

## Case Report

# $\gamma\delta$ T-cell lymphoma: a rare entity mimicking hemophagocytic syndrome-report of two cases

Ujwala Maheshwari, Kalyani Mahore\*, Evith Pereira, Reeta Dhar

Department of Pathology, Mahatma Gandhi Missions Medical College, Kamothe, Navi Mumbai, Maharashtra, India

**Received:** 27 May 2017

**Accepted:** 23 June 2017

**\*Correspondence:**

Dr. Kalyani Mahore,

E-mail: mahore.kalyani@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

$\gamma\delta$  T-cell lymphoma is a rare extranodal and systemic neoplasm which accounts for less than 1% of all NHL having peak incidence in adolescents and young adults with a male predominance. Study report two cases, 29 and 25 years male presented with fever, abdominal pain and pancytopenia; one had hepatosplenomegaly while other had marked splenomegaly respectively and both showing feature of hemophagocytosis. Both underwent splenectomy. On gross examination, the spleen was markedly enlarged and shows a deep brown cut-surface. Histologically the normal structure of the spleen is totally effaced by a monotonous lymphoid population consisting of medium-large sized lymphoid cells with vesicular chromatin and small eosinophilic nucleolus with tumor cells showing moderate amount of eosinophilic cytoplasm. Liver biopsy showed regenerative changes in parenchyma and sinusoidal involvement by tumour cells. Peripheral smear revealed atypical lymphocytes with pancytopenia. Bone marrow aspiration showed moderate neoplastic infiltrate by lymphoid cells. Immunophenotypic study showed tumour cells expressing CD3, CD56, CD 2 (dim), TIA-1, TCR-gamma. The tumour cells were immunonegative for CD20, CD5, CD4, CD8, granzyme B, CD7, CD10 and CD 23. Immunophenotypic study is must for diagnosis of  $\gamma\delta$  T-cell lymphoma which can mimic hemophagocytic syndrome.

**Keywords:** Splenomegaly,  $\gamma\delta$  T-cell lymphoma

### INTRODUCTION

$\gamma\delta$  T-cell lymphoma (HSTL) is a rare extranodal and systemic neoplasm derived from cytotoxic T-cells usually of gamma-delta T-cell receptor type. A minority of cases appear to be of alpha-beta type. HSTL accounts for less than 1% of all NHL.<sup>1</sup> Peak incidence is in adolescents and young adults, with a median age of 20 years (range 15-65) and male to female ratio of 9:1.

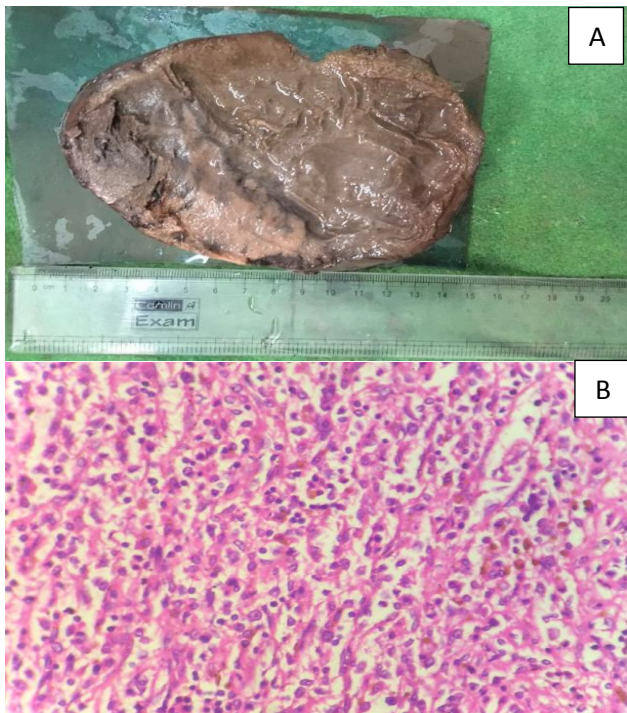
### CASE REPORT

Study report two cases, the one with 29 years male presented with fever, abdominal pain, pancytopenia with

hepatosplenomegaly and another with 25 years male presented with fever, abdominal pain, pancytopenia with marked splenomegaly. Both patient were showing feature of hemophagocytosis. For hematological study, blood samples from both the patients were collected for CBC and peripheral smear examination which revealed atypical lymphocytes and pancytopenia. USG abdomen done in one showed marked hepatosplenomegaly and in another showed moderate to marked splenomegaly. Considering the peripheral smear findings, bone marrow aspiration was planned which revealed moderate neoplastic infiltrate by lymphoid cells. After that a liver biopsy was done in a patient with hepatosplenomegaly and both underwent splenectomy.

