Case Number 15
Pleomorphic Sarcoma

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Case summary:

Demographic details:
Ms. AC, female, 67
Referred from home by GP

67-year-old female who was referred from her general practitioner because of uncontrolled right popliteal knee pain which was very severe and continuously deteriorating. She could not bend her knee and sleep because of the pain. She could only walk on tiptoes with increased pain on weight bearing. Originally the popliteal swelling was thought to be a baker's cyst. Arthroscopy showed no changes and MRI showed a large, primarily solid lesion in the popliteal fossa measuring 6x6x9 cms. This was biopsied and histopathology showed a sarcoma and an above knee amputation had to be performed. The patient is now well undergoing physiotherapy and occupational therapy to get back to her life.

Presenting complaint:

Severe pain in the right knee leading to decrease mobility.

History of presenting complaint:

The patient complained that after a fall in April 2011, in which she hit her knee, she felt an ever growing knee pain. She also complained of swelling and was noted that she could not extend her knee. Her pain increased with weight bearing and could only walk on tiptoes.

The pain was very severe and crushing in nature. It did not allow her to sleep at night. She was very desperate and has spent the last two weeks unable to move unless assisted by someone. The patient did not find a way to reduce the pain and not even powerful painkillers prescribed by her general practitioner were working. The patient was also given two cortisol injections in her knee joint but these had no beneficial effect on her.

Past medical and surgical history:

Past medical history:

Hypertension
Hypercholesterolaemia

Past surgical history:

Tonsillectomy as a child
Excision of benign lipoma of right shoulder (2000)

Drug history:

Drug	Dosage	Frequency	Type	Reason
Atenolol	50 mgs	daily	Beta blocker	Hypertension
Bumetanide	1 mgs	BD	Diuretic	Hypertension
Simvastatin	20 mgs	BD	Statin	Hypercholesterolaemia
Enalapril	20 mgs	BD	ACE inhibitor	Hypertension
Glucosamine	1 tablet	BD	Joint care	Arthritis
Amlodipine	10 mgs	daily	Calcium channel blocker	Hypertension
Solpadol	30 mgs	TDS	Analgesic	Pain relief

Family history:

Mother died of a stroke at the age of 65.
Father died of a brain tumour at the age of 83.
There is a history of hypertension and hypercholesterolaemia in the family.

Social history:

Married.
Lives with husband who is independent and helps her when needed. Her children also give her a helping hand.
She has one flight of stairs but does not need to use it as everything is found on the first floor.
No smoking.
No alcohol intake.
No recreational drugs.

Systemic inquiry:

- General Health: good and active. Patient looked comfortable after operation.
- Cardiovascular System: hypertension and hypercholesterolaemia.
- Respiratory System: nil to note.
- Gastrointestinal Tract: nil to note.
- Genitourinary System: nil to note.
- Central Nervous System: nil to note.
- Musculoskeletal System: after amputation she is already standing up and doing exercises with the help of physiotherapy.
- Endocrine System: nil to note.

Current therapy:

Patient was fast-tracked due to the amount of pain she was suffering and given powerful analgesics till the operation.

Discussion of results of general and specific examinations:

On examination: The patient had fixed flexion of the knee and painful ROM. Mass at the popliteal fossa was felt, which was tender on palpation.

Differential diagnosis:

- Baker's cyst
- Popliteal aneurysms

Diagnostic procedures:

Laboratory Investigations:

Test: Biopsy for histology (18/1/13)
Justification for test: Popliteal mass in right knee.
Result: Multiple biopsies show poorly differentiated spindle cell lesion composed of pleomorphic spindle cells with scattered abnormal mitosis and occasional bizarre nuclei which are forming sheets and fascicles. The cells are SMA positive but Desmin, Cytokeratin and HRF-35 negative.
Conclusion: Pleomorphic Sarcoma.

