Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Annals of Experimental Biology, 2022, 10 (6): 85-87

(http://www.scholarsresearchlibrary.com)

ISSN:2348-1935

Soporific and Humdrum-Monomorphic Epitheliotropic Intestinal T Cell Lymphoma

Anubha Bajaj*

Department of Pathology, Panjab University, Chandigarh, India

***Corresponding Author:** Anubha Bajaj, Department of Pathology, Panjab University, Chandigarh, India*

E-mail: anubha.bajaj@gmail.com

***Received:** 18-Nov-2022, Manuscript no. AEB-22-80403; **Editor assigned:** 21-Nov-2022, Pre QC no. AEB-22-80403 (PQ); **Reviewed:** 23-Nov-2022, QC no. AEB-22-80403 (Q); **Revised:** 25-Nov-2022, Manuscript no. AEB-22-80403 (R); **Published:** 31-Nov-2022*

INTRODUCTION

Monomorphic Epitheliotropic Intestinal T- Cell Lymphoma (MEITL) is an exceptional, aggressive, primary intestinal T cell lymphoma emerging from mature intestinal intraepithelial T-lymphocytes with a preceding nomenclature of Type II Enteropathy-Associated T-cell Lymphoma (EATL type II) or enteropathy-associated T-cell lymphoma type II, the lymphoma lacks association with celiac disease. The infrequently discerned primary T-cell lymphoma is constituted of monomorphic, miniature to medium T-lymphocytes expressing gamma/delta T-cell receptors and comprises an estimated <5% of malignant, primary gastrointestinal lymphomas. Monomorphic epitheliotropic intestinal T-cell lymphoma manifests an inferior clinical outcome with an average over-all survival of ~10 months [1,2].

The lymphoma is preponderantly discerned within Asians or Hispanics whereas Caucasians are uncommonly implicated. The median age of disease emergence is the sixth decade. A male preponderance is observed with male to female proportion of 2:1. Monomorphic epitheliotropic intestinal T cell lymphoma commonly arises within the small bowel as jejunum followed in frequency by the ileum. Of obscure aetiology, neoplastic T cells engendering monomorphic epitheliotropic intestinal T cell lymphoma are posited to arise from intestinal intraepithelial lymphocytes [1,2].

Neoplastic lymphocytes demonstrate a phenotype of CD8+, CD56+ and Megakaryocyte-Associated Tyrosine Kinase (MATK) which contributes to lymphomagenesis. Besides, altered T-Cell Receptor (TCR) signalling may engender lymphoma [1,2]. Aberrant overexpression of SYK occurring due to hypo-methylation of SYK promoter induces anomalous proliferation of intestinal intraepithelial T lymphocytes.

Chromosomal alterations appear pathogenic along with chromosomal copy number variations, gains within chromosomal region 9q33-q34 and amplification of chromosome locus 8q24 with consequent neoplastic cellular proliferation. Characteristically, activating mutations of the *JAK/STAT* pathway with genetic mutations of *STAT5B* are commonly discerned. Besides, genomic mutations within *JAK3*, *GNAI2*, *CREBBP* and *SETD2* genes appear to contribute to the pathogenesis of monomorphic epitheliotropic intestinal T-cell lymphoma [1,2].

Whole genome sequencing appears confirmatory for evaluating cytogenetic and molecular mutations encountered within *CREBBP, STAT5B, SETD2, GNAI2, JAK3 and AXSL3* genes. Monomorphic epitheliotropic intestinal T cell lymphoma commonly manifests extra signals for the MYC gene denominated at chromosome 8q24. Besides, gains at chromosome 9q34.3 discernible with Fluorescent *In Situ* Hybridization (FISH) and copy number analysis are observed. Additionally, aberrations such as gain at chromosomes 1q32.3, 4p15.1, 5q34, 7q34, 8p11.23, 9q22.31, 9q33.2, 8q24 (MYC locus) and 12p13.31 and losses at chromosome 7p14.1 and 16q12.1 are discerned.

The majority (>90%) of instances delineate chromosomal mutations within SETD2 whereas STAT5B appears mutated upon whole exome sequencing. *JAK3* and *GNAI2* genes appear mutated. Overexpression of Spleen Tyrosine Kinase (SYK) ensues, possibly due to hypo-methylation of SYK promoter [1,2].