### Gross examination

We received the specimen of spleen of one patient and the spleen along with 3 linear cores of liver biopsy of another patient for histopathological examination. Grossly, both the spleen were moderately to markedly enlarged one measuring 22x15x11 cm weighing 2.8 kg, another measuring 19.5x14x9 cm weighing 2.2 kg. External surface was grey-brown and firm in consistency with a deep brown cut-surface. (Figure 1A). Both the spleen were kept for overnight fixation and routine protocol for tissue processing was carried out.



**Figure 1: A) gross image of a slice of enlarged spleen of deep brown cut surface. B) microscopic image (H and E, 10 x) of splenic architecture totally replaced by monotonous population of lymphoid cells.**

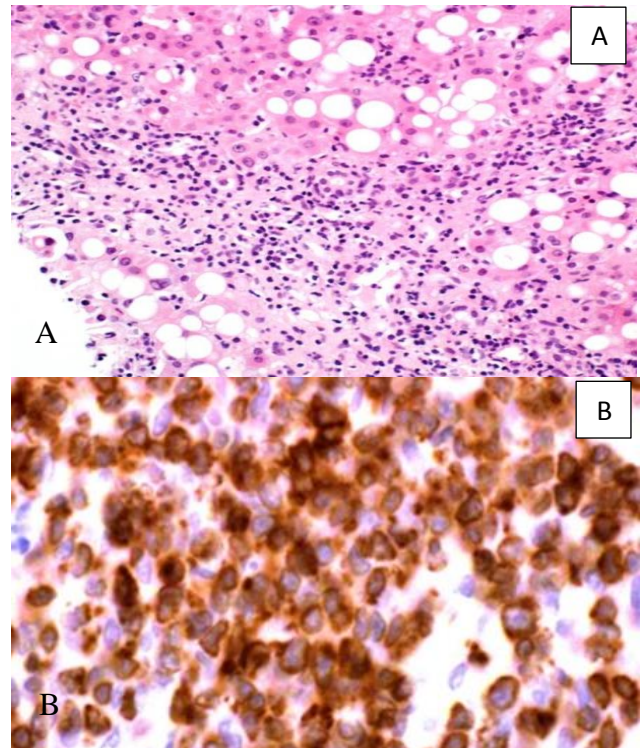
### Microscopic examination

On histopathological examination, the splenic architecture was totally effaced and replaced by a monotonous lymphoid population consisting of medium-large sized lymphoid cells. Individual lymphoid cells show round to oval nucleus, vesicular chromatin and small clearly visible eosinophilic nucleolus with tumor cells showing moderate amount of eosinophilic cytoplasm. (Figure 1B). On microscopy, liver biopsy showed regenerative changes in parenchyma and sinusoidal involvement by tumour cells (Figure 2A).

### Immunophenotypical study

Immunophenotypic study from both the spleen showed tumour cells expressing CD3, CD56, CD 2 (dim), TIA-1, TCR-gamma. The tumour cells were immunonegative for

CD20, CD5, CD4, CD8, granzyme B, CD7, CD10 and CD 23. (Figure 2B).



**Figure 2: A) microscopic image (H and E, 10x) liver biopsy of regenerative changes in parenchyma and sinusoidal involvement by tumour cells. B) microscopic image (40x), IHC study of CD 3 positivity in spleen by lymphoid cells.**

### DISCUSSION

$\gamma\delta$  T-cell lymphomas are rare and aggressive histological type. It is less common than B-cell lymphoma and the diagnosis is difficult on histopathology. There are fewer than 100 cases in reported literature till today. A minority of cases appear to be of alpha-beta type. HSTL accounts for less than 1% of all NHL.<sup>1</sup> The prognosis is poor with average survival of less than 2 years has been reported. This entity should be distinguished from other lymphomas of T-cell and natural-killer cell (NK)-like T-cell derivation.

