INTRODUCTION: Primary bone lymphoma is a rare disease, accounting for about 3% of all primary bone malignancies in adults. Patients with primary NHL of bone commonly present with local bone pain, soft tissue swelling, and a mass or a pathological fracture. There is a slight male preponderance, and most patients are over 45-50 years of age. Primary NHL of bone can arise in any part of skeleton, but long bones (femur) is the most common sites of presentation but distal tibia is an unusual, rare site of presentation. The outcome of patients with primary lymphoma of bone is relatively favorable with multidrug regimen chemotherapy +/- radiation therapy.

CASE PRESENTATION: A 50 year old female presented with chief complaints of pain and swelling over the left leg since 2 months, which was insidious in onset, gradually progressive in nature and with low grade intermittent fever since 1 month. There was no preceding history of trauma, joint stiffness or other associated constitutional symptoms. She had an episode of enteric fever 2 months ago, which was treated with IV antibiotics. She gives history of chemo-radiation for oral malignancy 17 years back, the details of which were not available to us at presentation. She has also undergone hysterectomy 14 years back, following which she had no complications. On general examination, patient had stable vitals, with no pallor or generalised lymphadenopathy. She had left sided non-pitting pedal edema upto the level of mid-calf. On examination of the right leg, we found that she had multiple localized swellings noted over the distal third of leg. The skin over the swelling was normal, with no wounds, scars, sinuses or dilated veins over the leg. On palpation, there was local rise of temperature with tenderness over the leg. Swelling had a smooth surface with ill-defined margins, soft in consistency with no evidence of crepitus or abnormal movements. Peripheral pulsations were well palpated, and there was no sensory or motor deficits. On movement of left ankle joint, the terminal movements were painful and restricted. Patient was referred to the Oncology department for chemotherapy. Patient is on regular follow-up since then, and remains asymptomatic.

CONCLUSION: Primary lymphoma of the bone involving distal tibia is a very rare entity, with chemotherapy and radiotherapy being the mainstay of treatment. Surgery has a limited role. Early diagnosis and treatment can help reduce significant morbidity and mortality.

KEYWORDS

NHL, CHOP, primary lymphoma
MRI of right leg was done to rule out soft tissue infections or osteomyelitis - which revealed a large infiltrative soft tissue lesion over the ankle and lower one third of right leg encasing the tendons, distal tibia and fibula, muscles, skin and subcutaneous tissue with cortical erosions and marrow edema in distal tibia and fibula. A differential diagnosis of synovial sarcoma or metastatic lesion to distal tibia/fibula was suggested based on the MRI report (Figure 3).

In view of features suggestive of metastasis, oncology opinion was sought, where they advised USG abdomen and pelvis & chest x-ray.

USG abdomen and pelvis was suggestive of bilateral metastases to adrenal glands with retroperitoneal lymphadenopathy. To confirm the same, CECT abdomen and pelvis, with thorax screening was ordered. This revealed multiple retroperitoneal enlarged lymph nodes with multiple metastases to adrenal and kidneys. Hence, we considered a possibility of lymphoma based on these findings (Figure 4).

For the purposes of staging, bone marrow aspiration and biopsy was done, which was found to be normal.

With all the preliminary investigation done to diagnose the primary lesion, it was decided to perform a biopsy of the lesion from left distal tibial metaphysis and soft tissue swelling. Histopathology revealed a lymphoproliferative lesion suggestive of Non Hodgkin’s Lymphoma (Figure 5).

Immunohistochemistry markers were ordered on the histopathology specimen, which showed positivity for CD 45, CD 20, Ki 67 and was confirmed to have Diffuse Large B cell Lymphoma.

Patient was then referred to the Oncology department for chemotherapy. Patient is on regular follow-up since then, and remains asymptomatic.

DISCUSSION:-

Non-Hodgkin's lymphoma belongs to a group of hematological malignancies that originate either from T cell or B cell. These vary significantly in their cell of origin, cytogenetics, morphology and prognosis. Generalised lymphadenopathy remains the most common presentation of NHL, which may or may not be associated with hepatosplenomegaly. Involvement of bone as a primary lesion is relatively rare, accounting for less than 2% of the lymphomas affecting adults [1]. This is seen more common in paediatric population, seen in 3-9% of cases of NHL. Men are affected more frequently than women, with a ratio ranging from 1.2 to 1.8 [2-5]. The most common age of presentation is more than 30 years, with over 50% of patients being over 60 years.

The most common presentation of patients with primary lymphoma of bone is deep seated bone pain, not relieving upon rest. There can be associated symptoms such as fever, loss of weight and night sweats. Occasionally, patient presents with features of pathologic fractures following trivial trauma and even features of spinal cord compression.

Diagnosis is confirmed by histopathology, where the tissue sample is obtained via percutaneous or open biopsy. A comprehensive history and physical examination is essential in a case of primary lymphoma of bone as it is required to identify all involved sites and any evidence of constitutional symptoms. Imaging is required to identify the primary as well as to look for other extranodal sites of involvement, which includes CT/MRI of the primary site, along with PET/CT of the thorax and abdomen.

Multidrug regimen chemotherapy +/- radiation therapy is the preferred treatment of adults with PLB. Given that the majority of PLB are aggressive B cell lymphoma, patients are typically treated with anthracycline-based, multi-agent chemotherapy, such as CHOP regimen (cyclophosphamide, doxorubicin, vincristine and prednisone) with the addition of the anti-CD20 monoclonal antibody Rituximab [5-7]. In patients with unifocal disease, consolidative involved-field radiotherapy is reasonable, but should be individualized with particular attention to the location of disease. Radiation to areas, such as the pelvis, which contain significant marrow production, should be considered carefully. A dose of 30 to 36 Gy is reasonable in patients who attain a complete response following chemotherapy. A higher dose (eg, 40 Gy) is offered to patients with an indeterminant response [7-10].

The role of surgery is generally limited to diagnostic biopsy and stabilization of a pathologic fracture. Orthopedic management is important during the treatment and recovery period because the potential for fracture persists until there is complete bone healing. Rarely, patients with involvement of the weight-bearing bones may require internal stabilization or bracing until bone healing occurs.

CONCLUSION:

Primary lymphoma of the bone involving distal tibia is a very rare entity, with chemotherapy and radiotherapy being the mainstay of treatment. Surgery has a limited role. Early diagnosis and treatment can help reduce significant morbidity and mortality.

Clinical Message: Non Hodgkin's Lymphoma involving the distal tibia is a rare entity with diffuse large B cell lymphoma being the most commonest type. Chemoradiation is regarded as the mainstay of treatment with regular follow up.

FIGURES-

Figure 1: Initial clinical presentation of swelling over right distal third of leg extending to ankle.

Figure 2: Radiograph of right leg with ankle appears normal.

Figure 3: MRI showing large infiltrative soft tissue lesion in the ankle and lower one third of right leg encasing the tendons, distal tibia and fibula and invading the muscles, skin and subcutaneous tissue with cortical erosions and marrow edema in the distal third of tibia and fibula.

Figure 4: CECT abdomen and pelvis revealed multiple retroperitoneal enlarged lymph nodes with multiple metastases to adrenal and kidneys.
Figure 5: Sections from distal tibial biopsy shows necrotic and sclerotic bony bits with admixed atypical lymphoid cells with mildly pleomorphic nucleus, condensed chromatin and scanty cytoplasm.

Competing Interests:
The authors declare that they have no competing interests.

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REFERENCES