Monomorphic epitheliotropic intestinal T-cell lymphoma commonly exhibits nonspecific clinical symptoms such as altered bowel habits, chronic abdominal pain, chronic diarrhoea or weight loss. Besides, complications such as intestinal obstruction, gastrointestinal perforation or haemorrhage may ensue. B clinical symptoms manifesting fever, night sweats or >10% loss of body weight are commonly encountered.

Upon gross or endoscopic examination, neoplasm represents mucosal ulceration with granular configuration, nodules, plaques, diffuse mucosal thickening, intestinal strictures or enlarged singular or multifocal tumour masses. Generally, gastrointestinal malabsorption or celiac disease is absent. Macroscopically, features are concordant to the tumour stage and vary from oedematous or granular mucosa, diffuse thickening of the gastrointestinal wall or tumefaction along with or devoid of mucosal ulceration. Tumour magnitude varies from sub-centimetres to a few centimetres.

Upon microscopy, neoplastic lymphocytes occur as monotonous cells of intermediate magnitude imbued with the scanty rim of pale staining cytoplasm, spherical nuclei with mildly irregular nuclear contour, dispersed chromatin and inconspicuous nucleoli (Figure 1 and 2). Characteristically, lymphoma exhibits prominent epitheliotropism along with transmural tumour cell infiltrate. Inflammatory cell infiltration is minimal, except within the foci of mucosal ulceration (Table 1).

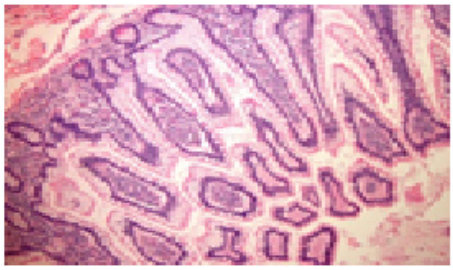

Figure 1. Monomorphic epitheliotropic intestinal T cell lymphoma demonstrating epithelial infiltration of atypical small to medium lymphocytes with scanty cytoplasm, spherical nuclei, dispersed chromatin and inconspicuous nuclei. Focal red cell extravasation is seen

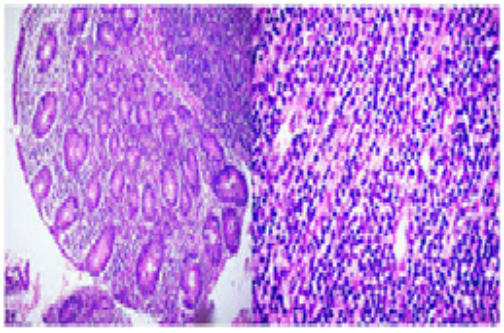

Figure 2. Monomorphic epitheliotropic intestinal T cell lymphoma delineating mucosal infiltration of small to intermediate atypical lymphocytes with minimal cytoplasm, spherical nuclei, dispersed chromatin and invisible nucleoli

Table 1. Modified WHO classification of primary extra-nodal and leukemic mature T cell neoplasms

Disorder	Alterations	Significance
T cell lymphomas of the gastrointestinal tract	EATL	EATL type I associated with celiac disease
	MEITL	EATL type II non-concurrent with celiac disease
	Indolent TLPD of gastrointestinal tract	Indolent clinical behaviour with occasional progression
Cutaneous T-cell lymphoma	Primary cutaneous CD4+ small/medium TLPD	Indolent biological behaviour
	Primary cutaneous acral CD8+ T cell lymphoma	Indolent clinical behaviour, incriminating the ear
	Primary cutaneous δγT cell lymphoma	Elimination of lymphomas with δγ T cell phenotype as MF or LyP.
EBV+ NK/T cell neoplasms	Systemic EBV+ T cell lymphoma of childhood	Lymphoma with aggressive clinical behaviour
	Hydro a vacciniforme-like lymphoproliferative disorder	Lymphoproliferative disorder reflects wide spectrum of clinical behaviour
WHO: World Health Organization, EATL: enteropathy associated T cell lymphoma, MEITL: monomorphic epitheliotropic intestinal T cell lymphoma, MF: mycosis fungoides, LyP: lymphomatoid papulosis, TLPD: T cell lymphoproliferative disorder, EBV: Epstein Barr virus, NK: natural killer cell, δγ: gamma/delta.		

