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An Interesting Differential for Orthopnoea: Leiomyosarcomas

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Abstract

Background

Primary cardiac tumors are very rare. The autopsy incidence is between 0.0001-0.030%. 25% of the tumors are malignant and 95% of them represent primary cardiac sarcomas. Primary Cardiac Sarcomas (PCS) can be histologically divided into angiosarcomas, leiomyosarcoma and fibrosarcoma. This case report describes a rare case of leiomyosarcoma that presented late with metastasis.

Case Summary

Mrs. H, 67, presented with an 18-month history of dry cough, and 3 months of worsening breathlessness and orthopnoea. Chest X-ray and CT chest findings prompted an urgent transthoracic echocardiogram which showed a large sessile mass filling in the right atrium with some obstruction to the mitral valve (MV) and appeared attached to the posterior MV annulus. Under Cardiology, patient had a CT Chest-Abdomen-Pelvis with contrast which showed an obstructing lesion involving the left atrium, infiltrating through the MV into the left ventricle and disseminated bony metastasis. A core biopsy of L3 paravertebral mass showed moderately differentiated leiomyosarcoma. The patient had an MRI spine after reporting back pain which showed metastasis to the vertebral bodies of T3, T10, T12 and L3 (posteriorly eroded and infiltrated by soft tissue mass). A multi-disciplinary team discussion yielded that this patient receives palliative radiotherapy to L3 vertebrae.

Conclusion

PCS should be considered as a differential when patients present with worsening cardiovascular symptoms, albeit rare. This case report adds to the existing literature of primary cardiac sarcomas and advocates for primary care services to have open access for requesting echocardiograms for early diagnosis of such tumours.

Abbreviations: None to be mentioned
Keywords: Orthopnoea; Primary Cardiac Sarcomas; oncology; echocardiogram; pericardial effusion; leiomyosarcomas.

Introduction

Primary cardiac sarcomas are very rare. The autopsy incidence is between 0.0001%-0.030%. 25% of the tumours are malignant and 95% of them represent primary cardiac sarcomas. Primary Cardiac Sarcomas (PCS) can be histologically divided into angiosarcoma, leiomyosarcoma and fibrosarcoma of which angiosarcomas constitute the most common histological subtype (1). It is believed that PCS arises de novo. The presentation is highly dependent on the site of the tumour however patients can present with murmurs or pulmonary emboli secondary to thrombi (2). It is not uncommon for patients to also present with shortness of breath and weight loss although many tumours remain asymptomatic until it reaches an advanced stage of disease. This case report describes a 67-year-old lady who was diagnosed with PCS and reached a palliative outcome as a result of advanced metastases.

Case Presentation

Mrs. H, a 67-year-old Caucasian female with a background of hypertension and hyperthyroidism, was referred to the Respiratory Outpatient Clinic with an eighteen-month history of dry cough and a three-month history of worsening breathlessness/orthopnoea. There were no associated weight loss, fever or night sweats. Her exercise tolerance had declined to half a mile over this period. Mrs H was a non-smoker and

a retired clerical worker. She had no allergies, had a cat at home and had no significant exposure to any chemicals/dust in the past. On examination, there were no signs of clubbing, jaundice or lymphadenopathy. Respiratory, cardiovascular, abdominal and breast examinations were unremarkable. Pulmonary function tests and Radio allergosorbent Test were normal. Initial blood results showed raised ESR, CRP and ALP (Table 1).

Initial chest x-ray revealed clear lung fields and mild cardiomegaly (Figure 1.1). A non-contrast HRCT showed findings as described (Figure 1.2).

Mrs. H returned for an urgent Transthoracic Echocardiogram. This revealed a large sessile unencapsulated mass filling in the left atrium with some Mitral Valve (MV) obstruction and appeared to be attached to the posterior MV annulus rather than the inter-atrial septum. The biventricular function was good and there was no evidence of pulmonary hypertension. A small circumferential pericardial effusion was noted.

With these findings, she was admitted under Cardiology for further evaluation. A contrast-enhanced CT CAP was performed (Figure 3.3) showing an obstructing lesion involving the left atrium, infiltrating through the MV into the left ventricle and a mild pericardial effusion. There was no mediastinal lymphadenopathy. There were disseminated bony metastasis involving both proximal femurs, T12 vertebral body, posterior elements of L3 vertebra and the body of the sternum. There was also a small right pleural effusion.

Her case was discussed with the regional tertiary center and was included in the multidisciplinary team (MDT) case discussion. Meanwhile, a core biopsy of the lumbar paravertebral mass was performed showing two cores of a moderately differentiated sarcoma composed of slender and slightly plump cells arranged in fascicles of varying size and intersecting at right angles. The neoplastic cells had light eosinophilic and blunt ended nuclei. They were non-necrotic, mitotic and had focal areas of hyalinization of stroma. The neoplastic cells were positive with smooth muscle Actin (SMA) and Desmin (Figure 3). CD99 stains cytoplasm. The neoplastic cells were negative for S100 proteins, MCK, CD34, NF 200 and WT1. The morphological appearances and immunoprofile were consistent with moderately differentiated leiomyosarcoma. An urgent spine MRI was performed as the patient reported new lower back pain. This showed metastasis to the vertebral bodies as described with posterior elements of L3 eroded and infiltrated by a soft tissue mass (Figure 4).