Imaging:

Test: MRI (17/1/13)
Justification for test: Popliteal mass of right knee.
Result: There is a large primarily solid mass lesion within the popliteal fossa measuring 6x6x9 cm. It is of intermediate to high signal intensity on fluid-sensitive sequences and low signal intensity on T1. Its solid component is seen to avidly enhance post contrast administration. A few central cystic components are noted within the mass lesion. The lesion is seen to encase the popliteal neurovascular bundle. It displaces the gastrocnemius muscle belly posteriorly. A small effusion is also noted.
Conclusion: Large mixed solid cystic popliteal mass lesion appearances of which are suspicious for sarcomatous change.

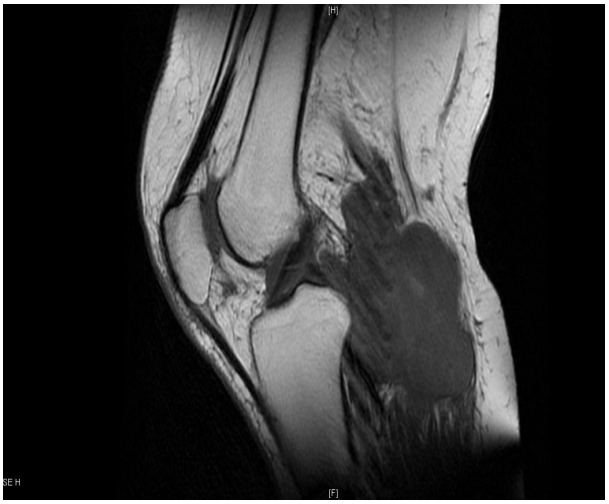

Figure 1: MRI (Coronal Section) of the knee showing clearly the popliteal mass

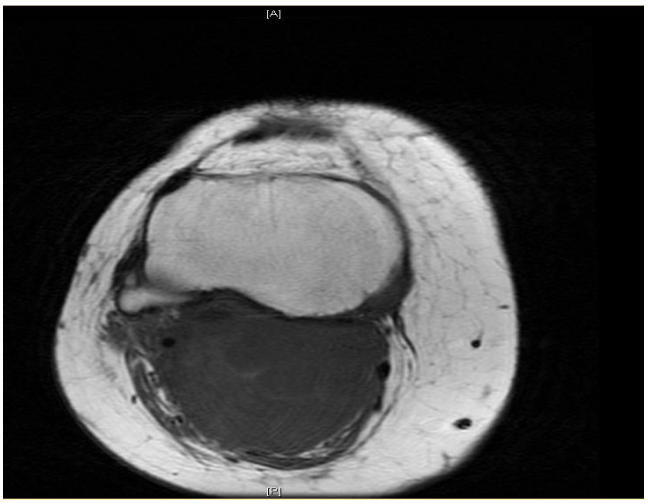

Figure 2: Cross sectional MRI view of the right knee showing the popliteal mass

Test: CT Abdomen, CT pelvis and CT thorax
Justification for test: Staging.
Result: No abnormality seen in the chest. In the abdomen and pelvis, the liver is seen to contain four tiny lesions likely to be simple cysts. Both kidneys are noted to have cortical lumps which probably represent foetal lobulations. The remaining structures are intact. No free fluid or enlarged lymph nodes are observed.

Conclusion: No abnormality in chest but cortical lumps noted in kidney which might need further investigation.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Atenolol	50mgs	daily	Beta blocker	Hypertension
Bumetanide	1 mgs	BD	Diuretic	Hypertension
Simvastatin	20 mgs	BD	Statin	Hypercholesterolaemia
Enalapril	20 mgs	BD	ACE inhibitor	Hypertension
Glucosamine	1 tablet	BD	Joint care	Arthritis
Amlodipine	10 mgs	daily	Calcium channel blocker	Hypertension
Solpadol	30mgs	TDS	Analgesic	Pain relief
Enoxaparin (SC)		daily	Low molecular weight heparin	Given post-operatively for pain relief
Pethidine (IM)		PRN	Opioid analgesic	Given post-operatively for pain relief

Surgical therapy:

Pre-operative: The tumour in the right popliteal fossa had infiltrated the nerve bundle and thus the limb was unsalvageable. Patient was fit for general anesthetic and prepared the night before. There was discussion with oncologist and radiologist before undergoing surgery and the multidisciplinary team decided that the limb should be operated on because it was invading the neurovascular bundle.

