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RESEARCH ARTICLE

A RARE CLINICAL CASE SERIES OF LEIOMYOSARCOMA OF BONE WITH REVIEW OF LITERATURE

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Abstract

Introduction: Leiomyosarcoma is a rare malignant sarcoma which occurs in different anatomic sites including bone with similar histological characteristics but heterogenous clinical behaviour and prognosis. Primary LMS of bone is a rare aggressive sarcoma which presents as a high grade destructive tumour with poor prognosis and limited treatment options. Final diagnosis of LMS includes a combination of histomorphological features along with immunohistochemistry. Due to rarity of disease there is limited understanding of its pathology , prognosis and treatment .

Objective: Due to rarity of this disease a case series of primary LMS of bone is prepared to understand its behaviour and management in accordance with the current literature.

Material And Methods: 3 cases of primary LMS of Bone is documented in this case series along with history, imaging , diagnosis and treatment.

1] LMS Left Fibula :- A 55 year old male patient reported with pain and partial limitation of motion of the left knee joint. Patient managed with Surgery and Radiotherapy.

2] LMS Right Shoulder :- A 40 year old female patient reported with complaints of lump over right back with associated pain and restriction of joint movements. Patient managed with Surgery, Radiotherapy and Chemotherapy.

3] LMS Right Hip :- A 50 year old male patient reported with lump over right hip with pus discharge. Patient managed with Chemotherapy , Surgery and Radiotherapy .

Conclusion: Due to rarity of LMS Bone cases little is known about its clinical behaviour and treatment outcomes. A multidisciplinary approach is needed for the optimal management of the disease. Surgery with a curative intent is the corner stone of treatment of localised disease along with the combination of neoadjuvant or adjuvant chemotherapy and radiotherapy. Further research is needed to identify more effective outcomes.

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Introduction:-

Review Of Literature:-

Leiomyosarcoma is a common subtype of soft tissue sarcoma , accounting 10 – 20 % of all sarcomas[1] . LMS of Bone accounts for < 0.7% of all primary malignant bone tumors. Sarcomas are malignant tumors arising from the embryonic mesoderm. LMS originate from smooth muscle cells of uterine, gastrointestinal or soft tissue origin. The behaviour of LMS and its response to the treatment depends on the organ of origin. LMS typically occur in the 5^{th} – 6^{th} decades of life, however it can present in childhood[2]. Women are affected more than men which is attributed to the proliferation of smooth muscles that occur in the response to the estrogen. Leiomyosarcomas are aggressive tumors that are often difficult to treat. The prognosis is poor with survival rates among the lowest of all soft tissue sarcomas[3].

Etiology

The risk factors for LMS include :-

1. Prior history of radiotherapy is the most significant risk factor[4].
2. Genetic syndromes like hereditary retinoblastoma (RB 1 gene deletion) and Li- Fraumeni syndrome (Mutation in TP 53 gene).
3. Exposure to certain chemical like pesticides.
4. The prolonged used of tamoxifen is associated with uterine LMS.

Clinical Features

There are no specific symptoms related to LMS. Prognosis and treatment varies with the location, stage and grade of the primary tumor as well as presence of metastatic disease. The most common site is Retroperitoneum.

Site wise symptoms are as follows :-

1. LMS of Retroperitoneum :- abdominal mass , pain , swelling , weight loss , nausea or vomiting .
2. LMS of Soft Tissue :- enlarging painless mass , symptoms of vascular compression, leg edema , neurologic symptoms.
3. LMS of Bone :- bone pain , palpable mass and restriction of Joint movement.

Histopathology

Histologically LMS can be divided into spindle cell and non spindle cell morphology ,a spindle cell neoplasm with similar characteristics shared between the osseous and soft tissue forms of the disease, with the presence of cigar shaped nuclei cells arranged into fascicles along with myofibers running parallel[5]. Typically there is devoid of osteoid and chondroid matrix.

IHC

For confirmation of the diagnosis IHC studies are done. Certain stains like Desmin , smooth muscle actin and H-caldesmon can be used for confirmation of smooth muscle origin. To differentiate between LMS and leiomyomas, p16 and p53 with high Ki 67 proliferation index provide better sensitivity and specificity. Generally LMS have lower estrogen and progesterone receptors[6].

