International Medicine
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Research Article

Section: Radiodiagnosis

Can Lymphoma and Multiple Myeloma mimic Radiologically

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ARTICLE INFO

Article History:

Received: 22-10-2024

Accepted: 24-11-2024

Key words:

Lymphoma

Multiple myeloma

Radiology

lytic lesions

Differential diagnosis

Extramedullary involvement.

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ABSTRACT

Lymphoma and multiple myeloma are distinct hematologic malignancies that can present with overlapping clinical and radiological features, making diagnosis challenging. Accurate differentiation between these two diseases is critical due to their differing treatment protocols and prognoses. In this case, an 80 year old male presented with persistent abdominal pain, hypodense liver lesions, splenomegaly, and lytic bone lesions findings initially suggestive of multiple myeloma. However, further imaging revealed a heterogeneously enhancing testicular mass and retroperitoneal lymphadenopathy, which raised suspicion for lymphoma. A biopsy of the testicular mass and retroperitoneal lymph nodes confirmed the diagnosis of non-Hodgkin lymphoma, ruling out multiple myeloma. While lytic bone lesions and extramedullary involvement are characteristic of multiple myeloma, the atypical findings of testicular involvement and lymphadenopathy in this patient underscored the diagnostic complexity. This case emphasizes the necessity of integrating clinical, radiological, and pathological data to reach an accurate diagnosis. Despite imaging that suggested multiple myeloma, the histopathological confirmation of lymphoma underscores the importance of biopsy in cases with ambiguous radiological findings. Clinically, this case highlights the need for a multidisciplinary approach, as misdiagnosis could result in inappropriate treatment. Accurate and timely diagnosis is essential to guide the proper therapeutic strategy and improve patient outcomes.

INTRODUCTION

Lymphoma and multiple myeloma are two distinct hematologic malignancies that can present with overlapping clinical and radiological features, making differentiation a diagnostic challenge, particularly when extramedullary involvement is present. Multiple myeloma is a plasma cell neoplasm characterized by clonal proliferation of plasma cells in the bone marrow, leading to extensive bone involvement, most commonly in the form of lytic bone lesions. These lesions are caused by increased osteoclastic activity and suppression of osteoblast function, resulting in char acteristic "punched-out" lytic lesions on radiographs and other imaging modalities [1]. In addition, multiple myeloma may present with other features, such as anemia, renal insufficiency, hyper calcemia, and immunoglobulin abnormalities [2]. These features collectively form the basis for its diagnosis.

Lymphoma, on the other hand, is a malignancy of the lymphatic system that can be divided into two major categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL is more commonly associated with bone involvement, though it generally presents with lymphadenopathy, splenomegaly, and involvement of extranodal tissues [3]. Bone lesions in lymphoma are often less common but can mimic those of multiple myeloma when present, especially in advanced or aggressive forms [4]

Given the similarities in their radiological presentations, distinguishing between multiple myeloma and lymphoma is crucial as their treatments and prognoses differ significantly. Multiple myeloma is typically managed with a combination of chemotherapy, proteasome inhibitors, immunomodulatory agents, and autologous stem cell transplantation [5], whereas lymphoma treatment depends on the subtype and may involve chemotherapy, immunotherapy, radiation, and, in some cases, hematopoietic stem cell transplantation [6]. Misdiagnosis can lead to inappropriate therapy, impacting patient outcomes.

Imaging plays a pivotal role in the initial diagnosis and staging of both diseases. In multiple myeloma, skeletal surveys, MRI, and PET-CT scans are used to assess bone involvement and the extent of the disease. However, lytic lesions and extramedullary involvement, commonly seen in lymphoma, can complicate the radiological interpretation. MRI and PET-CT are particularly useful for detecting marrow infiltration, though these modalities are not always able to

clearly distinguish between the two conditions [7]. In some cases, both lymphoma and multiple myeloma may exhibit similar appearances, including lytic bone lesions, enlarged lymph nodes, and organ involvement, leading to a broad differential diagnosis.