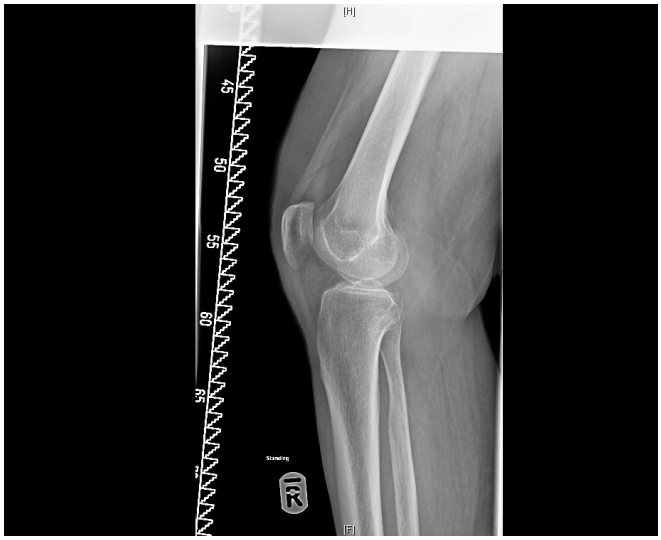

Figure 3: X-ray of right Knee showing a mass in the popliteal fossa

Operation – Above-Knee Amputation: The patient was administered general anesthetic and put in a supine position. Co-amoxiclav was given intravenously and the skin was prepared and draped. Fish-mouth flaps were fashioned. This was followed by sharp dissection down to the bone. The vessels were identified medially and divided between clips and transfixed to the proximal stump with PDS 0. The sciatic nerve was identified and infiltrated with 1% 10 ml of lignocaine. This was done for better analgesia as well as reducing the chances of phantom limb.

Then the periosteum was elevated from the bone and the bone was divided 5cms above the lower border of the stump. The stump was then sanded down to round edges and bone wax was applied to the bone marrow.

After haemostasis was achieved, the bone was covered with muscle using Vicryl 2/0 and the fascia was sutured to the opposite fascia by using Vicryl 0. Finally the skin was stapled and the wound was infiltrated with bupivacaine 0.25% once again for better pain management of the patient.

The leg and fat from the stump were sent to the histology lab for further investigations. The fat from the stump required analysis in order to determine whether the cancer was resected completely or otherwise, as this would change the future treatment regimen.

Post-operative: The patient was watched till awake and was given 1L 8 hourly intravenous infusions of Hartmann's solution. Hartmann's IV Infusion is used to replace body fluid (as it is isotonic to blood) and mineral salts that may be lost for a variety of medical reasons. For the first 6 hours temperature, blood pressure and pulse were taken 2 hourly and then 6 hourly. The patient was allowed to drink and eat when feeling well and was monitored for any bleeding. Also analgesia was continued and clexane was given to prevent deep vein thrombosis.

Diagnosis:

Pleomorphic sarcoma in right popliteal fossa which was compressing her nerve bundle.

Final treatment and follow-ups:

Patient is undergoing physiotherapy and occupational therapy to regain her mobility and independence. Patient looks healthy and strong and it seems that she will recover well.

Cell Pathology report (6/3/13):
Macro: Above-knee amputation measuring 600mm in length. Skin over the knee and popliteal fossa are erythematous. On sectioning there is an ill-defined pale and brown necrotic intravascular mass which measures 440mmx50mmx60mm. This mass appears to be intramuscular and doesn't infiltrate bone.
Micro: Sections show an infiltrative, poorly differentiated sarcoma composed of spindle pleomorphic neoplastic cells which in places show fascicular arrangement. There is prominent focal necrosis. Small residual aggregates of fat cells resembling lipoblasts are also identified suggesting that the tumour is very likely a dedifferentiated liposarcoma with extensive pleomorphic component. It is completely excised. Separate biopsies include fat from stump show no notable abnormalities.