Most of uterine LMS express the platelet derived growth factor – alfa, Wilms tumor gene 1, aromatase and gonadotropin releasing hormone receptors.

Investigation

CT scan is better for retroperitoneal and visceral lesions.

1. MRI for evaluating tumors arising in the extremities and head and neck.
2. As the disease spreads mainly through the hematogenous route it is essential to rule out lung or liver metastasis:- CT / MRI/ PET- CT .
3. A biopsy of the suspected lesion is needed to make a definitive diagnosis.
4. A core needle biopsy or an open incisional biopsy is needed to obtain adequate tissue to identify histologic subtype and grade to distinguish it from other sarcomas.

Staging
Tnm Staging
T1 :- Tumor less than or equal to 5 cm in greatest dimension.
T2 :- Tumor over 5 cm and less than or equal to 10 cm in greatest dimension.
T3 :- Tumor over 10 cm and less than or equal to 15 cm in greatest dimension.
T4 :- Tumor over 15 cm in greatest dimension.

Node Staging :-
N0 :- No regional lymph node metastasis or unknown lymph node status.
N1 :- Regional lymph node metastasis.

Metastatic Staging :-
M0 :- No distant metastasis
M1 :- Distant Metastasis.

Grading :-
G1 :- Well differentiated
G2 :- Moderately differentiated
G3 :- Poorly Differentiated or Undifferentiated.

Stage Group :-
Stage IA :- T1 , N0 , M0 , G1
Stage IB :- T2 , T3 , T4 , N0 , M0 , G1
Stage II :- T1, N0 , M0 , G2/3
Stage III
Stage III A :- T2 , N0, M0, G2/3
Stage IIIB :- T3, T4, N0 , M0 , G2/3
Stage IV :- Any T , N1, M0 any G
Any T, any N , M1 ,
Any G

Treatment
Treatment of LMS depends on the stage of the disease and is a multidisciplinary approach. The goal of the treatment is to control the symptoms, debulking the tumor and prolong the survival. The treatment plan is formulated in combination with surgery, chemotherapy and radiotherapy depending on the site of LMS.

Case 1
Lms Of Left Fibula
A 55 year male patient reported in the OPD of Government cancer Hospital , Aurangabad with clinical complaint of pain in the left knee which was throbbing in nature since 1 year. Physical examination revealed partial limitation of motion of the left knee joint. On palpation a tender subtle swelling was present on the lateral aspect of left knee. There was no palpable lymphadenopathy in the draining regional lymph node. Patient had history of same swelling 2 years back for which angiography was done. Wide local excision with reconstruction and fibular flap was done. Histopathological report was suggestive of large mass size 13 x 11 cm removed from leg spindle cell arranged in storeform pattern features suggestive of dermatofibrosarcoma protuberance.

Patient received no adjuvant treatment and then defaulted for 2 years. Medical history revealed no contributory family and past histories and no neurological deficit on physical examination. MRI Left Knee (plain + contrast) [Figure 1[A]] was done with features suggestive of well defined multiloculated lesion measuring 10.4 x 2.6 x 10.7 cm appearing hypointense on T2 in the subcutaneous and cutaneous plane on the lateral aspect of left knee extending from level of lateral femoral condyle to upper 1/3rd of fibula abutting underlying deep fascia without any obvious involvement.

