ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24MAY2008

Clinical Approach to Advanced Mantle Cell Lymphoma: A Detailed Case Analysis

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Abstract:- Mantle cell lymphoma (MCL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL) originating from cells in the mantle zone. Herein, we present a case report of a 49-year-old male patient diagnosed with stage VI MCL, illustrating various diagnostic methods and procedures utilized in his evaluation. The patient presented with progressively enlarging cervical lymph nodes, fatigue, weight loss, anorexia, chronic diarrhea, abdominal pain, and rectal bleeding. Clinical examination revealed cutaneomucosal pallor, tachycardia, expiratory polypnea, bilateral jugulocarotid adenopathies, and splenomegaly. Laboratory investigations showed normocytic normochromic anemia, hyperleukocytosis, lymphocytic predominance, and thrombocytopenia. Peripheral blood smear analysis indicated a lymphoproliferative disorder, confirmed by flow cytometry revealing monotypic lymphoid cells. Bone marrow biopsy showed hypoplastic marrow with atypical cells. Immunohistochemistry confirmed mantle cell lymphoma localization. Subsequent thoraco-abdomino-pelvic CT scan revealed mediastinal and abdominal adenopathy with splenomegaly, leading to a diagnosis of stage IV MCL. The case highlights the importance of early and comprehensive diagnostic approaches in MCL management.

Keywords:- *Mantle Cell Lymphoma; Diagnosis; Rare; Case Report.*

I. INTRODUCTION

Mantle cell lymphoma (MCL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL) originating from cells in the "mantle zone." This zone comprises the outer ring of small lymphocytes surrounding the central area of a lymphatic nodule(1–3). It is often diagnosed at an advanced stage of disease, frequently involving the gastrointestinal tract and bone marrow(4,5). More than 90 percent of patients with MCL exhibit overproduction of a protein called cyclin D1 in the lymphoma cells(6,7). Here, we present the case of a young male patient diagnosed with stage VI MCL, highlighting the various diagnostic methods and procedures employed in his evaluation.

II. CASE REPORT

A 49-year-old male patient, devoid of significant personal or familial medical history, presented with a chief complaint of progressively enlarging cervical lymph nodes over a two-month period. Notably, these nodes were non-compressive and lacked associated symptoms such as hoarseness, dyspnea, or dysphagia. Concurrently, the patient experienced fatigue, weight loss, anorexia, chronic diarrhea, and abdominal pain. Furthermore, one week prior to seeking emergency care, rectal bleeding emerged, further complicating his clinical presentation.

General examination unveiled cutaneomucosal pallor, tachycardia, and expiratory polypnea, which resolved following saline solution administration. Examination of the cervical lymph nodes revealed multiple large bilateral jugulocarotid adenopathies. Additionally, splenomegaly was noted, along with tenderness upon palpation of the colonic framework, and rectal examination revealed blood-soaked findings.

Considering these symptoms, a blood count was ordered, revealing normocytic normochromic anemia (Hemoglobin 8.3 g/dl; Mean corpuscular volume (MCV) 91 fl; Mean corpuscular hemoglobin (MCH) 29 pg.) with a hyperleukocytosis of 144,270 per cubic millimeter, predominantly lymphocytic (139,942 per cubic millimeter), and thrombocytopenia of 104,000 per cubic millimeter.

Peripheral blood smear analysis indicated a peripheral hyperlymphocytosis with a monomorphic appearance of small mature lymphocytes, rare prolymphocytes, and a few Gumprecht shadows, suggestive of a lymphoproliferative disorder (figure 1).

