

Leukaemia Section

Short Communication

Mediastinal Gray Zone Lymphoma

Luis Miguel Juárez Salcedo, Samir Dalia

Principe de Asturias University Hospital, Madrid, Spain (LMJS); Oncology and Hematology, Mercy Clinic Joplin, Joplin, MO, USA (SD). Dr.luisjuarez@gmail.com; sdalia@gmail.com

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Abstract

Review on Mediastinal gray zone lymphoma, with data on the genes involved.

Keywords

Unclassified B-cell Lymphoma, mediastinal gray zone lymphoma, primary mediastinal B-cell lymphoma, nodular sclerosis Hodgkin lymphoma.

Identity

Other names

MGZL (mediastinal gray zone lymphoma)

Clinics and pathology

Disease

The new WHO lymphoma classification introduced the provisional category of B-cell lymphoma, unclassifiable with features that are intermediate between diffuse large cell lymphoma (DLBCL) and classical Hodgkin lymphoma (CHL) to encompass cases that do not fulfill the morphological and/or phenotypic criteria for primary mediastinal B-cell lymphoma (PMBL) or nodular sclerosis Hodgkin lymphoma (NSHL) in the mediastinum but exhibit transitional features between these two entities. (Swerdlow S, et al., 2008; Savage KJ, et al., 2003; Rosenwald A, et al., 2003).

Mediastinal gray zone lymphoma (MGZL) is a rare and new entity that shares clinical characteristics with PMBCL and NSHL. Historically, these patients were often included in series of Hodgkin-like anaplastic large cell lymphoma, which is a heterogeneous group. (Zinzani PL, et al., 1998; Grant C, et al., 2011).

Epidemiology

MGZL is more frequently seen in young men, with a median patient age of 30 years. (Traverse-Glehen A, et al., 2005; Rieger M, et al., 2011).

Clinics

The patients present a mediastinal mass larger than 10 cm, and most of 50% of them are associated with elevated LDH. A minority of patients had extranodal involvement or pleural or pericardial effusions. Also, patients had low peripheral blood absolute lymphocyte counts (ALCs) at the time of presentation. (Poppema S et al., 2005).

Treatment

Their indeterminate pathobiology has led to uncertainty about what the optimal therapeutic strategy should be in MGZL. MGZLs are often found to be refractory to different chemotherapy regimens used in either DLBCL or CHL such as R-CHOP, R-CHOEP, ABVD, BEACOPP. Although patients with MGZL have been treated as aggressively as patients with B-cell lymphoma, they generally exhibit worse outcomes than patients with PMBCL. (Wilson W, et al., 2014; Song H, et al., 2016).

Lacking other options either R-CHOP or DA-EPOCH-R have been regarded as the most suitable treatments courses for patients with MGZL since those who did not receive these regimen as frontline therapy displayed disease progression.

For relapses, salvage chemotherapy followed by high-dose stem cell transplantation may be considered. Allogeneic transplantation is another option, but outcomes in patients with MGZL are inferior to that of PMBL.

Prognosis

The association of a Hodgkin-like microenvironment and the poor outcomes in MGZL raise the hypothesis that a predominant HL-like morphology and/or phenotype may also be associated with a worse outcome.

Additionally, the intensity of CD15, CD68, CD209 or Bcl-6 staining on the malignant MGZL cells is associated with poor prognosis. (Wilson W, et al., 2014, Song H, et al., 2016).

Genetics

Note

Gains of 2p15, 9p24 and 12q24 were detected by PCR amplification in PMBL and NSHL tumor cells, supporting the hypothesis of pathogenic relationship between these two entities. (Joos S, et al., 1996; Joos S, et al., 2000).

In PMBL and in NSHL tumor cells, within the smallest commonly amplified regions (2p15 and 9p24), two genes were identified, the REL and JAK2 oncogenes. REL is involved in the NF- κ B signaling pathway, which has been shown to be deregulated in cHL before. JAK2, which is important for cytokine signaling, plays a crucial role in PMBL and NSHL pathogenesis. (Joos S, et al., 2003).

On the basis of a gene expression analysis it has been identified that a dendritic cell gene expression signature that distinguished MGZL and NSHL from PMBL. This signature includes CD209, which encodes DC-SIGN, a marker of dendritic cells and activated macrophages. Interestingly, DC-SIGN gene expression was significantly associated with poor survival in NSHL, suggesting that it may be a biomarker of macrophage activity in MGZL. (Dunleavy K, et al., 2013; Wilson W, et al., 2014). MGZL shows a methylation profile related to but different from that of both PMBL and NSHL. The profile falls somewhere between the methylation profile of PMBL and NSHL. A unique feature found in MGZL is the hypomethylation of HOXA5 (DNA-binding transcription factor which may regulate gene expression, morphogenesis, and differentiation), but the importance of this finding for the pathogenesis of MGZL is still unknown.

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