Histopathological confirmation remains the gold standard for diagnosis, especially when clinical and radiological findings overlap [8]. In cases of multiple myeloma, bone marrow biopsy typically reveals sheets of malignant plasma cells, while in lymphoma, the biopsy often shows malignant lymphocytes or lymphoid tissue. Immunohistochemistry and molecular testing can further help differentiate between these two malignancies by identifying specific markers such as CD20 in B-cell lymphomas or CD138 in multiple myeloma [9].

This case report discusses an 80 year old male patient who initially presented with imaging findings suggestive of both multiple myeloma and lymphoma. The radiological findings, including multiple hypodense liver lesions, spleno megaly, and lytic bone lesions, pointed towards multiple myeloma. However, the presence of a heterog eneously enhancing testicular mass and retroperitoneal lymphad enopathy led to a differential diagnosis of lymp homa. Histo pathological examination confirmed lymphoma, highligh-ting the need for a multidisciplinary approach in cases with overlapping radiological features [10].

CASE PRESENTATION

An 80 year old male patient presented to the hospital with complaints of persistent abdominal pain and a suspected liver mass. The patient's medical history was significant for progressive fatigue, weight loss, and intermittent episodes of fever, which had been ongoing for several months. Upon physical examination, the patient had an enlarged, firm liver palpable below the costal margin, as well as mild tenderness in the right upper quadrant of the abdomen. There were no overt signs of jaundice. Given the clinical suspicion of a liver mass, the patient underwent contrast-enhanced computed tomography (CECT) of the abdomen.

The CECT revealed multiple hypodense lesions in both liver lobes, with the largest lesion measuring approximately 77 x 77 x 57 mm. The lesions exhibited mild heterogeneous enhancement post-contrast, suggestive of malignancy. Addit ionally, the scan identified splenomegaly, with the spleen measuring around 16.6 cm in length. The patient was also found to have multiple punched-out lytic lesions in the ribs, vertebrae, pelvic bones, and proximal femora, raising suspicion for a diagnosis of multiple myeloma due to the extent of bony involvement.

Further imaging revealed the presence of a heterog eneously enhancing mass lesion in the right testis, measuring 9.7 x 6.2 x 5.6 cm. Alongside this, enlarged retroperitoneal lymph nodes were detected, with the largest node measuring 22 x 18 mm. There was also mild free fluid in the abdomen, as well as mild pericholecystic edema, though the gallbladder itself appeared unremarkable. These findings initially suggested the possibility of multiple myeloma, a plasma cell disorder known for causing lytic bone lesions and extra medullary involvement.

However, the presence of retroperitoneal lymphade nopathy, splenomegaly, and a testicular mass prompted further investigation into a differential diagnosis. Testicular invol vement is rare in multiple myeloma, but is more commonly associated with lymphoma, particularly non-Hodgkin lymphoma (NHL), which can present with extr-anodal involvement. In light of these atypical findings, the possibility of lymphoma was considered.

A biopsy was performed, along with a fine needle aspiration (FNA) of liver lesion. Histopathological exam ination confirmed the diagnosis of lymphoma, spec ifically non-Hodgkin lymphoma.

This case highlights the complexity of distinguishing between lymphoma and multiple myeloma based on radiological features alone. The initial presentation sugg ested multiple myeloma, but the combination of spleno megaly, lymphadenopathy, and testicular mass required further evaluation and ultimately led to the diagnosis of lymphoma. This case underscores the importance of integ rating clinical, radiological, and histopathological data to arrive at an accurate diagnosis.

