

Intravascular large B cell lymphoma

Biji .K A^{1*}, K R Leenadevi²

¹Senior Consultant, ²Hon. Senior Consultant, Dept. of Pathology, KIIMS Hospital, Trivandrum, Kerala, India

Article Info

Received: 25th October, 2018

Accepted: 13th February, 2019

Published Online: 9th August, 2019

Keywords: Vascular, Lymphoma, B cell.

Abstract

Intravascular Large B Cell Lymphoma (IVLBCL) is a unique subset of Diffuse Large B cell lymphoma. No randomised trials have been done on IVBCL till date as this a very rare type of Non Hodgkin Lymphoma. The clinical presentations are varied. The awareness about the disease and a high index of suspicion are required to diagnose a case of IVBCL. We report a case of 71 year old lady who was extensively investigated for fever of unknown origin, and finally one vessel in the bone marrow biopsy showed Intravascular Large B Cells.

Introduction

Intravascular large B cell lymphoma (IVLBCL) is a rare type of extranodal large B cell lymphoma. Large lymphoid cells are seen within the lumina of blood vessels especially capillaries, with the exception of larger arteries and veins.¹ IVLBCL was first described 50 years back, but for pathologists and oncologists, IVBCL continues to be a diagnostic and therapeutic challenge.^{2,3} Delay of timely and accurate diagnosis due to the varied clinical presentation adds to the poor prognosis of IVBCL. We report a case of 71 year old lady who was brought to our centre in shock.

Case Report

71 year old lady was brought to the emergency department of our hospital in shock. Patient had fever for the past one month, and had thrombocytopenia.

As a part of extensive investigations done to know the cause of fever with thrombocytopenia, bonemarrow aspiration and biopsy were also done. The peripheral blood smear showed neutrophilic leucocytosis and bonemarrow aspiration smears showed normal marrow elements.

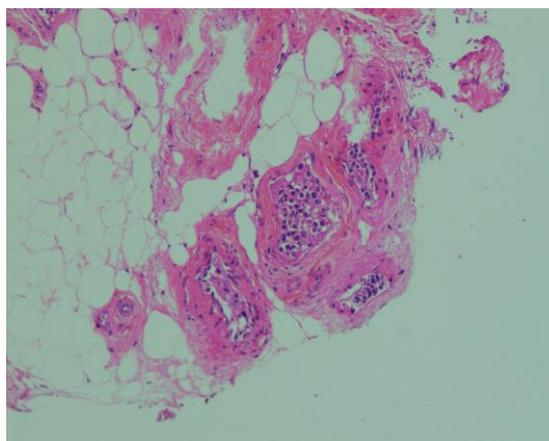


Fig. 1: Bonemarrow biopsy showing vessels with large cellsx40

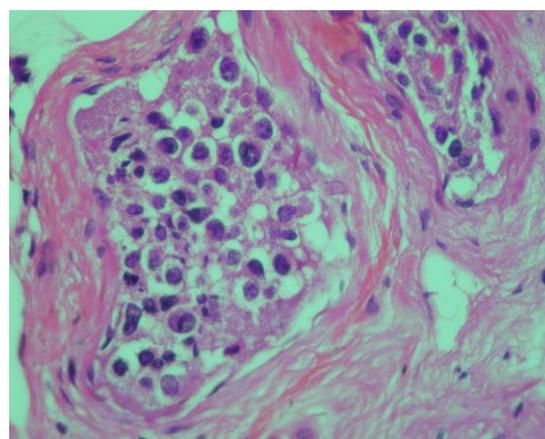


Fig. 2: Vessels filled with large cells x400

*Corresponding Author: Biji .K A, Senior Consultant, Dept. of Pathology, KIIMS Hospital, Trivandrum, Kerala, India
Email: drbijipath@gmail.com
<http://doi.org/10.18231/j.ijpo.2019.098>

Bone marrow biopsy had six small fragments of which five were showing only cartilage and one showed fibroadipose tissue with dilated blood vessels. These vessels were filled with large cells showing vesicular nuclei and single nucleoli. The large cells were limited to the vascular lumina and were not seen outside. Bonemarrow tissue was very scanty and showed foci of hemophagocytosis. The peripheral smear and bonemarrow smears were reviewed and occasional atypical cells were seen. On immunohistochemistry on bone marrow biopsy, these cells were positive for CD20, and negative for CD3, CD30, ALK and Cytokeratin.