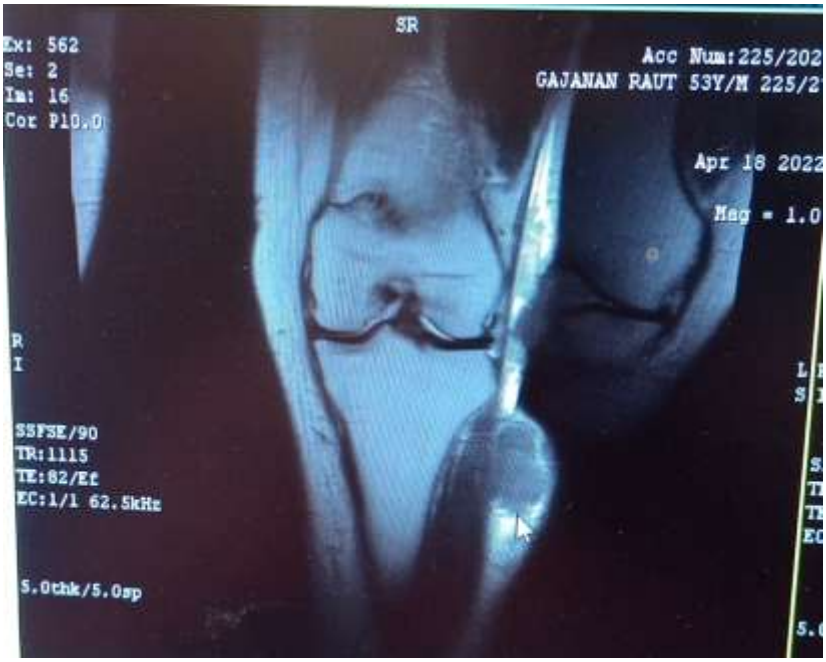

Figure 1[A] :- MRI left knee suggestive of well defined multiloculated lesion on T2.

The serum alkaline phosphatase , phosphorus, calcium and uric acid levels were within normal limits. Routine oncological work was done to rule out any metastasis. CT Thorax excluded any pulmonary metastasis. Patient underwent surgery with Wide local excision of DFSP with STSG. Post OP Histopathological report was suggestive of 13x11cm size growth hard in consistency base was involved by tumor, Spindle cell sarcoma suggestive of malignant transformation in known case of Dermatofibrosarcoma protuberance. All margins were free of tumour. Nodules from left thigh showed Tumor deposits. IHC [Figure 1[B]] was done suggestive of High grade Leiomyosarcoma with SMA and Desmin positive while CD24 and S100 were negative with high KI 67 Index.

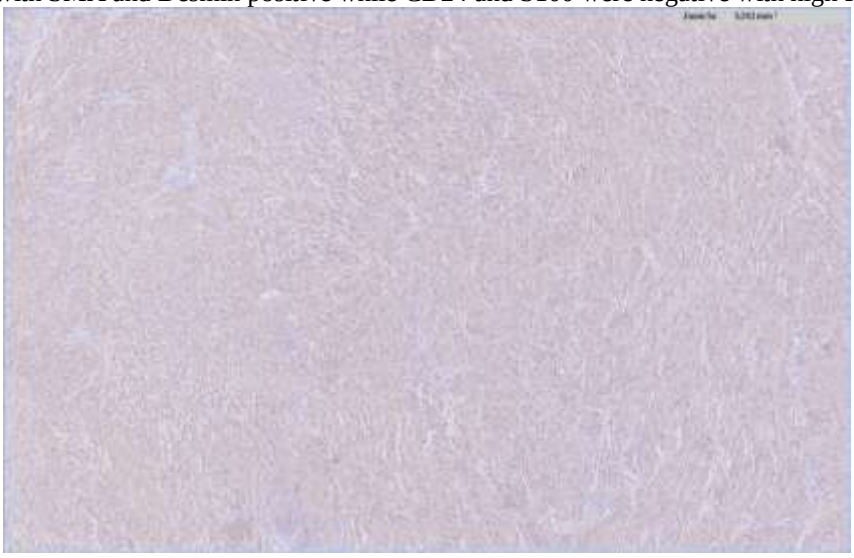

Figure 1[B]:- Figure showing IHC suggestive of High grade leiomyosarcoma with SMA positive.

Treatment with Post OP RT Dose of 60 Gy/ 30 # over 6 weeks using 2D techniques with field size of 8x11x3cm first field , second field 12x20x4cm was given on linear accelerator. Patient tolerated well. Now patient is on follow up and imaging will be planned after 2 months. Long term disease free survival is under assessment.

Case 2
Lms Of Right Shoulder
A 40 year female reported to our OPD with clinical complaint of lump over right back area gradually increasing in size since 2 years associated with pain and restriction of right shoulder joint movement. Imaging of 2 years back was not available with the patient. Patient had undergone excision for the swelling of right scapular region 2 years back. Histopathological report of suggestive of mass of size 5.5 x 4.5 in right scapular region showed undifferentiated sarcoma. (Figure 2 [A])