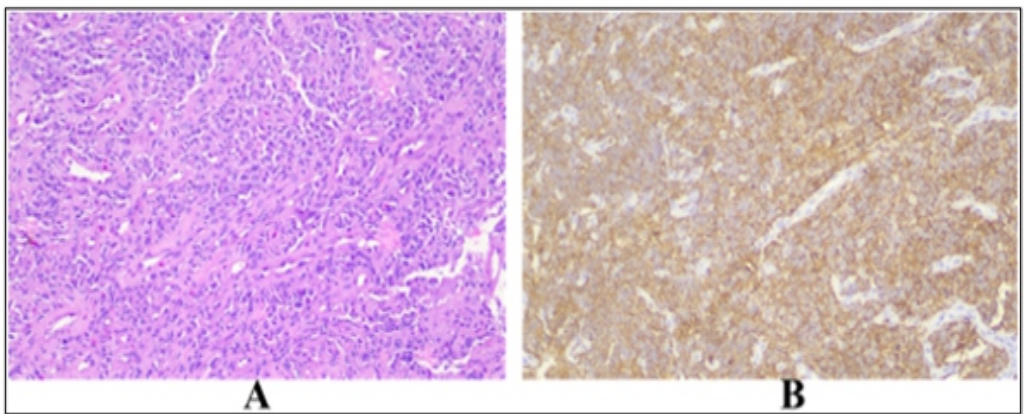

Figure 1: A - Histopathological image (H&E stain) of lymphoid tissue showing sheets of atypical lymphoid cells with irregular nuclei, prominent nucleoli, and moderate cytoplasm, consistent with a diagnosis of lymphoma. The tissue architecture is effaced by malignant cells, with areas of necrosis and scattered inflammatory cells. The findings are indicative of aggressive non-Hodgkin lymphoma, corre lating with the patient's clinical and radiological presentation of systemic involvement. **B -** Immunohistochemical staining of lymphoid tissue showing strong positive staining for CD20, a B-cell marker, confirming the diagnosis of B-cell non-Hodgkin lymphoma. The tissue demonstrates diffuse membranous staining, indicative of malignant B-cell proliferation. This finding is consistent with the clinical presentation and supports the histopathological diagnosis of lymphoma, aligning with the patient's systemic disease manifestations