Patient is now being evaluated at Boffa hospital to see if she will require additional treatment such as chemotherapy or radiotherapy, although this seems unlikely since the histology result suggests that the resection was complete and there seems to be no metastasis.

Fact Box 15:

Title: Pleomorphic Sarcoma

Also known as malignant fibrous histiocytoma (MFH), it is one type of sarcoma from about 50 other types of sarcoma. It is a malignant neoplasm of uncertain origin that arises both in soft tissue and bone. No true cell of origin has ever been identified[1]. Most commonly found in thigh.

Types: Pleomorphic sarcoma manifests itself as a broad range of histologic appearances with four sub-types described; Storiform-pleomorphic, Myxoid, Giant cell, Inflammatory [2].

Of these, the storiform-pleomorphic is the most common type, accounting for up to 70% of most cases. The myxoid variant is the second most common accounting for approximately 20% of case.

Risk factors:

- Age (50-70)
- Male

Symptoms:

- Very rare: pain only when a nerve is compressed
- Rarer: weight loss and fatigue
- Signs: a lump might be felt

Treatment:

- Surgery
- Radiation
- Chemotherapy

Prognosis: Prognostic factors that are known to correlate with survival in patients with pleomorphic sarcoma include tumour grade, depth, size, metastatic status, patient's age and histologic subtype [3]. Favourable prognostic factors include age less than 60 years old, tumor size less than 5 cm, superficial location, low grade, the absence of metastatic disease and a myxoid subtype. Older patients with large (> 5cm), deeply seated, high grade tumors do not have as favourable an outcome. For example, patients with a small low grade tumor are likely to be cured completely. Patients with large, deep, high grade tumors (Stage III) have a 5 year survival estimate which ranges from 34 to 70% [4].

Recurrence: Local recurrence (LR), i.e. recurrence of the tumor in the same location, will occur in approximately 20-30% of all patients with soft tissue sarcomas [5]. LR is lowest in extremity sarcomas and highest in retroperitoneal and head and neck sarcomas. This distribution is directly related to the ability to completely resect a tumor at the time of surgery. Higher LR rates are observed in the setting of positive surgical margins, which are more difficult to achieve in anatomic locations outside of the extremity [6]. Whether local control has an impact on overall survival is unclear and remains controversial.

Summary:

MFH is a curable disease.

The term "Malignant Fibrous Histiocytoma" has been changed by the WHO to Undifferentiated Pleomorphic Sarcoma Not Otherwise Specified.

The mainstays of treatment for MFH are complete surgical excision, most often supplemented with adjuvant radiation therapy.

Chemotherapy is reserved for patients with the highest risk of disease recurrence or patients that already have recurrence.

Patients with recurrent MFH can still be cured.

Favorable prognostic factors that correspond to superior survival include small tumor size, low grade, extremity location, superficial location and localised disease.

References:

1. Kauffman, S. L., and Stout, A. P.: Histiocytic tumors (fibrous xanthoma and histiocytoma) in children. Cancer, 14: 469-82, 1961.
2. Enzinger and Weiss's Soft Tissue Tumors. Edited by Weiss SW, G. J., St. Louis, Mosby, 2001.
3. Coindre, J. M. et al.: Prognostic factors in adult patients with locally controlled soft tissue sarcoma. A study of 546 patients from the French Federation of Cancer Centers Sarcoma Group. J Clin Oncol, 14(3): 869-77, 1996.
4. Le Doussal, V. et al.: Prognostic factors for patients with localized primary malignant fibrous histiocytoma: a multicenter study of 216 patients with multivariate analysis. Cancer, 77(9): 1823-30, 1996.
5. Salo, J. C.; Lewis, J. J.; Woodruff, J. M.; Leung, D. H.; and Brennan, M. F.: Malignant fibrous histiocytoma of the extremity. Cancer, 85(8): 1765-72, 1999.
6. Heslin, M. J.; Woodruff, J.; and Brennan, M. F.: Prognostic significance of a positive microscopic margin in high-risk extremity soft tissue sarcoma: implications for management. J Clin Oncol, 14(2): 473-8, 1996.