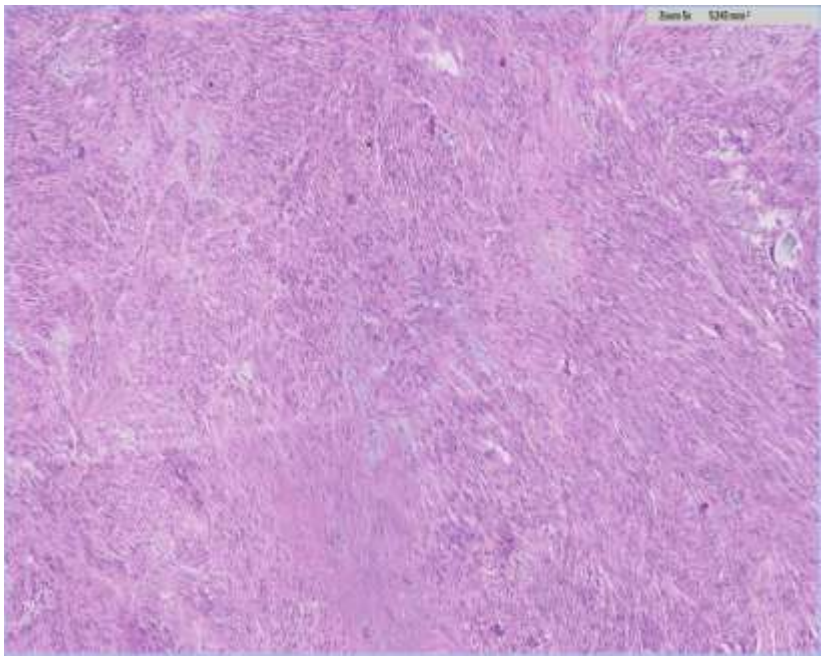

Figure 2[A]:- Showing Microscopic slide of Histopathological examination showing cells arranged in fascicles along with myofibrils running parallel.

Post OP USG showed mild scar in region of right scapula below incision with no evidence of residual or recurrent disease in Right scapular region. MDCT Scan chest also done suggestive of no evidence of disease, no enlarged nodes in the right scapular region. Patient received no adjuvant treatment with disease free interval of 1.4 years. Patient developed recurrence in right scapular region. Local examination showed a lump of 3 x 4 cm at operative site, not fixed to underlying structures, mobile, nontender. MRI imaging showed a solid lesion of 3.6 x 4.4 x 1.6 cm at the operative bed with increased vascularity surrounding the lesion.

Re-excision of the swelling was done. Patient was not affordable for IHC, so post op RT to tumor bed 60Gy / 30 # over 6 weeks using 3DCRT technique on linear accelerator was given with bolus to tumor site. Patient completed treatment successfully. Followed by 3 cycles of AI Day 1 to Day 3 [inj Adriamycin 60mg/m2 , inj ifosphamide 1.5gm/m2 , inj Mesna 225mg/m2] regimen. Patient completed 3 cycles of chemotherapy after which MRI was done suggestive of low grade edema at site of lesion with no obvious mass lesion, excellent response to the treatment (Figure 2[B]). Hence patient planned for 3 more cycles of AI Regimen. Long term disease free survival is under assessment.

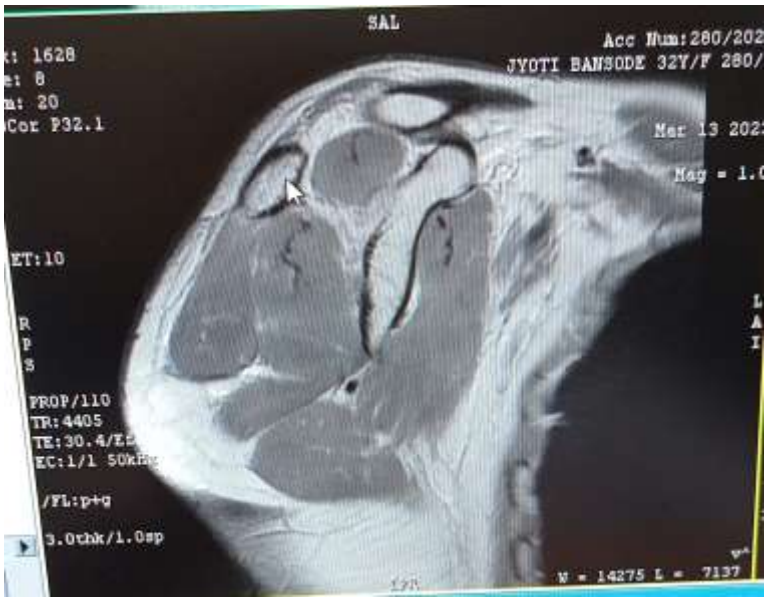

Figure 2[B]:- MRI image showing low grade edema with no obvious mass lesion at operative site.