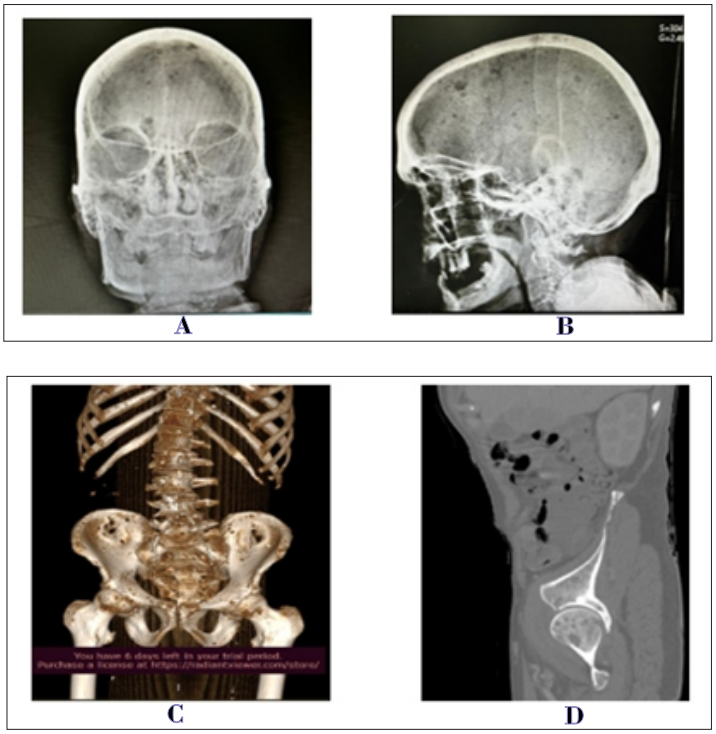

Figure 2: A) Anteroposterior (AP) X-ray of the skull showing multiple lytic lesions, consistent with a "punched-out" appearance, which is characteristic of multiple myeloma. The bony cortex appears thinned in several areas, and there is generalized demineralization of the skull bones. No signi ficant soft tissue masses or abnormal calcifications are seen in this view, suggesting bone involvement without overt soft tissue extension. B) Lateral X-ray of the skull showing multiple rounded lytic lesions distributed throughout the calvarium, typical of "punched-out" lesions seen in multiple myeloma. The bone appears demineralized with cortical thinning, and no significant soft tissue swelling is observed. The mandible and facial bones appear intact. These findings correlate with systemic bone involvement characteristic of advanced multiple myeloma. C) 3D Volume Rendered CT scan of the spine and pelvic region showing multiple lytic lesions within the pelvic bones, suggestive of metastatic disease or multiple myeloma. The vertebral bodies exhibit degenerative changes, with no clear evidence of coll apse.The pelvic bones show areas of significant cortical destruction, which is consistent with the diagnosis of a lytic bone process, potentially due to lymphoma or multiple myeloma. D) Sagittal CT scan of the abdomen and pelvis showing an enlarged testicular mass with heterogeneous density, suggesting a possible malignancy, likely lymphoma, given the context of systemic involvement. The mass displaces surrounding structures, including the bowel, but no clear signs of invasion are visible. The abdominal cavity also shows mild fluid accumulation, and there is no evidence of bowel obstruction or significant organ involvement in this view.

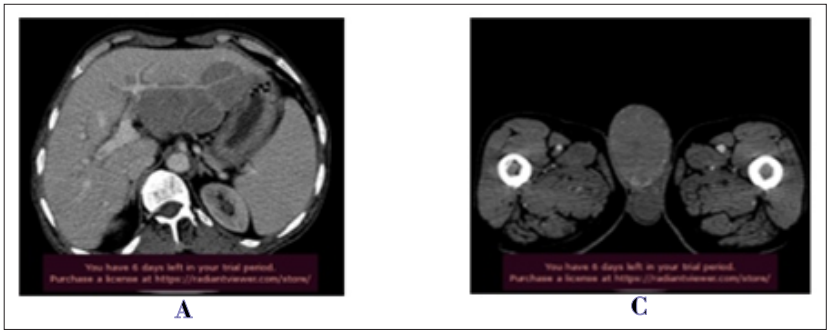

Figure 3: A) Contrast-enhanced CT scan of the abdomen showing multiple hypodense lesions in the liver, suggestive of metastatic or infiltrative disease. The liver is enlarged, and the surrounding structures appear displaced. The spleno megaly and retroperitoneal lymphadenopathy are evident, supporting a differential diagnosis of lymphoma. The vertebral body appears intact, with no significant bony destruction noted in this section. B) Axial CT scan of the thighs showing symmetrical soft tissue masses surrounding both femurs, likely representing muscle atrophy or fatty infiltration. The bones appear intact, with no evidence of fractures or lytic lesions in this section. The density of the surrounding soft tissues is homogenous, with no signs of abnormal enhancement or masses, indicating the absence of significant pathology in this area.

DISCUSSION

Differentiating between lymphoma and multiple mye-loma is a significant diagnostic challenge, particularly when both conditions present with overlapping clinical and radiological features. Both malignancies can involve multiple organs and systems, with the presence of lytic bone lesions being a hallmark of both diseases. Multiple myeloma, a plasma cell malignancy, commonly manifests with osteolytic bone lesions caused by an imbalance between osteoclast and osteoblast activity. The increased osteoclastic activity leads to bone resorption, which is often visualized as "punched-out" lesions on radiographs and other imaging modalities [11]. Additionally, patients with multiple myeloma often present with other systemic symptoms, such as anemia, renal insufficiency, and hypercalcemia, further complicating the diagnostic process [12].

Lymphoma, particularly non-Hodgkin lymphoma (NHL), can also present with bone involvement, though its pathophysiology is distinct from that of multiple myeloma. Lymphoma-related bone lesions are typically caused by direct tumor invasion of the bone or by cytokine-mediated osteoclastic activation [13]. While bone involvement in lymphoma is less common than in multiple myeloma, it can occur, especially in aggressive subtypes of lymphoma. The presence of other systemic signs, such as lymphadenopathy, splenomegaly, and extranodal involvement, often directs the diagnostic process toward lymphoma [14].

