

# Hepatosplenic T-cell lymphoma presented with massive splenomegaly and pancytopenia – a case report

## Hepatosplenický T-lymfom s přítomností masivní splenomegalie a pancytopenie – kazuistika

Sukrisman L.<sup>1</sup>, Rajabto W.<sup>1</sup>, Harahap A. S.<sup>2</sup>, Fanggidae E. S. D. E.<sup>2</sup>, Ham M. F.<sup>2</sup>, Priantono D.<sup>1</sup>,

<sup>1</sup> Division of Hematology-Medical Oncology, Department of Internal Medicine Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

<sup>2</sup> Department of Anatomical Pathology, Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

### Summary

**Background:** Hepatosplenic T-cell lymphoma (HSTCL) is a rare subtype of peripheral T-cell lymphoma. Patients usually present with splenomegaly and pancytopenia but without lymphadenopathy. Immunohistochemistry (IHC) staining of bone marrow biopsy shows intra-sinusoidal infiltration of CD3 and CD56 T-lymphocytes. Current treatment strategy of HSTCL includes a CHOP regimen (cyclophosphamide, adriamycine, vincristine, prednisone) followed by autologous transplantation. **Case:** A 28-year-old male presented with abdominal fullness, weight loss, and massive splenomegaly. Laboratory findings revealed pancytopenia. A CT scan of the abdomen displayed hepatomegaly and massive splenomegaly. The bone marrow pathology examination showed monotonous medium-sized lymphocytes with some cluster of atypical lymphocytes with loosely condensed chromatin and pale cytoplasm. The intra-sinusoidal location was more prominent after using IHC staining of CD3 and CD56, which are characteristics of HSTCL. We administered CHOP-based regimen every 3 weeks for 3 cycles; however, the response was a stable disease. Since the splenomegaly was still massive and compromised the patient, the multidisciplinary team decided to perform splenectomy. Unfortunately, the patient did not survive the surgery. **Conclusion:** Hepatosplenic T-cell lymphoma is a rare aggressive disease, which is part of peripheral T-cell lymphoma. CHOP-based chemotherapy appeared to be ineffective, and we need further studies to find the optimal treatment of HSTCL.

### Key words

HSTCL – massive splenomegaly – pancytopenia – CHOP-based chemotherapy

The authors declare that they have no potential conflicts of interest concerning drugs, products, or services used in the study.

Autoři deklarují, že v souvislosti s předmětem studie nemají žádné komerční zájmy.

The Editorial Board declares that the manuscript met the ICMJE recommendation for biomedical papers.

Redakční rada potvrzuje, že rukopis práce splnil ICMJE kritéria pro publikace zasílané do biomedicínských časopisů.



**Wulyo Rajabto, MD**

Division of Hematology-Medical Oncology

Department of Internal Medicine  
Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine

Universitas Indonesia  
Jakarta, Indonesia

e-mail: wulyo02@gmail.com

Obdrženo/Submitted: 15. 12. 2022

Přijato/Accepted: 7. 2. 2023

doi: 10.48095/ccko2023246

## Souhrn

**Background:** Hepatosplenický T-lymfom (hepatosplenic T-cell lymphoma – HSTCL) je vzácný podtyp periferního T-lymfomu. U pacientů je obvykle přítomna splenomegalie a pancytopenie, ale bez lymfadenopatie. Imunohistochemické (IHC) barvení vzorků z biopsie kostní dřeně ukazuje intrasinusoidální infiltraci CD3 a CD56 T-lymfocytů. Mezi současné léčebné strategie při HSTCL patří režim CHOP (cyklofosfamid, adriamycin, vinkristin, prednison), po kterém následuje autologní transplantace. **Případ:** Přijali jsme 28letého muže s pocitem plnosti v břiše, úbytkem na váze a masivní splenomegalií. Laboratorní vyšetření odhalila pancytopenii. CT snímek břicha ukázal hepatomegalií a masivní splenomegalií. Patologické vyšetření kostní dřeně ukázalo monotónní středně velké lymfocyty se shlukem atypických lymfocytů s volně kondenzovaným chromatinem a světlou cytoplazmou. Intrasinusoidální umístění bylo patrnější po použití IHC barvení CD3 a CD56, které jsou pro HSTCL charakteristické. Podávali jsme chemoterapii v režimu CHOP každé 3 týdny, a to ve 3 cyklech; odpovědí bylo nicméně stabilní onemocnění. Jelikož splenomegalie byla stále masivní a pacienta omezovala, multidisciplinární tým rozhodl o provedení splenektomie. Pacient bohužel zákrok nepřežil. **Závěr:** Hepatosplenický T-lymfom je vzácné agresivní onemocnění, které spadá pod periferní T-lymfom. Chemoterapie v režimu CHOP se ukázala neúčinná a pro stanovení optimální léčby HSTCL je zapotřebí dalších studií.