The WHO classification recognizes two main T-cell lymphoma (TCL) entities: HSTL and primary cutaneous T-cell lymphoma (PCGD-TCL). Neoplastic cells localize in epithelial-rich tissue and within sinusoidal areas of the splenic red pulp.<sup>2</sup> HSTL typically presents with hepatosplenomegaly and systemic symptoms, usually manifest with pancytopenia. Up to 20% arise in the setting of chronic immune suppression, most commonly in solid organ transplantation or prolonged antigenic stimulation.<sup>3-5</sup> Epstein Barr Virus has been detected in a minority of HSTL cases and may have a pathogenic role by stimulating and expanding T-cells.<sup>6</sup> Few cases

associated with hepatitis-B virus infection have been reported.<sup>7</sup>

HSTL is characterized by a monotonous neoplastic infiltrate consisting of medium-sized lymphocytes with a moderate amount of cytoplasm and indistinct cellular borders.<sup>8-14</sup> The nucleus is oval, often slightly indented or clearly folded, with chromatin less condensed than that of small lymphocytes. The nucleoli, when present, are small, clearly visible. These cells usually involve the spleen, liver, bone-marrow and peripheral blood. Microscopic observation reveals an expansion of the red pulp, where neoplastic cells infiltrate both cords and sinuses with atrophy of the white pulp, though residual Malpighi corpuscles can be seen. In the liver, lymphomatous elements regularly affect the distended sinusoids but usually spare portal triads. The bone marrow is always readily aspirable and the smears highlight a moderate neoplastic infiltrate.

Trephine biopsy commonly shows a hypercellular marrow with sinusoids containing variable amounts of tumor cells, whose detection is greatly facilitated by immuno-histochemical techniques. With progression, the pattern of bone-marrow involvement becomes increasingly interstitial and shows a shift toward larger blastic cells. Bone marrow infiltration by large, highly atypical lymphocytes can be observed already on presentation when the infiltration is mostly confined to the sinusoidal compartment. Haemophagocytic histiocytosis is not uncommon, it can be pronounced and sustain a full-blown haemophagocytic syndrome. Leukemic cells can be detected because of their atypical morphology, even if as few as 1-2%. Lymph nodes are rarely involved at diagnosis, with sinusoidal infiltration by medium-sized cells; nodal architecture can be well preserved.<sup>15</sup>

HSTL usually carries the following phenotype: CD2+, CD3+, CD4-, CD5-, CD7+, CD8-, TCR+. One or more NK markers (CD16, CD56, CD57) are frequently expressed. Most of HSTL show an inactive cytotoxic profile (TIA-1+, Granzyme-, Perforin-).<sup>16</sup> An accurate diagnosis can be made on bone marrow histology with immunophenotypic evaluation, liver biopsy and/or cytological and immunocytochemical examinations.<sup>17</sup>

Considering presenting symptoms, differential diagnosis includes Acute hepatitis; in cases of myelodysplastic syndrome who presents with uninvolved bone marrow; In patients with autoimmune thrombocytopenic purpura presenting with isolated thrombocytopenia; in patients with acute lymphoblastic leukemia, with a high number of circulating blast cells; and T-cell lymphoblastic lymphoma expressing TCRs.<sup>18</sup>

## CONCLUSION

The diagnosis of  $\gamma\delta$  T-cell lymphoma was difficult on histopathological examination and it should be

