Original Research Paper

Volume - 13 | Issue - 02 | February - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Internal Medicine

EBV ASSOCIATED HODGKIN'S LYMPHOMA IN A MIDDLE AGED MALE

Dr.C.Arshad Akeel* MD Gen Med, FRCP Glasg, FRCP Ireland, FRCP Edin, FACP USA , DABTM USA, FCCP USA, FICA USA,Senior Consultant, Department of Internal Medicine, Apollo Hospitals, Greams Road, Chennai Adjunct Professor, The Tamil Nadu Dr.MGR Medical University. *Corresponding Author

Dr.J.Divyalakshmi DNB Internal Medicine Resident, Apollo Hospitals, Greams Road, Chennai.

ABSTRACT Hodgkin's Lymphoma, also known as Hodgkin's disease is an uncommon neoplasm arising from B Lymphocytes. It is a highly curable lymphoid malignancy, with a 5 year overall survival rate of more than 80% in advanced cases. Here we present a case of advanced Hodgkin's lymphoma, in a 46 year old male from Kolkata, presenting as PUO.

KEYWORDS :

INTRODUCTION-

Lymphomas, both Hodgkin's and NHL comprise approximately 5-6% of all malignancies, half of all newly diagnosed hematological tumours (1,2). Hodgkin's Lymphoma is a rare monoclonal lymphoid neoplasm. It is classified into two types. Nodular lymphocyte predominant type and Classical Hodgkin's Lymphoma which is further sub classified into Nodular Sclerosis, Lymphocyte Rich, Lymphocyte Depleted and Mixed Cellularity.

It has a bimodal age distribution , with the first peak between the ages of 20-30 years and second peak at ages older than 50 years and is frequently associated with Epstein Barr Virus(3).

About 80% of the patients have lymphadenopathy above the diaphragm. Fewer than 20% have lymphadenopathy below the diaphragm. Extra nodal lymphomas account for 2-16% of cases . Approximately one-third of the patients present with disease related symptoms such as unexplained fever, night sweats and weight loss (4). Global age standard incidence rate was 0.98 per 1,00,000 population. There is an increasing trend in the incidence of Hodgkin's Lymphoma especially in females and Asian population.

CASE REPORT-

46 year old male patient, from Kolkata, with no known co-morbidities, presented with complaints of fever for the past 45 days, associated with chills and rigors. Fever was high grade and intermittent in nature. Complaints of generalised weakness . Patient also had complaints of nausea and reduced appetite, loss of weight of about 5kgs in past 1 month.

On examination, patient was conscious, oriented and febrile. General Examination and Systemic Examination was unremarkable.

His baseline investigations are given in Table 1. CXR was within normal limits. Transthoracic Echocardiography showed no evidence of vegetations with normal LV function.

Tropical screening for infections including Dengue, Malaria, Leptospirosis and Scrub Typhus were negative. Blood and urine cultures showed no growth.

In view of persistent fever spikes with pancytopenia, Haematologist was involved and BMA and Biopsy was done. Bone Marrow Aspirate showed Hypercellular Marrow with tri-lineage haematopoiesis with plasmacytosis.

Considering plasmacytosis and A-G Reversal , further investigations including S. Protein Electrophoresis, S. Capillary Immunotyping and Free Kappa and Lambda levels were sent. Serum Protein Electrophoresis showed Hypergammaglobulinemia with no evidence of M Band. Serum Capillary Immunotyping showed polyclonal increase of IgG and IgA. Kappa and Lambda ratio were within normal limits.

Vasculitis panel including ANA, ANCA and Anti dsDNA were negative. Bone Marrow Biopsy showed Interstitial and Paratrabecular Lymphohistiocytic Infiltrate with Atypical Mononuclear cells and Fibrosis. Fever Spikes were persistent and therefore, PET CT was done which revealed, Hyper metabolic extensive Lymphadenopathy bilaterally , above and below the diaphragm, Extensive bone marrow deposits and mild Hepatosplenomegaly (Figure1 and 2).

Left Axillary Lymph node Biopsy was carried out by a General Surgeon and sample was sent for analysis. Lymph node X Pert MTb was negative. IHC was suggestive of Classical Hodgkin's Lymphoma, CD 15+ and CD 30+. He was classified as Stage 4B disease in view of extensive involvement of Lymph nodes and Bone Marrow.

Patient was started on ABVD regimen (Doxorubicin, Bleomycin, Vinblastine and Dacarbazine) along with Dexamethasone. Patient tolerated the treatment well and was discharged with stable vitals and planned for dose 1B after 14 days.

DISCUSSION-

Although Lymphoma is one of the major causes of PUO, it has always been a challenge to diagnose a patient presenting with PUO as Lymphoma. PET CT plays a vital role in such situations. PET CT is currently the modality of choice for pretreatment disease localization and response assessment in Hodgkin's Lymphoma.

Staging of Hodgkin's Lymphoma is based on Lugnano's classification, which is derived from the Ann Arbor Staging System.(TABLE2)

Stages 1 and 2 are considered early stages, whereas stages 3 and 4 are considered advanced stage . Patients with advanced CHL should be evaluated with International Prognostic Score. (TABLE 3).The freedom from progression of disease and Overall Survival is calculated based on IPS.(5,6)

The choice of treatment of CHL is based on the stage at presentation and IPS Score. Presence of EBV is generally associated with poor prognosis . Highest percentage of EBV positive cases are in children <10 years and adults >55 years. In a study of 922 patients, EBV was independently associated with increased HL-specific mortality and inferior survival in adults >45 years of age.(7)

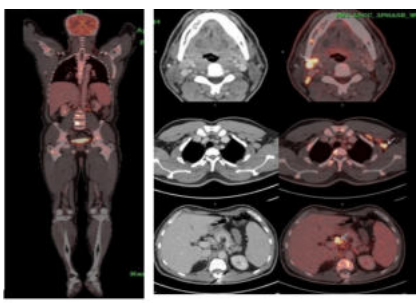
Combination chemotherapy with ABVD, is the preferred treatment modality in most patients with advanced CHL. ABVD is administered 2 weekly once and 2 treatments are considered as one complete cycle. Response to the therapy is assessed after 2 cycles. Approximately 80% of the patients with advanced stage CHL will attain a complete response to treatment with ABVD .(8,9,10) Up to one quarter of the patients will have disease progression requiring further therapy, half of those will have long term survival with Hematopoietic stem cell transplant.