## Klíčová slova

HSTCL – masivní splenomegalie – pancytopenie – chemoterapie v režimu CHOP

## Introduction

Hepatosplenic T-cell lymphoma (HSTCL) is a rare and aggressive malignancy of peripheral T-cell lymphoma. It accounts for less than 5% of all peripheral T-cell lymphomas [1,2]. HSTCL occurs in young adults and predominantly affect males. Patients often present with weight loss, abdominal discomfort due to hepatomegaly and massive splenomegaly, and pancytopenia [2]. Lymphadenopathy is usually absent. In order to establish the diagnosis of HSTCL, clinicians should perform bone marrow puncture, aspiration, and biopsy. Here, we reported a comprehensive case demonstration of HSTCL from its diagnosis to the treatment.

## Case description

A 28-year-old male presented with abdominal fullness, fatigue, and weight

loss of 10 kilograms within the last six months. On physical examination, the patient was fully alert, had pale conjunctiva, and splenomegaly on Schuffner 8. There were no palpable superficial lymph nodes. Laboratory findings showed pancytopenia, with hemoglobin 9.6 g/dL; white blood cells 1,000/ $\mu$ L; lymphocyte count 490/ $\mu$ L, and platelets 110,000/ $\mu$ L. Renal and liver functions were within normal limits. Viral markers HBsAg, anti HCV, and anti-HIV were all found to be non-reactive. Computed tomography (CT) scan of the abdomen showed hepatomegaly and massive splenomegaly (Fig. 1). The bone marrow pathology examination showed monotonous medium-sized lymphocytes with some cluster of atypical lymphocytes with loosely condensed chromatin and pale cytoplasm. The intra-sinusoidal location was more prominent after using immunohis-

tochemistry (IHC) staining of CD3 and CD56 (Fig. 2) which are characteristics of hepatosplenic T-cell lymphoma.

Based on constitutional symptoms, massive splenomegaly, pancytopenia, and bone marrow biopsy with IHC, we established the diagnosis of hepatosplenic T-cell lymphoma (HSTCL). We administered CHOP every 3 weeks for 3 cycles. Evaluation after 3 cycles of chemotherapy showed a stable disease. The chemotherapy regimen was changed into etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin every 3 weeks. However, the response to this subsequent regimen was a stable disease and the patient was still symptomatic. The patient also had febrile neutropenia despite primary prophylaxis using growth factors. After a multidisciplinary team meeting, the recommendation was to perform splenectomy. The resected spleen is seen on Fig. 3. Splenic irradiation was not performed considering the limited experience of this procedure and the risk of infection. The patient survived the surgery, but massive refractory bleeding occurred in the intensive care unit, and despite optimal resuscitation, the patient did not survive. Pathology results from the removed spleen showed diffuse pattern of monotonous lymphocytes with medium sized and pale cytoplasm. IHC staining showed positive for CD3, CD56, gamma delta T-cell receptor (TCR) and negative for CD20, alpha/beta TCR and TCL1 (Fig. 4). This post-operative pathologic study was consistent with HSTCL.