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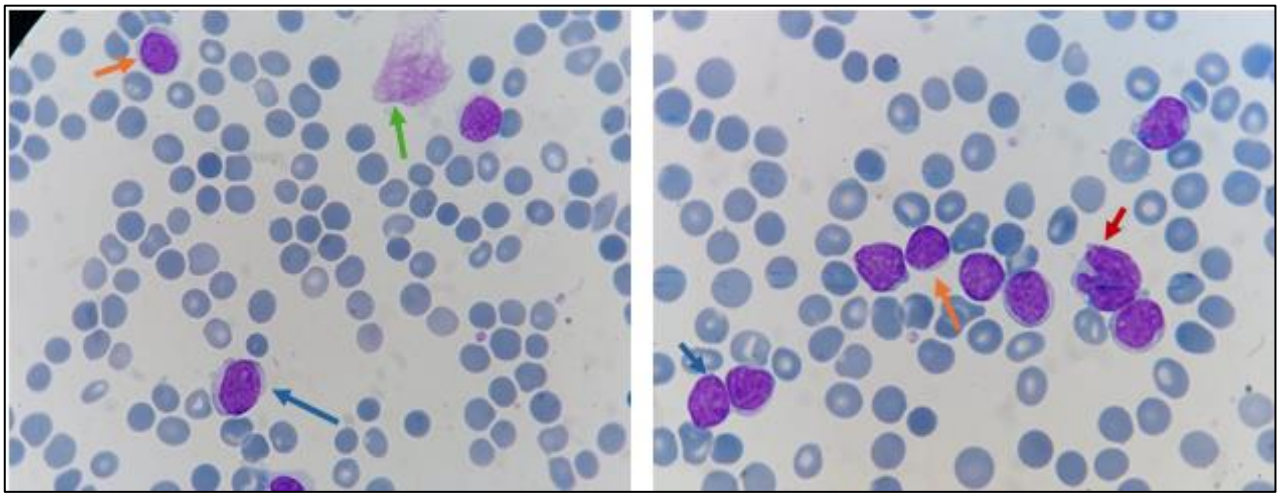

Fig 1: Microscopic Image of the Blood Smear Showing Small Mature Lymphocytes (Orange Arrows), Prolymphocytes (Blue Arrows), Gumprecht Shadows (Green Arrow), And Lymphomatous Cells Suggesting Mantle Cell Lymphoma (Red Arrow).

Cytometry revealed monotypic lymphoid cells with specific markers (CD19 +, CD23 -, CD43 +, FMC +, CD79b +, CD200 -, CD20 +, CD38 +) and kappa light chain present; Matutes score 1/5. Blood smear showed medium to large atypical lymphoid cells with irregular nuclei, scattered chromatin, conspicuous nucleoli, and moderately basophilic cytoplasm of variable size. A bone marrow biopsy was performed in the presence of anemia, showing marrow richness of 2 to 3. All 3 lineages were hypoplastic with minor maturation disorders. Rare medium-sized scattered cells with discreetly hyperchromic nuclei were observed.

Immunohistochemistry revealed: anti-Bcl2 +++, anti-CD5 +++, anti-CD20+++, anti-Cyclin D1 +++, anti-Ki-67 positive on 20% of tumor cells, anti-CD10 and anti-CD3 negative, concluding a medullary localization of mantle cell lymphoma (figure 2).