DECLARATION-

Funding- None
Conflict of Interest- None
Ethical Approval- Not required

TABLE1-BASELINEINVESTIGATIONS

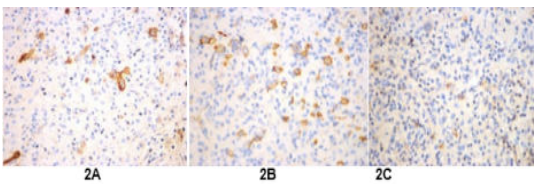
TESTPARAMETERS	PATIENT'SDATA	NORMALRANGE
HEMOGLOBIN	10.7	13-18gm/dl
WBC	3350	4000-11000cells/Microlitre
DIFFERENTIALCOUNTS	NEUTROPHILS-68% EOSINOPHILS-1% BASOPHILS-0% MONOCYTES-14% LYMPHOCYTES-17%	
PLATELETCOUNTS	120	150-450/Microlitre
UREA	18	13-43mg/dl
CREATININE	0.9	0.7-1.3mg/dl
TOTALBILIRUBIN	1.1 CONJUGATED-0.5 UNCONJUGATED-0.6	0.0-1.3mg/dl
AST	38	<35U/L
ALT	126	<46U/L
ALP	194	<128
GGTP	84	<64U/L
ALBUMIN		
GLOBULIN		
LDH	136	125-220U/L
SERUMFERRITIN	681.3	20-250ng/ml
RAFACTOR	<11.2	Negative-<30
HbsAG	Negative	
HIV	Negative	
AntiHCV	Negative	



1A 1B

FIGURE 1A- PET-CT -Increased uptake in multiple levels of lymph nodes above and below diaphragm, hepatosplenomegaly and extensive bone marrow deposits

FIGURE 1B- Hypermetabolic cervical, axillary and periportal lymph nodes



2A 2B 2C

FIGURE 2 : IHC 2A-CD15+ 2B-CD30+ 2C-EBV+

TABLE2- LUGNANO'SCLASSIFICATION

STAGE1	Involvement of a single Lymph Node region(I) or of a single Extra lymphatic organ or site Without nodal involvement.
STAGE2	Involvement of two or more Lymph node regions on the same side of the diaphragm alone (II) or with involvement of limited contiguous Extra lymphatic organ.
STAGE3	Involvement of lymph node regions or lymphoid structures on both Sides of the diaphragm.
STAGE4	Additional non-contiguous extra lymphatic involvement, with or without associated lymphatic involvement.

The International Prognostic Score for Hodgkin lymphoma

One point is given for each of the characteristics below present in the patient, for a total score ranging from zero to seven
Serum albumin <4 g/dL
Hemoglobin <10.5 g/dL
Male gender
Age >45 years
Stage IV disease
White blood cell count ≥15,000/microL
Absolute lymphocyte count <600/microL and/or <8 percent of the total white blood cell count

TABLE 3-INTERNATIONALPROGNOSTICSCORE

REFERENCES-

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65:5–29.
2. Razek AAKA, Shamaa S, Lattif MA, Yousef HH. Inter-Observer Agreement of Whole-Body Computed Tomography in Staging and Response Assessment in Lymphoma: The Lugano Classification. Pol J Radiol.2017;82:441–447.
3. Brice, Pauline et al. "Classical Hodgkin lymphoma." Lancet (London,England) vol.39810310(2021):1518-1527.doi:10.1016/S0140- 6736(20)32207-8.
4. Ellen Mullen, Yazhen Zhong, Hodgkin Lymphoma: An Update, The Journal for Nurse Practitioners, Volume 3,Issue 6,2007,Pages393-403,ISSN 1555-4155.
5. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med1998;339:1506.
6. Moccia AA, Donaldson J, Chhanabhai M, et al. International Prognostic Score in Advanced-stage Hodgkin's Lymphoma: Altered Utility in the Modern Era. J Clin Oncol 2012;30:3383.
7. Keegan TH, Glaser SL, Clarke CA, et al. Epstein Barr virus as a marker of survival after Hodgkin's lymphoma: a population-based study. J Clin Oncol 2005;23:7604.
8. Bonadonna G, Zucali R, Monfardini S, et al. Combination chemotherapy of Hodgkin's disease with adriamycin, bleomycin, vinblastine, and imidazole carboxamide versus MOPP. Cancer 1975;36:252.
9. Canellos GP, Anderson JR, Propert KJ, et al. Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Engl J Med 1992;327:1478.
10. Somers R, Carde P, Henry-Amar M, et al. A randomized study in stage IIIB and IV Hodgkin's disease comparing eight courses of MOPP versus an alteration of MOPP with ABVD: a European Organization for Research and Treatment of Cancer Lymphoma Cooperative Group and Groupe Pierre-et-Marie-Curie controlled clinical trial. J Clin Oncol 1994;12:279.