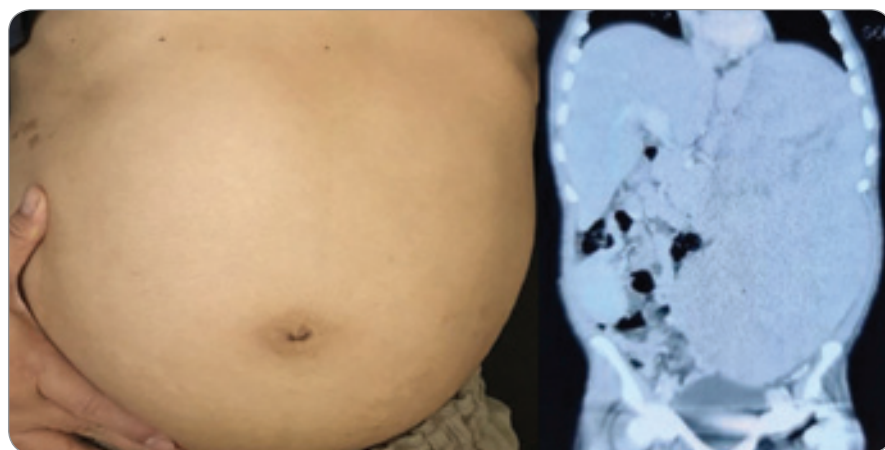


Fig. 1. Clinical examination and abdominal CT-scan showing massive splenomegaly.