Case 3 – Lms Of Right HIP :-

A 50yr old male patient presented in our OPD with complains of lump over right hip gradually increasing in size with foul smelling pus discharge from wound in the lump since 2yrs. Patient had done MRI Hip joint in June 21 suggestive of solid altered signal intensity lesion in subcutaneous plane of SuperoLateral Region of Right Hip Size 6.5x4.2cm abutting the gluteal muscle. An enlarged Oval region was also there in Right Inguinal Iliac region Largest 4.8x4.1cm abutting iliac arteries. Trucut Biopsy from Right Gluteal mass done in June 21 suggestive of high grade malignancy favoured sarcoma. Patient was not Affording for IHC at that time on the basis of HPR patient received 3 cycles of chemotherapy AI 3 weekly apart last cycle completed in august 21. IHC [Figure 3[A]] was done Features suggestive of Leiomyosarcoma in which desmin was focally weakly positive high KI67 Index along with CK8 Vimentin positive.

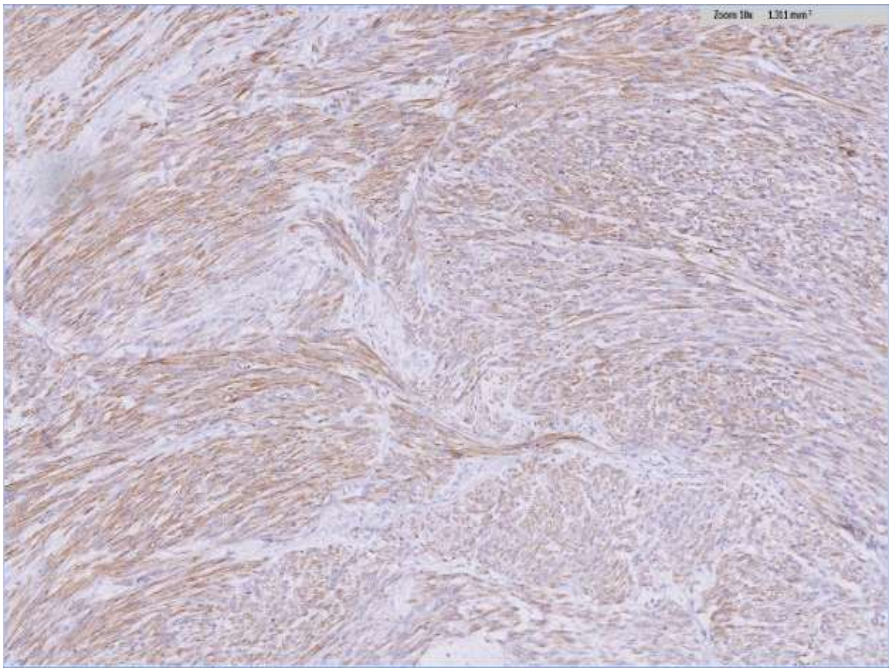

Figure 3[A]:- IHC suggestive of Leiomyosarcoma with Desmin Positive.

Patient defaulted for further treatment MRI PBH [Figure 3[B]] was done in April 22 suggestive of lesion size 10x6x9.7cm noted in subcutaneous plane of lateral aspect of right hip involving adjacent skin and subcutaneous tissue causing a focal bulge. 3.2x2.4cm size satellite lesion in ipsilateral Iliacus muscle was also there, Lymph node in Right external iliac and superficial inguinal lesion involving forming a conglomerated mass of size 5.7x5.9x7.3cm in superficial inguinal region.