Monomorphic epitheliotropic intestinal T cell lymphoma is immune reactive to CD3, CD8, CD56, T cell intracellular antigen (TIA1), granzyme B and aberrantly immune reactive to CD20. Besides, diverse cytotoxic markers may be variably expressed. Monomorphic epitheliotropic intestinal T-cell lymphoma is immune and non-reactive to CD2, CD4, CD5, PAX5 or CD30.

Upon flow cytometry, neoplastic lymphocytes manifest surface CD3, CD56, granzyme B or T cell receptor gamma /delta(TCRδγ). Molecules such as CD4, CD8, surface T cell receptor alpha/beta (TCRαβ) or cytoplasmic perforin are absent. Also, a subset of neoplasms may lack manifestation of TCRδγ or TCRαβ and are designated as 'silent TCR'[3,4]. Monomorphic epitheliotropic intestinal T cell lymphoma requires segregation from neoplasms such as enteropathy-associated T cell lymphoma, intestinal T cell lymphoma not otherwise specified (NOS), indolent T cell lymphoproliferative disorder of gastrointestinal tract, extra-nodal NK/T cell lymphoma, peripheral T cell lymphoma not otherwise specified (NOS) with intestinal spread or mycosis fungoides with gastrointestinal involvement.

Appropriate discernment of monomorphic epitheliotropic intestinal T-cell lymphoma necessitates cogent clinical and pathological concurrence [3,4]. Incriminated subjects devoid of a history of celiac disease represent chronic abdominal pain, diarrhoea and associated symptoms. Abdominal imaging can be suitably obtained with techniques such as abdominal ultrasonography, Computerized Tomography (CT) along with or devoid of contrast enhancement, Magnetic Resonance Imaging (MRI) and endoscopy. Endoscopic assessment exemplifies fine granularity or diffuse thickening of mucosa along with semicircular, shallow mucosal ulcerations.

Abdominal Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI) enunciates the thickening of the bowel wall and mesenteric lymphadenopathy [3,4]. Surgical tissue sampling demonstrates monomorphic, neoplastic lymphocytes delineating aberrant T cell phenotype which appear immune reactive to CD3, CD8, CD56, TIA1 and T cell receptor gamma or delta. Elimination of celiac disease may be obtained by demonstrating immune non-reactive endomysial antibodies, and human leukocyte antigen DQ2 or DQ8 (HLA DQ2 or HLA DQ8) [3,4].

Computerized Tomography (CT) of the abdomen may demonstrate tumefaction encircling the small bowel along with thickened intestinal wall or distension of the small bowel on account of gastrointestinal obstruction and ascites. Gastrointestinal perforation exhibits free air under the diaphragm. Mesenteric lymphadenopathy is indicative of neoplastic dissemination and metastasis [3,4].

Apart from surgical tumour eradication, monomorphic epitheliotropic intestinal T-cell lymphoma can be appropriately treated by regimens such as cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone(CHOEP), cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP 14/CHOP21), dose adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin (EPOCH), hyper-fractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone (hyper-CVAD) or rituximab, methotrexate, cytarabine (R-MTX-Ara-C) [3-5]. Besides, stem cell transplantation can be advantageously employed.

Monomorphic epitheliotropic intestinal T-cell lymphoma represents an overall inferior prognostic outcome. On account of the absence of specific, targeted therapy, the estimated average survival is ~10 months and median survival is ~7 months [3,4].

REFERENCES

1. Muramoto, K., et al., Rare monomorphic epithelial intestinal T-cell lymphoma of the stomach with a giant gastric perforation rescued by liver-covering sutures followed by a total gastrectomy and lateral hepatectomy: a case report. *Surgical Case Reports*, **2022**.8(1):1-7.
2. Zhong, H., Zheng, Y. and Zhang, F., Monomorphic epitheliotropic intestinal T-cell lymphomas: a case report. *Diagnostic Pathology*, **2021**. 16(1):1-5.
3. Veloza, L., et al., Monomorphic epitheliotropic intestinal T-cell lymphoma comprises morphologic and genomic heterogeneity impacting outcome. *Haematologica*, **2020**.
4. Fukushima, M., et al., Initial and advanced endoscopic findings of monomorphic epitheliotropic intestinal T-cell lymphoma in the duodenum: A case report. *DEN Open*, **2022**. 2(1):p. e118.
5. Du, Q., et al., Methyl-CpG-binding domain proteins: readers of the epigenome. *Epigenomics*, **2015**.7(6) : p. 1051-73.