distinguished from other lymphomas of T-cell and natural-killer cell (NK)-like T-cell derivation. Immunophenotypic study is must for diagnosis of  $\gamma\delta$  T-cell lymphoma which can be misdiagnosed as it can mimic hemophagocytic syndrome.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Cooke CB, Krenacs L, Stetler-Stevenson M, Greiner TC, Raffeld M, Kingma DW, et al. Hepatosplenic T-cell lymphoma: a distinct clinicopathologic entity of cytotoxic gamma delta T-cell origin. *Blood.* 1996;88:4265-74.
2. Bordessoule D, Gaulard P, Mason DY. Preferential localisation of human lymphocytes bearing gamma delta T cell receptors to the red pulp of the spleen. *J Clin Pathol.* 1990;43(6):461-4.
3. Ross CW, Schnitzer B, Sheldon S, Braun DK, Hanson CA. Gamma/delta T-cell post transplantation lymphoproliferative disorder primarily in the spleen. *Am J Clin Pathol.* 1994;102:310-5.
4. Salhany KE, Feldman M, Peritt D, Nowell PC. Cytotoxic T-lymphocyte differentiation and cytogenetic alterations in gamma delta hepatosplenic T-cell lymphoma and posttransplant lymphoproliferative disorders. *Blood.* 1997;89:3490-1.
5. Roelandt PR, Maertens J, Vandenberghe P, Verslype C, Roskams T, Aerts R, et al. Hepatosplenic gamma delta T-cell lymphoma after liver transplantation: report of the first 2 cases and review of the literature. *Liver Transplant.* 2009;15(7):686-92.
6. Rothenberg ME, Weber WE, Longtine JA, Hafler DA. Cytotoxic gamma delta I lymphocytes associated with an Epstein-Barr virus-induced post transplantation lymphoproliferative disorder. *Clin Immunol Immunopathol.* 1996;80(3):266-72.
7. Ozaki S, Ogasahara K, Kosaka M, Inoshita T, Wakatsuki S, Uehara H, et al. Hepatosplenic gamma delta T-cell lymphoma associated with hepatitis B virus infection. *J Med Invest.* 1998;44:215-7.
8. Gaulard P, Jaffe E, Krenacs L, Macon WR. Hepatosplenic T-cell lymphoma. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, eds. WHO classification of tumours of hematopoietic and lymphoid tissues. 4<sup>th</sup> ed. Lyon: IARC; 2008:292-293.
9. Farcet JP, Gaulard P, Marolleau JP, Le Couedic JP, Henni T, Gourdin MF, et al. Hepatosplenic T-cell lymphoma: sinusal/sinusoidal localization of malignant cells expressing the T-cell receptor gamma delta. *Blood.* 1990;75:2213-9.
10. Gaulard P, Bourquelot P, Kanavaros P, Haioun C, Le Couedic JP, Divine M, et al. Expression of the

- alpha/beta and gamma/delta T-cell receptors in 57 cases of peripheral T-cell lymphomas. Identification of a subset of gamma/delta T-cell lymphomas. *Am J Pathol.* 1990;137(3):617-28.
11. De Wolf-Peeters C, Achten R. Gamma delta T-cell lymphomas: a homogeneous entity? *Histopathol.* 2000;36(4):294-305.
  12. Allory Y, Challine D, Haioun C, Copie-Bergman C, Delfau-Larue MH, Boucher E, et al. Bone marrow involvement in lymphomas with hemophagocytic syndrome at presentation: a clinicopathologic study of 11 patients in a Western institution. *Am J Surg Pathol.* 2001;25(7):865-74.
  13. Gaulard P, Belhadj K, Reyes F. Gamma delta T-cell lymphomas. *Semin Hematol.* 2003;40(3):233-43.
  14. 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.
  15. Swerdlow S, McColl K, Rong Y, Lam M, Gupta A, Distelhorst CW. Apoptosis inhibition by Bcl-2 gives way to autophagy in glucocorticoid-treated lymphocytes. *Autophagy.* 2008;4(5):612-20.
  16. Weidmann E. Hepatosplenic T cell lymphoma. A review on 45 cases since the first report describing the disease as a distinct lymphoma entity in 1990. *Leukaemia.* 2000;14(6):991-7.
  17. Iannitto E, Tripodo C. How I diagnose and treat splenic lymphomas. *Blood.* 2011;117(9):2585-95.
  18. Vega F, Medeiros LJ, Gaulard P. Hepatosplenic and other gamma delta T-cell lymphomas. *Am J Clin Pathol.* 2007;127(6):869-80.

**Cite this article as:** Maheshwari U, Mahore K, Pereira E, Dhar R.  $\gamma\delta$  T-cell lymphoma: a rare entity mimicking hemophagocytic syndrome-report of two cases. *Int J Res Med Sci* 2017;5:3751-4.