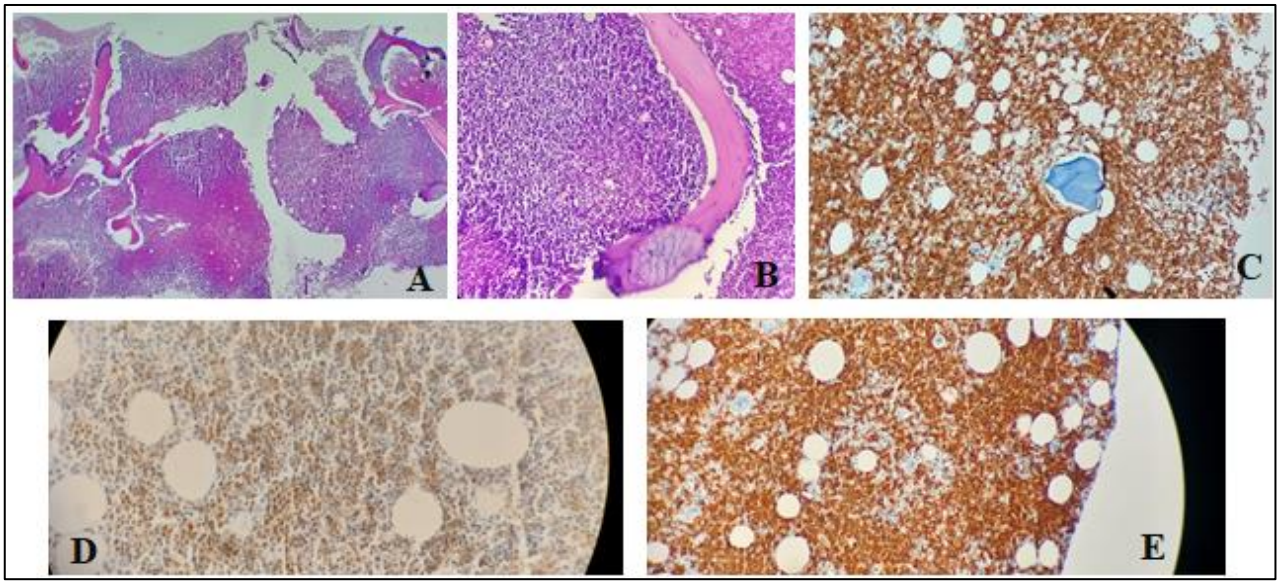

Fig 2: Image Under Optical Microscope With Standard Hematoxylin-Eosin Staining And Immunohistochemistry: A Magnification HE X40, B Magnification HE X60, C Positive Immunohistochemistry For CD20, D Positive Immunohistochemistry For Cyclin D1, E Positive Immunohistochemistry For Bcl-2.

Subsequent diagnostic colonoscopy disclosed multiple colonic polyps with inflammatory mucosa (Figure 3), although biopsies were inconclusive.

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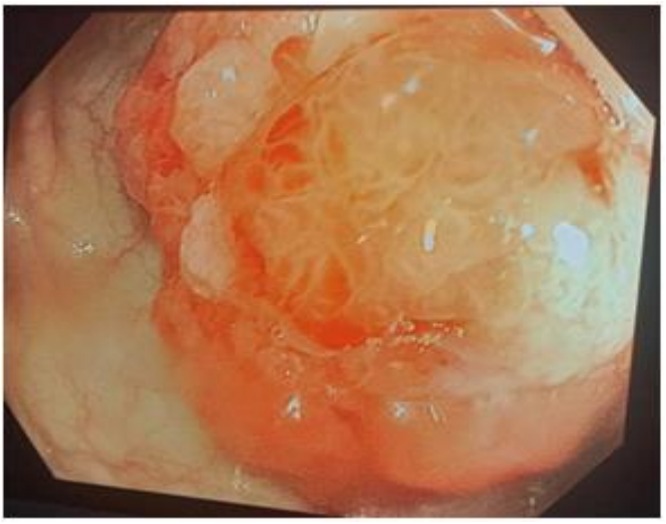

Fig 3: Image Taken During the Colonoscopy, Showing a Polypoid Mass in the Colonic Mucosa.

Further investigation via thoraco-abdomino-pelvic CT scan unveiled mediastinal and abdominal adenopathy in conjunction with splenomegaly (Figure 4-5).

Based on the findings, the patient was diagnosed with mantle cell lymphoma, Ann Arbor stage IV. Consequently, the patient was referred to the hematology department for further management.

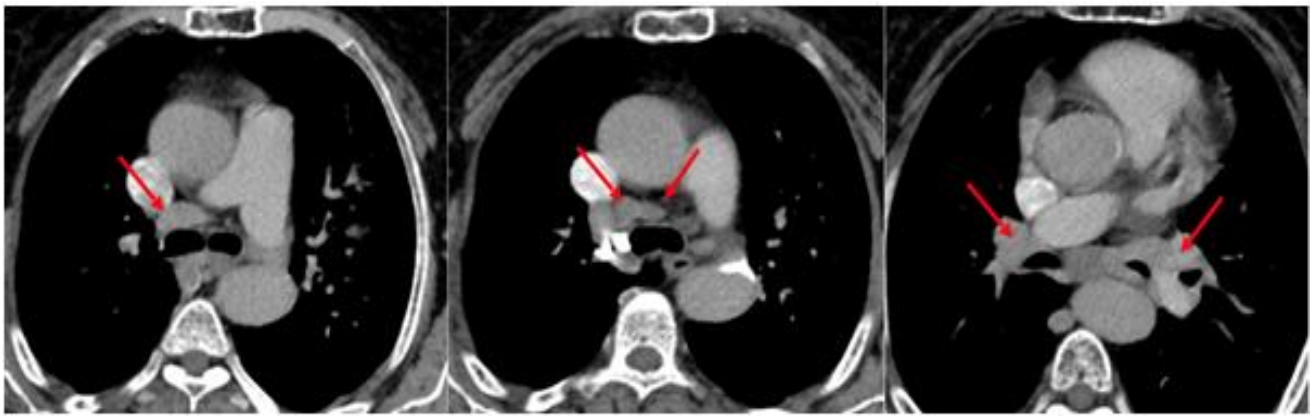

Fig 4: Abdominal CT Scan, Multiple Lymphadenopathies of The Celiac, Gastric, Para-Aortic, And Retrocaval Chains (Arrow).