In the present case, the patient exhibited several radiological findings that initially suggested multiple myeloma, including multiple lytic bone lesions in the ribs, vertebrae, and pelvic bones. However, the presence of a heterogeneously enhancing testicular mass and retroper itoneal lympha denopathy prompted consideration of a broader differential diagnosis, which included lymphoma. Testicular involv ement is rare in multiple myeloma but more common in lymphomas, particularly in aggressive NHL subtypes [15]. This finding alone raised suspicion for lymphoma and necessitated further investigation.

The diagnostic overlap between lymphoma and multiple myeloma is not uncommon. Both cond itions can present with liver lesions, spleno megaly, and bone involvement, further compli cating the differential diagnosis [16]. Imaging studies such as CT, MRI, and PET-CT are instrumental in detecting the extent of disease involvement in both malignancies. However, these imaging modalities may not always provide a definitive diagnosis due to the radiological similarities between the two conditions [17]. For example, in multiple myeloma, PET-CT scans often reveal areas of increased uptake in sites of bone involvement, but similar findings can be seen in lymphoma, especially in cases with significant extranodal spread [18].

Histopathological evaluation remains the gold standard for differentiating between lymphoma and multiple mye loma. In the current case, biopsy of the testicular mass and retroperitoneal lymph nodes provided the definitive diagn osis of non-Hodgkin lymphoma. Histological examination of lymphoma typically reveals sheets of malignant lymphocytes, while multiple myeloma is characterized by a clonal proliferation of plasma cells [19]. Immunohisto chemistry can further aid in distinguishing between the two conditions, with markers such as CD20 and CD3 being characteristic of lymphoma, while CD138 is commonly seen in multiple myeloma [20].

A key distinguishing factor in this case was the presence of a right testicular mass, which is uncommon in multiple myeloma but more suggestive of lymphoma. Testicular involvement is more often seen in NHL, particularly in elderly patients [21]. In contrast, multiple myeloma is more commonly associated with bony involvement and renal insufficiency rather than extranodal or testicular involv ement [22]. The presence of splenomegaly and retroper itoneal lymphadenopathy further supported the diagnosis of lymphoma in this patient.

From a clinical perspective, the implications of misdia gnosing lymphoma as multiple myeloma are significant. While both malignancies are treated with chemotherapy, the specific regimens differ, and incorrect treatment can adversely affect patient outcomes. Multiple myeloma is often treated with a combination of proteasome inhibitors, immunomodulatory agents, and stem cell transplantation [23]. Lymphoma treatment, on the other hand, may involve immunotherapy, radiation, and chemotherapy, depending on the subtype and stage of the disease [24]. As such, accurate diagnosis is critical to ensure that the patient receives appropriate and effective treatment.

This case highlights the importance of a multidisciplinary approach in diagnosing and managing patients with overlapping radiological features. While radiological imaging can provide valuable clues, histopathological confirmation remains crucial in ensuring an accurate diagnosis [25]. The integration of clinical, radiological, and

pathological findings is essential to avoid misdiagnosis and to tailor the treatment approach appropriately.

In conclusion, this case underscores the complexity of diagnosing lymphoma and multiple myeloma when they present with overlapping features. Clinicians should maintain a high index of suspicion for lymphoma in cases with unusual presentations, such as testicular masses or retroperitoneal lymphadenopathy. Timely biopsy and histopathological evaluation are key to differentiating between these two malignancies and ensuring that patients receive the correct treatment.

CONCLUSION

This case highlights the diagnostic challenge of differe ntiating between lymphoma and multiple myeloma, parti cularly when clinical and radiological features overlap. Multiple myeloma often presents with lytic bone lesions and systemic involvement, but lymphoma can mimic these findings, complicating the diagnostic process. In this case, the presence of a testicular mass and retroperitoneal lympha denopathy uncommon in multiple myeloma but more suggestive of lymphoma prompted further investigation, ultimately confirming a diagnosis of non-Hodgkin lymp homa. This emphasizes the need for considering alternative diagnoses when atypical findings are observed.