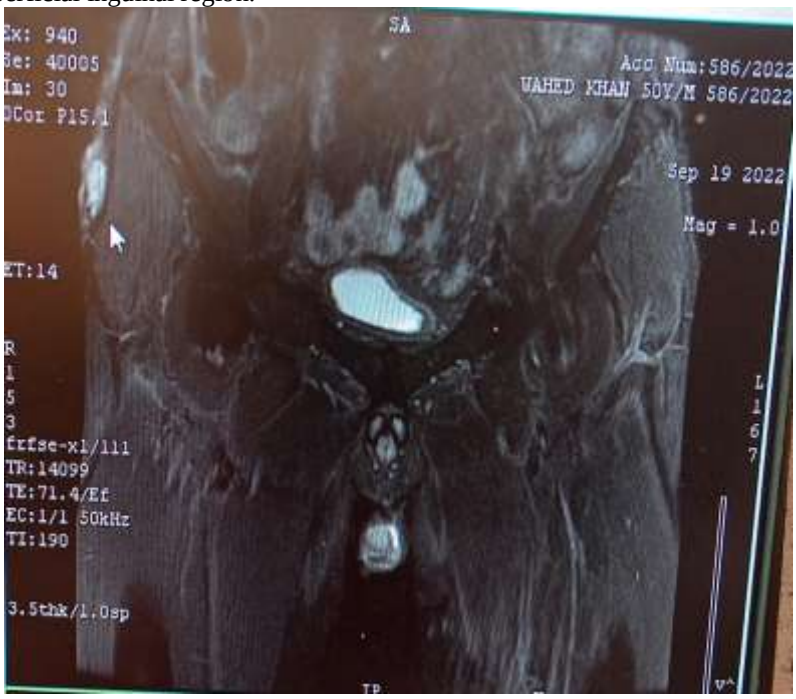

Figure 3[B]:- MRI suggestive of lesion in subcutaneous plane over lateral aspect of right hip.

Patient received 3 cycles of AI Day 1 to Day 3 [inj Adriamycin 60mg/m2 , inj ifosphamide 1.5gm/m2 , inj Mesna 225mg/m2] 3 weeks apart which completed on June 21. CT done on July 21 was suggestive of 9.4x4.6x6.2cm size lesion involving skin and subcutaneous tissue of superolateral aspect of Hip on right side laterally causing focal bulge of skin abutting right gluteal muscle. Along with lesion in subcutaneous plane size 1.4x1.2cm suggestive of satellite nodules conglomerated lymph node deposit 4.7x3.8x6cm along right external iliac vessel discrete lymph node noted in right inguinal region along right common iliac and external iliac vessel Largest 1.5x1.8cm lesion in Intramuscular plane involving right internal oblique and transverse abdominus muscle largest 1.5x1.6cm.

Patient then defaulted to surgery and then turned up in April 2022 with progressive lesion MRI PBH done revealed legion of size 10x6x9.7cm noted in subcutaneous plane of lateral aspect of right hip involving adjacent skin and subcutaneous tissue causing a focal bulge with 3.2x2.4cm satellite region in ipsilateral iliacus muscle. Lymph node in Right external iliac and superficial Inguinal region conglomerated forming a mass of size 5.7x5.9x7.3cm in superficial inguinal region.

Patient then reinducted with 2nd line chemotherapy with inj Gemcitabine 75mg/m2 and inj Docetaxel 100mg/m2 , 3 cycles 3 weeks apart followed by CT scan suggestive of Ulceroproliferative legion measuring 8x1.9x7cm noted in subcutaneous plane over lateral aspect of Right gluteal region with loss of Fat plane with right gluteus medius muscle conglomerated lymph nodal mass in right external iliac region size 5x4.6x6.2cm along right superficial inguinal region 3x2.8cm . Patient underwent surgery with wide local excision of Hip sarcoma with lymph node dissection right anterolateral thigh flap with STSG in December 2022. [Figure 3[C]]

Figure 3[C]:- Suggestive of intraoperative image while undergoing Wide Local Excision of Hip Sarcoma.

Post op HPR :-

ulcer over skin size 5 x 2 cm with base abutting < 1mm away from inked cauterized margin. Malignant neoplasm suggestive of sarcoma , anterior margin with skin and overlying skin ulcerated and involved. Right inguinal lymph node ¼ positive without ENE. Right external iliac 3/3 positive with ENE. Post op adjuvant RT to post op site is now planned after wound healing. Long term disease free survival is under assessment.

Conclusion:-

Leiomyosarcoma of bone is a rare disease. Proper diagnosis and multidisciplinary treatment in combination with surgery, chemotherapy and radiotherapy along with proper counselling of the patient and relatives regarding the treatment strategy is required. Long term disease free survival is under assessment.

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