of-the-best: unique contributions of γδ T cells to immunology. Nat Rev Immunol. Nature Publishing Group; 2013;13(2):88-100.