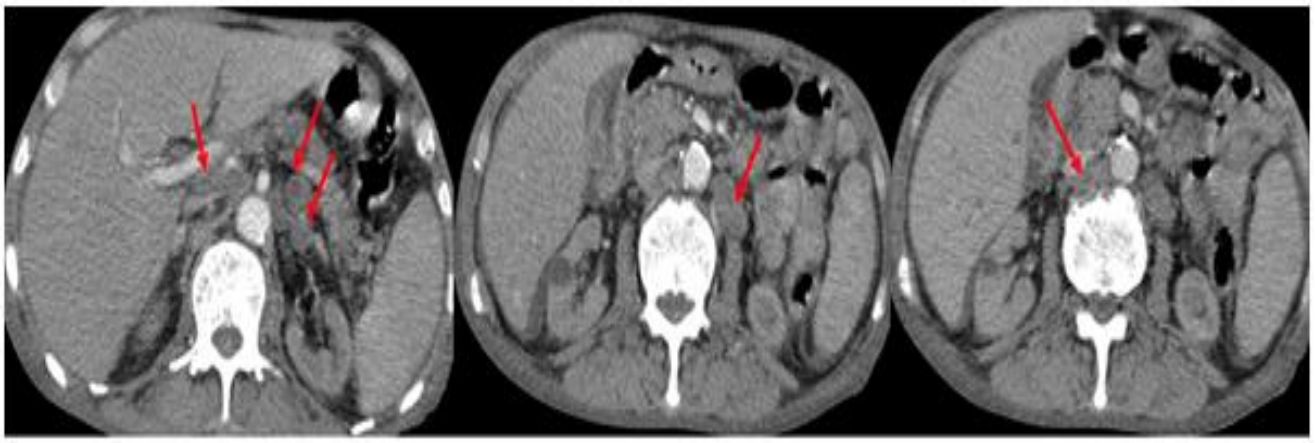

Fig 5: A Thoracic CT Scan in Mediastinal Window, Multiple Mediastinal Lymphadenopathies Visible in the Prevascular Area, Barety's Space, Pre- and Subcarinal Areas, and Bilateral Hilar Regions (Arrow).

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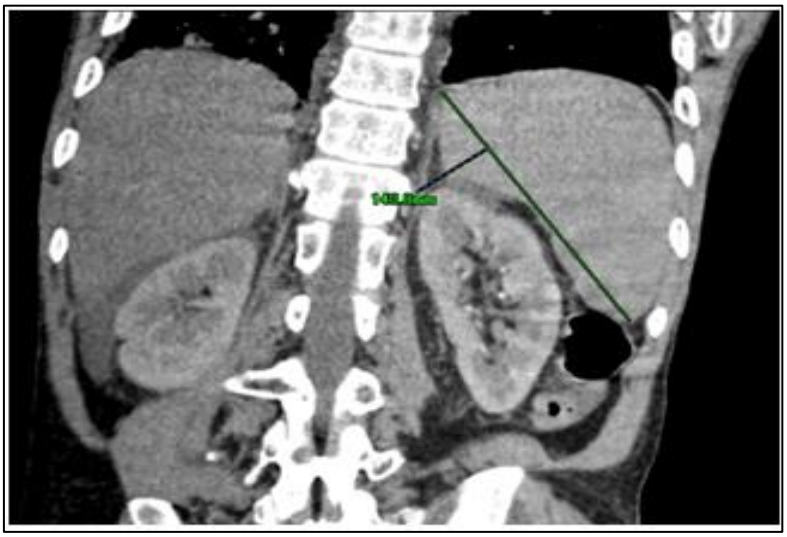

Fig 6: Abdominal CT Scan in Coronal Reconstruction, Homogeneous Splenomegaly with the Splenic Length Measured at 14 Cm (Arrow).

III. DISCUSSION

Mantle Cell Lymphoma (MCL) is a subtype of non-Hodgkin lymphoma (NHL) distinguished by the proliferation of malignant B-type lymphocytes originating from the mantle zone of lymphoid follicles(3). Before 1992, it fell under the classification of lymphocytic lymphoma with 'intermediate differentiation', as it appeared to occupy a position between well-differentiated lymphocytic lymphoma and poorly-differentiated lymphoma(2,5,8). It has been recognized as a new distinct entity, characterized by unique cytogenetic, immunophenotypic, and clinicopathological traits(4).