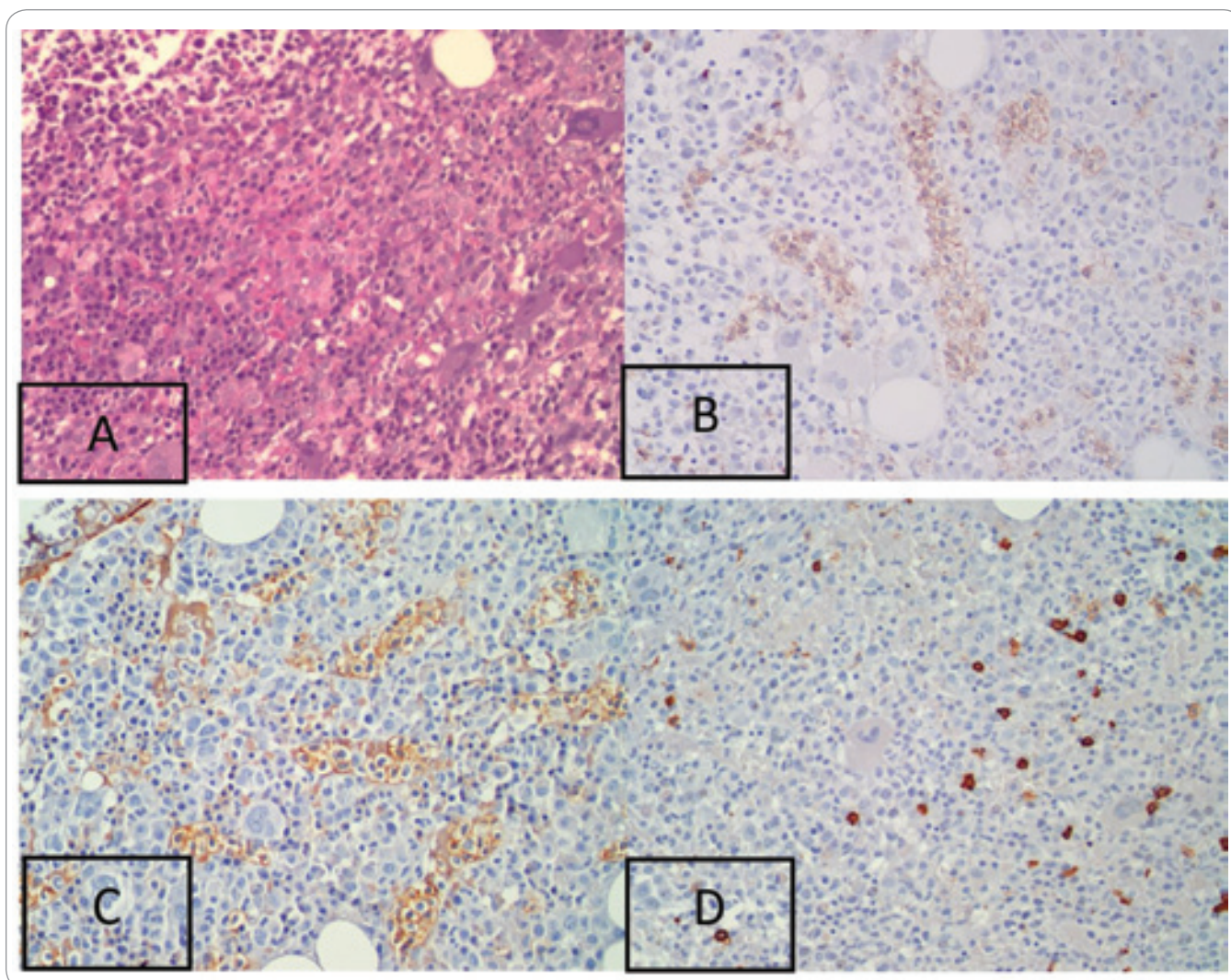
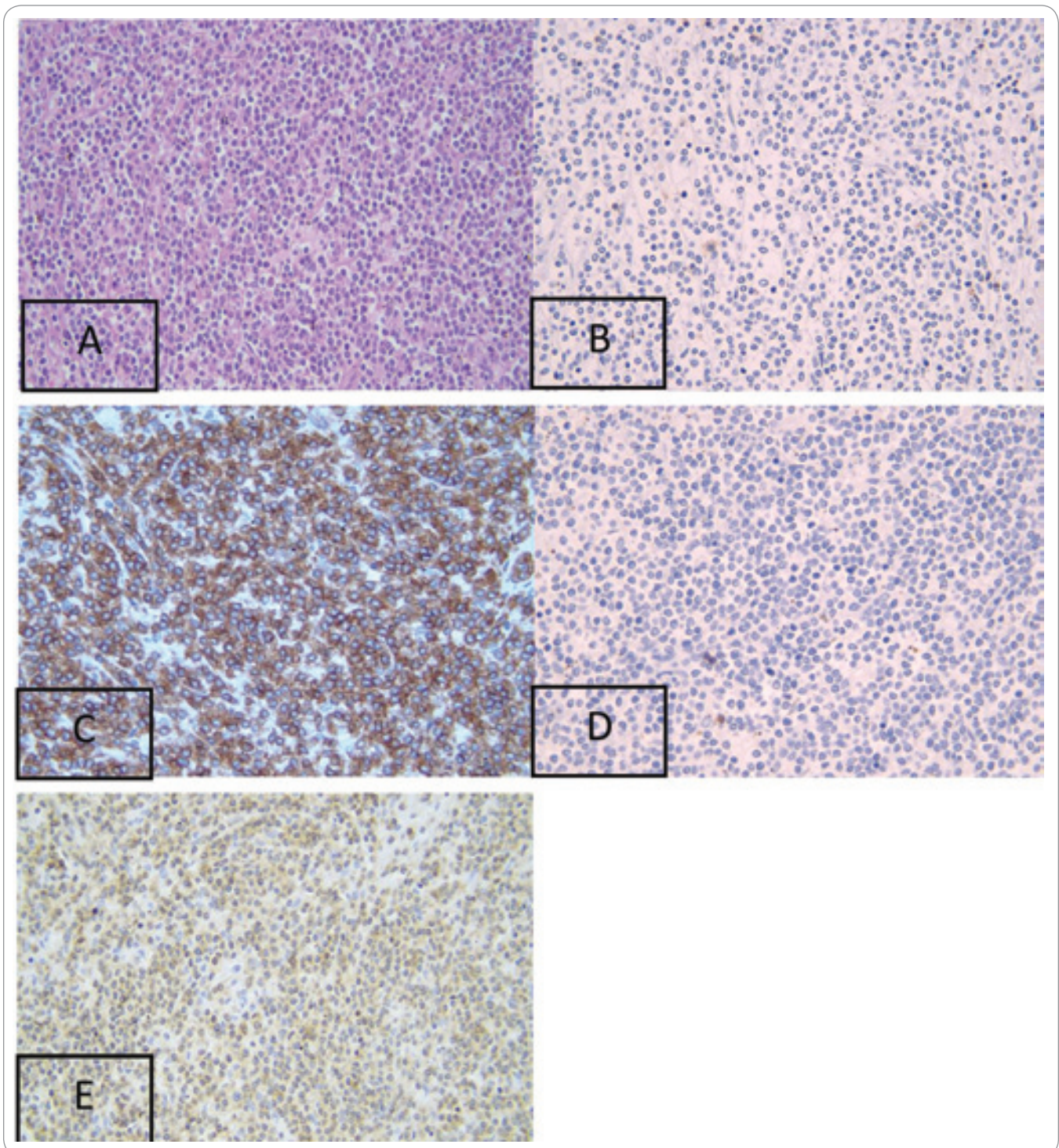