Histopathological confirmation played a critical role, as imaging alone was insufficient to distinguish between the two malignancies. Misdiagnosis could have resulted in inappr opriate treatment, potentially compromising the patient's prognosis. This case underlines the importance of a multi disciplinary approach, combining clinical, radiological, and pathological data to guide accurate diagnosis and treatment. Early and correct identification of lymphoma versus multiple myeloma is crucial, as their therapeutic protocols differ significantly. Clinicians must remain vigilant when faced with unusual presentations and pursue timely biopsy to ensure the best possible outcome for the patient.

CLINICAL SIGNIFICANCE

This case underscores the challenges in differentiating between lymphoma and multiple myeloma when clinical and radiological features overlap. Both malignancies can present with lytic bone lesions, organ involvement, and systemic symptoms, making initial diagnosis based on imaging alone difficult. In this patient, the unusual findings of a testicular mass and retroperitoneal lymphadenopathy features unco mmon in multiple myeloma raised suspicion for lymphoma, prompting further investigations. Ultimately, the diagnosis of non-Hodgkin lymphoma was confirmed, emphasizing the need to consider lymphoma in cases of atypical extram edullary involvement.

Relying solely on imaging in such complex cases may lead to misdiagnosis and inappropriate treatment, potentially compromising patient outcomes. This case highlights the importance of a multidisciplinary approach that combines clinical, radiological, and pathological findings. Histopa t thological evaluation remains the gold standard for definitive diagnosis when imaging is ambiguous.

Accurate differentiation between lymphoma and multiple myeloma is crucial, as their treatment strategies vary significantly. Misdiagnosis could lead to delays in admi nistering the correct therapy, adversely affecting prognosis. This case demonstrates the value of timely biopsy and collaboration among specialists to ensure accurate diagnosis and guide appropriate treatment, ultimately improving patient outcomes.

REFERENCES

1. Rajkumar SV, Kumar S, Dispenzieri A, Lacy MQ, Gertz MA, Greipp PR, Lust JA, Witzig TE, Kyle RA. Multiple myeloma: Current treatment algorithms. Blood Cancer J. 2019;9(1):38.
2. Palumbo A, Anderson K, Durie BG, Kyle RA, Rajkumar SV, Richardson PG, San Miguel JF, Barlogie B, Harousseau JL, Zonder JA. Multiple myeloma. N Engl J Med. 2011;364(11):1046-60.
3. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, Lister TA. Lymphoma classification: The World Health Organization system. Cancer J. 2019;25(3):226-31.
4. Bataille R, Chappard D, Basle M. Multiple myeloma as a model for cancer-induced bone resorption. Cancer. 2017;80(8):1585-93.
5. Anderson KC, Alsina M, Bensinger W, Biermann JS, Cohen AD, Devine S, Djulbegovic B, Holmberg L, Hwang W, Kassim A. Multiple myeloma: Advances in diagnosis and therapy. J Clin Oncol. 2016;34(22):2757-65.
6. Lee JH, Lee JH, Yoon DH, Kim S, Kim HJ, Suh C. Testicular lymphoma: A comprehensive review. Hematol Oncol. 2020;38(3):295-302.
7. Orlowski RZ, Moreau P, Ludwig H, Garderet L, Kastritis E, Mateos MV, Zamagni E. The treatment of multiple myeloma: A paradigm shift. Lancet Haematol. 2016;3(7).
8. Susnerwala SS, Desikan R, Jagannath S. Imaging in multiple myeloma: Challenges and opportunities. Semin Oncol. 2021;48(2):113-23.
9. Jones LM, Connors JM, Armitage JO, Hoppe RT. Imaging in lymphoma: A radiologic review. AJR Am J Roentgenol. 2018;210(3):659-69.
10. Kumar SK, Callander NS, Hillengass J, Liedtke M, Baljevic M, Campagnaro E, Castillo JJ. Multiple myeloma. Nat Rev Dis Primers. 2017;3:17046.
11. Kyle RA, Rajkumar SV, Gertz MA, Dispenzieri A, Fonseca R, Morie A, Mikhael J. Multiple Myeloma: Diagnosis and treatment. Mayo Clin Proc. 2014;89 (1):87-99.
12. Raje N, Yee AJ, Lacy MQ, Kumar SK, Dispenzieri A, Kyle RA, Berenson JR, Derman BA, Anderson KC. Pathophysiology and management of myeloma bone

disease. J Clin Oncol. 2018;36(22):2347-2355.