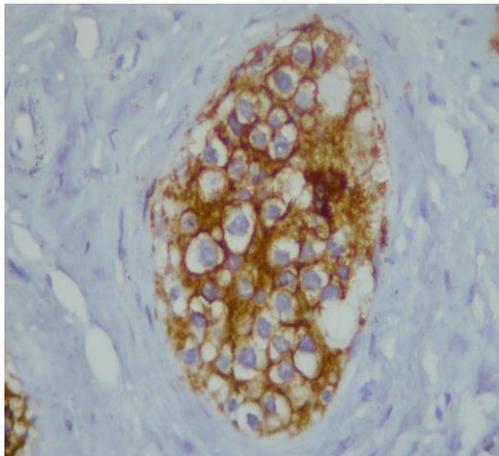


Fig. 3: CD 20 positive large cellsx400

Treatment and Follow up-The patient was not physically fit for starting chemotherapy. She expired on the second day of admission before the final Immunohistochemistry report was ready.

Discussion

IVLBCL is a unique subset of Diffuse Large B Cell Lymphoma(DLBCL) and is defined as the intravascular proliferation of clonal lymphocytes with little or no involvement of the organ parenchyma.³ Limited study and research were done on this disease mainly due to its rarity.³ The disease was first reported by Pflieger and Tappeiner from Germany in 1959 and was described as “angioendotheliomatous proliferans systemisata”.³ We have not acquired much knowledge on this disease even after 59 years.³ Very less case reports have been published due to the rarity of the disease, the incidence is less than one person per million.³ Randomised case studies or research have not been done as the numbers are less and the available information is mainly from individual case reports.³ Prognosis is bad and to make an antemortem diagnosis is difficult in most of the cases. The incidence is so less that a practicing oncologist and pathologist may encounter a case of IVL only once or twice in a career.³

IVLBCL has varied clinical presentation and can affect the small vessels of almost all organs.³ However, the lymphnodes are not involved by the neoplasm usually.¹ The neoplastic cells are limited to the vessels and the surrounding

soft tissue is not infiltrated. This feature along with the sparing of the lymph nodes and reticuloendothelial system is a hallmark of the disease. Due to this feature the patient will not have significant lymphadenopathy, hepatosplenomegaly or malignant cells in peripheral blood. This makes a timely diagnosis of lymphoma very difficult.³

Previously IVLBCL was classified into a Western form and an Asian variant. But recent classification as per WHO is into a classic form and a Hemophagocytic syndrome associated form.¹ The classic form mainly presents with neurological and cutaneous symptoms and the hemophagocytic syndrome associated form presents with multiorgan failure, hepatosplenomegaly and pancytopenia. B symptoms are very common in both the types, especially fever, as in our patient. Fever of unknown origin is seen in 55-76% cases.³ Extensive investigations for the cause of fever delays the diagnosis in many patients. Our patient was diagnosed after extensive investigations for one month and she passed away one day before the final diagnosis was made.

One rare variant is also suggested which is identified almost exclusively in Western females. This variant is associated with a better prognosis.