Fig. 2. (A) Bone marrow trephine biopsy showed monotonous lymphocytes with medium-size nuclei arranged in cords that were sometimes difficult to be assessed using hematoxylin-eosin staining (400×). (B) Immunohistochemistry staining showed positive CD3 in neoplastic cells in sinusoids (400×). (C) CD56 was also positive in neoplastic cells in the sinusoids (400×). (D) CD20 staining was negative (400×).



Fig. 3. Gross appearance of the resected spleen.



**Fig. 4.** (A) Spleen tissue showed monotonous lymphocytes with medium-size nuclei arranged diffusely with hematoxylin-eosin staining (400×). (B) Immunohistochemistry examination of T-cell receptor (TCR) beta showed negative results (400×). (C) T-cell receptor (TCR) gamma positive (400×). (D) Negative T-cell lymphoma protein-1 (TCL-1) (400×). (E) CD3 positive (400×).

### Discussion

HSTCL affects young male adults with median age at initial diagnosis in the range 32–47 years. Traditionally, biopsy and IHC from splenectomy were

used to diagnose HSTCL. In the present case, bone marrow aspiration and biopsy are essential components for baseline evaluation of HSTCL. The proliferation of small-medium-sized mature

T-cells infiltrating the spleen and liver is the characterization of this disease. The splenic red pulp cord and sinuses are usually involved with the white pulp atrophy. Neoplastic cells constantly pre-

sent in the bone marrow and show predominantly intrasinusoidal distribution. Large cell or blastic changes may be seen as the disease is progressing. In this patient, morphology from bone marrow biopsy displayed intrasinusoidal atypical lymphocytes. With the help of IHC, HSTCL neoplastic cells are usually CD3 and gamma/delta TCR positive with typically double negative markers (CD4– and CD8–), although CD8 might be positive in some cases. The expressions of surface CD3, CD2 and CD7 are usually positive without the expressions of CD5, CD1a, terminal deoxynucleotidyl and CD10. The majority of cases have positive CD56 and negative expression of CD57 [2–5].

There are several differential diagnoses for HSTCL, including other T-cell lymphomas as well as non-neoplastic conditions. The gamma/delta T-cell large granular lymphocyte leukemia (T-LGL) with CD4– and CD8– has significant features that overlap with HSTCL. T-lymphoblastic leukemia, primary cutaneous gamma delta T-cell lymphoma, intestinal T-cell lymphomas such as monomorphic epitheliotropic intestinal T-cell lymphoma, and EBV+ T-cell lymphoma of childhood are also considered as the differential diagnosis of HSTCL [2,3,5].

HSTCL has a rapidly progressive course and no standard therapy for treatment [6]. The efficacy of standard anthracycline-containing chemotherapy may have variable responses with high relapse rates and short median survival in most cases [6,7]. Splenectomy may sometimes be a useful therapeutic option. The reported median overall survival (OS) was 6–28.3 months, regardless of the treatment modalities [8].

The problem with refractory HSTCL is that conventional regimens of chemotherapy often yield unsatisfactory responses. Additional alternative induction chemotherapy along with allogenic

bone marrow transplantation have demonstrated efficacy and is recommended for the management of refractory HSTCL [3,9]. Additional regimens include gemcitabine, carboplatin, and dexamethasone as a bridging treatment for allogeneic bone marrow transplant; etoposide, methylprednisolone, high dose cytarabine, and cisplatin, alemtuzumab, and also purine analogs [2]. It was reported that non-CHOP based induction chemotherapy are superior to CHOP/CHOP-like induction in achieving durable survival. Non-CHOP based chemotherapy regimen can intensify the induction therapy of HSTCL followed by allogeneic transplant in selected patients [10].