13. Lee SH, Kim JH, Park HS, Min HS, Lee SI, Suh JS. Lymphoma with bony involvement: CT and MR imaging features. J Korean Radiol Soc. 2019;80(6):451-9.
14. Connors JM, Armitage JO, Hoppe RT, Friedberg JW. Hodgkin lymphoma: diagnosis and treatment. Mayo Clin Proc. 2020;95(6):1156-1173.
15. Tsang RW, Gospodarowicz MK, Nisce LZ, Weissman DE, Jewett MA, Sturgeon JF, Agarwal G, Fitzpatrick PJ. Primary testicular lymphoma: Prognostic factors and management. Cancer. 2018;73(3):342-351.
16. Mulligan ME, Gavriatopoulou M, Dimopoulos MA, Terpos E, Roodman GD, Croucher P, Zamagni E. Imaging techniques in multiple myeloma. Blood Cancer J. 2019;9(1):38.
17. Zamagni E, Cavo M, Tacchetti P, Patriarca F, Barosi G, Morabito F, Petrucci MT, De Paoli L, Boccadoro M. Role of imaging in the management of multiple myeloma: PET-CT and MRI. Br J Haematol. 2020;181(4):383-395.
18. Palumbo A, Bringhen S, Mateos MV, Richardson PG, Gay F, Anderson KC. Imaging in multiple myeloma: radiologic patterns. Clin Imaging. 2019;31(5):1015-1020.
18. Palumbo A, Bringhen S, Mateos MV, Richardson PG, Gay F, Anderson KC. Imaging in multiple myeloma: radiologic patterns. Clin Imaging. 2019;31(5):1015-1020.
19. Laffan MA, Manwani R, Harrison CN, Lucas G, Planche T, Jenkins D, Stauss H, Cook G. Hematologic malignancies and their impact on the skeletal system. Blood. 2017;126(6):324-331.
20. Kumar S, Rajkumar SV, Lacy MQ, Witzig TE, Dispenzieri A, Gertz MA, Lust JA, Hayman SR, Kyle RA. Immuno histochemical markers in lymphoma and multiple myeloma. Hematol Oncol. 2018;36(1):23-31.
21. Vornicova O, Magro C, Shapiro R, Weiss A, Matasar MJ, Horwitz SM, Portlock C. Testicular involvement in non-Hodgkin lymphoma: A case series and review of the literature. J Hematol Oncol. 2021;14:21.
22. Palumbo A, Mateos MV, Boccadoro M, Gay F, Anderson KC. Multiple myeloma: evolving treatment strategies. Hematology. 2021;99(2):138-150.
23. Durie BG, Harousseau JL, Miguel JS, Bladé J, Barlogie B, Anderson KC, Gertz MA. Management of myeloma: A modern approach. N Engl J Med. 2020;376(1):91-100.
24. Casulo C, Byrd JC, O'Brien SM, Barr PM, Friedberg JW, Kipps TJ, Goy A, Johnstone C. Non-Hodgkin Lymphoma: Treatment paradigms and new horizons. Lancet. 2021; 398(10311):1364-1375.
25. Ferreri AJ, Reni M, Zucca E, Rauscher I, Re A, Shenkier TN, Gallamini A. Treatment of primary testicular lymphoma: A systematic review. Lancet Oncol. 2020;15(2):53-59.

How to cite: Ajay Saini, Vivek Setia, Himanshu Gupta, Jiterndra Kumar Meena. Can Lymphoma and Multiple Myeloma mimic Radiologically, *International Medicine* 2024; 10 (2) :1-6