IVLBCL lacks detectable tumour masses and conventional staging procedures lead to a false negative staging. However, experts recommend staging work up with contrasted whole-body computerized tomography scan, contrasted whole-brain magnetic resonance imaging, peripheral blood smear, cerebrospinal fluid cytology and biochemical examination and bone marrow biopsy.⁵ FDG-positron emission tomography may also be useful for the early diagnosis of IVLBCL and can guide biopsies of affected organs. False negatives have been reported especially in skin and bronchial biopsies after FDG-PET.⁶

On immunohistochemistry, the tumour cells are positive for mature B Cell associated antigens like CD19, CD20, CD22, CD79a. A few cases are positive for CD5 and CD10.¹ These cells lack homing receptors like CD 29 and CD 54 adhesion beta-molecules and this is suggested as the reason for the intravascular growth pattern.¹ IVBCL carries poor prognosis except for the isolated cutaneous variant. This is partly due to varied clinical presentation leading to the delay in accurate diagnosis. The survival rate has been improved to 3 year overall survival of 60-81% using chemotherapeutic regimens with Rituximab. CNS relapse is seen in 25% of cases and is a serious complication.¹ If malignant cells of IVLBCL are seen in CSF by cytopathology or on PCR for IgH gene rearrangement, regimens for primary or secondary CNS Lymphoma should be used for treatment. R-CHOP will not penetrate blood brain barrier.³ Transient clinical improvement can be attained by high dose corticosteroids. CNS relapse can be seen in any clinical type and cannot be predicted by any clinical parameters.¹ The isolated cutaneous variant is reported to be associated with better prognosis even though the reported numbers are less. They can be treated by local radiation therapy.³

Early diagnosis and timely representative biopsy is critical for the treatment. Abnormal brain lesions and suspicious skin lesions should be biopsied without delay. In

affected cases, the tumour cells can be seen in the subcutaneous tissue of normal appearing skin. A random skin biopsy should be done in the setting of fever of unknown origin.³ Our case was diagnosed by the cells in the vessels of fibroadipose tissue, present in bone marrow biopsy, which mainly showed cartilage and no marrow spaces. Even though 3 cases of diagnosis in random skin biopsy have been reported, diagnosis in the vessels of fibroadipose tissue present in a bonemarrow biopsy has never been reported. Because of the various modes of presentation and the rarity of IVLBCL, the diagnosis is often made postmortem.³ However, in recent years, the heightened awareness of IVLBCL with appropriate investigations has resulted in more patients being diagnosed during life.⁴ This emphasises the importance of detailed analysis of every tissue fragment in a biopsy. Also the awareness of this diagnosis is important when we analyse a case of pyrexia of unknown origin. A random skin biopsy done in a case of pyrexia of unknown origin can lead to a diagnosis in a case of IVBCL.³

Conflict of Interest: None.

Source of Funding: None.

References

1. Nakamura. S, Ponzoni M, Campo E. Intravascular Large B Cell Lymphoma. In: Swerdlow H Steven, Campo E, Harris L Nancy, editors. WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues. *Int Agency Res Cancer (IARC)* 2017:317-8.
2. Mohammad R, Sohail Q, Shahnaila R, Salil G. Intravascular B cell lymphoma: An elusive diagnosis. *J Clin Oncol* 2012;30(15):e144-e5.
3. Zuckerman D1, Seliem R, Hochberg E. Intravascular lymphoma: the oncologist's "great imitator". *Oncologist* 2006;11:496-502.
4. Garcia-Munoz Ricardo, Rubio-Mediavilla Susana, Robles-de-Castro Diego, Munoz Aura, Herrera-Perez Pilar, Rabasa Pilar. Intravascular large B Cell lymphoma. *Leuk Res Rep* 2014;3(1):21-3.
5. Ponzoni M., Ferreri A.J., Campo E. Definition, diagnosis, and management of intravascular large B cell lymphoma: proposals and perspectives from an international consensus meeting. *J Clin Oncol* 2007;25:3168.
6. Shimada K., Kosugi H., Shimada S. Evaluation of organ involvement in intravascular large B cell lymphoma by 18F-fluorodeoxyglucose position emission tomography. *Int J Hematol* 2008;88:149-53.
7. Shimada K. Treatment strategy for central nervous system involvement in intravascular large B cell lymphoma. *Brain Nerve* 2011;63:467-72.

How to cite this article: Biji KA, Leenadevi KR. Intravascular large B cell lymphoma. *Indian J Pathol Oncol* 2019;6(3):506-8.