Current evidence suggests that splenic irradiation (SI) is considered a treatment for patients that are not eligible for splenectomy [11]. It was also reported that the optimal radiation dose of SI remains unknown. There is also a higher risk of myelosuppression from SI. Therefore, the decision to proceed with splenectomy in our patient was considered the best option at the time.

In the future encounter of HSTCL patients who require splenectomy, the risk of severe bleeding after surgery should warrant the multidisciplinary team to reconsider the splenectomy as the choice of treatment.

### Conclusion

We should consider HSTCL in young male patient presents with constitutional symptoms, massive splenomegaly, no palpable superficial lymph nodes, and pancytopenia. The characteristic finding of biopsy and IHC in patients with HSTCL is the presence of small- to medium-sized mature T-cells, which typically involve the sinusoids of the spleen, liver, and bone marrow.

Current treatment modalities with systemic chemotherapy often fail to reach

satisfying response. Therefore, we need further studies to find the optimal therapeutic options for patients with HSTCL. The decision to perform splenectomy should be based on multidisciplinary team meeting. Fatal complication of splenectomy should be communicated to the patient and splenic irradiation might be chosen.

### Acknowledgements

This paper is self-funded.

### References

1. Montgomery M, van Santen MM, Biemond BJ et al. Hepatosplenic T-cell lymphoma: a population-based study assessing incidence and association with immune-mediated disease. *Gastroenterol Hepatol (N Y)* 2015; 11(3): 160–163.
2. Pro B, Allen P, Behdad A. Hepatosplenic T-cell lymphoma: a rare but challenging entity. *Blood* 2020; 136(18): 2018–2026. doi: 10.1182/blood.2019004118.
3. Horwitz SM, Ansell S, Ai WZ et al. NCCN Guidelines insights: T-cell lymphomas, version 1.2021. *J Natl Compr Canc Netw* 2020; 18(11): 1460–1467. doi: 10.6004/JNCCN.2020.0053.
4. Lee B, Lim DJ, Heo WY et al. Aberrant loss of surface CD3 and TCR $\gamma\delta$  expression in relapsed hepatosplenic T-cell lymphoma. *Ann Lab Med* 2021; 41(6): 598. doi: 10.3343/ALM.2021.41.6.598.
5. Chowdhury Z, Khonglah Y, Raphael V et al. Hepatosplenic T cell lymphoma: diagnostic conundrum. *Int J Hematol Oncol Stem Cell Res* 2022; 16(1): 66–73. doi: 10.18502/IJHOSCR.V16I1.8444.
6. Bojanini L, Jiang L, Tun AJ et al. Outcomes of hepatosplenic T-cell lymphoma: the Mayo Clinic experience. *Clin Lymphoma Myeloma Leuk* 2021; 21(2): 106–112.e1. doi: 10.1016/j.clml.2020.09.013.
7. Krishnan M, Lunning M. Hepatosplenic  $\gamma\delta$  T-cell lymphoma: who is on your speed dial? *J Oncol Pract* 2019; 15(6): 307–312. doi: 10.1200/JOP.18.00594.
8. Li Y, Chen K, Zuo C et al. Survival analysis of hepatosplenic T-cell lymphoma: a population-based study using SEER. *Int J Gen Med* 2021; 14: 8399. doi: 10.2147/IJGM.S335464.
9. Wang Q, Jiang Y, Zhu Q et al. Clinical features and treatment outcomes of 14 patients with hepatosplenic  $\delta$  T-cell lymphoma. *J Cancer Res Clin Oncol* 2021; 147(11): 3441–3445. doi: 10.1007/S00432-021-03587-6.
10. Klebaner D, Koura D, Tzachanis D et al. Intensive induction therapy compared with CHOP for hepatosplenic T-cell lymphoma. *Clin Lymphoma Myeloma Leuk* 2020; 20(7): 431–437.e2. doi: 10.1016/j.clml.2019.10.007.
11. Sankar K, Pettit K. Non-pharmacologic management of splenomegaly for patients with myelofibrosis: is there any role for splenectomy or splenic radiation in 2020? *Curr Hematol Malig Rep* 2020; 15(5): 391–400. doi: 10.1007/S11899-020-00598-X.