MCL represents roughly 5 to 7% of all lymphomas. Patients typically fall within the age range of 60 to 70 years and It is 70% more frequent in Men(1).

It differs from indolent lymphomas as the median survival is between three to five years(5,9). In over 75% of cases, staging reveals stage IV disease. Notably, there is a high frequency of extranodal involvement, particularly affecting the bone marrow, spleen, gastrointestinal tract, ENT area, and liver(4,5,10).

There is no typical mode of presentation for mantle cell lymphoma (MCL). Several modes of presentation have been described, including myeloproliferative syndrome(11), bone marrow aplasia(5), tumor lysis syndrome(12), colonic mass, or digestive symptoms(13,14). Some authors advocate for systematically performing both gastro-duodenal endoscopy and colonoscopy in cases of suspected MCL, as gastrointestinal involvement is present in 20% of cases(5). However, there is currently no recommendation regarding the routine use of these explorations(6). On the other hand, a search for bone marrow involvement should be conducted in all cases, as it is present in 55 to 80% of cases(4,6,7,9).

Clinically, it can be mistaken for chronic lymphoid leukemia(1), with diagnosis criteria recently updated by the latest guidelines from the British Society of Hematology(6).

In terms of peripheral blood morphology, characteristic features include small- to medium-sized lymphocytes with mature nuclei displaying a cleft, along with larger atypical lymphoid cells seen in blastoid and pleomorphic variants. Prolymphocytic morphology is occasionally observed.

Flow cytometry typically reveals expression of CD5, CD19, CD20, CD79b, CD22, FMC7, and ROR1, along with surface light chains, predominantly lambda. Mantle-cell lymphoma, despite being CD5-positive like CLL, usually exhibits bright CD20 expression and is typically negative for CD23 and CD200. In contrast, CLL tends to show dim CD20 expression and is positive for CD23 and CD200.

Immunohistochemistry shows consistent expression of pan B-cell markers like CD19, CD20, CD22, PAX5, and CD79a, along with moderately to strongly expressed surface immunoglobulins including IgM and IgD. CD5 is commonly expressed, but a small-cell variant may lack CD5 expression. Cyclin D1 expression is a constant and specific feature. SOX11 expression is common, except in small-cell and non-nodal leukemic variants. CD23 is usually negative, though weak expression may occur in a small percentage of cases. CD10 and BCL6 are usually negative, and CD200 is typically negative, although a small percentage of CD200-expressing cases with an indolent course may occur in SOX11-negative non-nodal leukemic cases. Intracellular LEF1 is typically expressed in CLL but rarely in MCL, mainly in blastoid/pleomorphic variants.

Additional diagnostic features such as histology, cytogenetics, and mutation search can be utilized to further determine prognosis factors.

As per the European Task Force on Lymphoma classification, mantle-cell lymphomas can be categorized into four histopathological subtypes(8):

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- Nodular pattern with residual germinal centers, akin to the mantle-zone pattern.
- Nodular pattern without residual germinal centers, featuring a loosely structured meshwork of follicular dendritic cells.
- Nodular pattern without residual germinal centers, characterized by tight clusters of follicular dendritic cells.
- Diffuse pattern, with or without residual germinal centers.

Currently, morphological research and determination of tumor immunopheno type are essential diagnostic procedures for all lymphoproliferative diseases. The advancement of diagnostic methods has allowed for a clearer definition of several lymphoproliferative diseases that previously could have been confused with other subtypes, thus delaying appropriate management(3,13).

IV. CONCLUSION

In conclusion, mantle cell lymphoma (MCL) presents a complex diagnostic challenge due to its varied clinical manifestations and overlapping features with other lymphoproliferative diseases. The evolution of diagnostic techniques has significantly improved our ability to accurately diagnose MCL and distinguish it from similar conditions, leading to more timely and appropriate management strategies. However, ongoing research and vigilance in clinical practice are necessary to further refine our understanding of MCL and optimize patient care.

➢ *Statement of Ethics*

The patient has provided written consent for the publication of his personal data, including personal images.

➢ *Disclosure Statement*

The authors declare that there are no conflicts of interest.

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