Following MDT discussion, a debulking procedure of the primary lesion or palliative chemotherapy was not performed as this was deemed to be hazardous, not curative and. of no benefit to Mrs. H symptoms or overall performance status. After discussing with the patient and her family, palliative radiotherapy to the lumbar spine (L3) was administered for pain control with good effect. The patient passed away 3 months post- presentation.

Discussion

Leiomyosarcomas are typically located in the atrium where it presents as a large mass (6). In rare cases such as this, a metastatic lesion is the first manifestation of the disease translating to a poor prognosis.

Echocardiography and cardiac MRI demonstrate the tumour itself and haemodynamic compromise. However, full body CT imaging better appreciates the extent of extra cardiac dissemination. There are no definitive pathognomonic features on echocardiogram that differentiate a malignant cardiac tumour from benign atrial myxomas. Tumours with a broad base and originate from pulmonary veins raise the possibility of leiomyosarcoma [4]. The gold standard investigation is biopsy with histopathology and immunohistochemistry.

Histological analysis of leiomyosarcomas includes spindle, epithelioid or myxoid features. Some of them contain osteoclast-like multinucleated giant cells. A typical cell of leiomyosarcoma is elongated and has abundant cytoplasm. The nucleus is centrally located and blunt-ended or cigar-shaped. In some cells, a vacuole is seen at one end of the nucleus, creating a slight indentation that results in the nucleus assuming a concave contour. These cells are arranged in fascicles of varying size and shape that intersect at right angles, which is the recognised pattern of growth of leiomyosarcoma. The neoplastic cells are often positive with SMA and Desmin immunohistochemical staining although Desmin positivity is more variable (9). The histopathological differential diagnoses of leiomyosarcomas include fibrosarcoma and malignant peripheral nerve sheath tumours. Histological analysis illustrated typical features of leiomyosarcoma. Immunoprofiling was in keeping with a similarly reported case (the specimen stained positive for SMA and Vimentin but negative for S100 proteins and CD31). A recent study suggests SMA is presumed to be the most sensitive marker of this disease (95%), followed by MSA (91%) and Calponin (88%) [3]. Desmin and Vimentin are less sensitive for leiomyosarcoma but more so for rhabdomyosarcoma and tumours of mesenchymal origin respectively [5,9].

There is a lack of consensus regarding treatment strategies (7,8). Historically, surgical resection and chemotherapy with doxorubicin and ifosfamide represented the mainstay of treatment (10,11,12). The benefits of adjuvant chemotherapy have not been fully recognized due to the low incidence of primary

cardiac sarcoma and recommendations only being based on case reports and retrospective analyses (11). The exact role of radiotherapy remains unestablished. Radiotherapy has been incorporated as part of a palliative approach and is also recognised as an adjunct for aggressive therapy but needs cautious use due to risk of direct damage to myocardium and pericardium.

Unfortunately, cardiac leiomyosarcomas have a high rate of local and distant recurrence, despite optimal resection of the primary tumour. Without treatment, the prognosis is thought to be six months from diagnosis [5]. Therefore, prognosis and treatment options are largely dependent upon tumour grading, extent of invasion, evidence of metastases and overall performance status of the individual.

Acknowledgements

In completing this case report, I would like to express my heartfelt gratitude to Dr. S.S Myagerimath who was directly involved in the patient's care in 2019 and has supported me throughout. I would also like to thank Krsty Nale and Rudi Schmiglyski for their hard work, determination and commitment compiling the histopathology specimens in order to provide an accurate diagnosis. All their efforts together ensured that we provided the best possible care to the patient.

Conflict of Interest

None declared.

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References

1) Figure 1: Represents imaging undertaken by the respiratory outpatient clinic, left to right. Figure 1.1: Mild Cardiomegaly was noted on posterior-anterior (PA) chest x-ray. Figure 1.2: Transverse section of Non-Contrast High Resolution CT scan: This showed a mild to moderate pericardial effusion (approximately 14 mm in size) with suspected cardiac enlargement and mild interstitial oedema.

2) Figure 2: Imaging undertaken after preliminary investigations. From left to right, top to bottom. Figure 2.1: Echocardiogram in Parasternal Long axis view shows a Large sessile mass in the Left Atrium attached to the mitral valve annulus. Figure 2.2: Echocardiogram in Apical 4-chamber view shows eccentric mitral regurgitation jet hugging the mass. Figure 2.3: Transverse section of Contrast-enhanced CT chest-abdomen-pelvis- the above slices demonstrate a left atrial infiltrating mass represented by the white arrow. Figure 2.4: Sagittal section of Contrast-enhanced CT chest-abdomen-pelvis demonstrates metastatic deposits at T12 and L3. The blue arrows indicate the metastatic deposits.

3) Figure 3: From left to right, Histopathology specimen- neoplastic cells staining positive with A) Smooth Muscle Actin and B) Desmin.

4) Figure 4: MRI Spine: Sagittal T1, T2, STIR and axial T2 sequences were obtained. This STIR images demonstrate the bone metastases at T12 and L3 levels. No clear signs of cauda compression, spinal stenosis and myelopathy were noted on it.

Table

Test	Value	Normal Range (Units)
Haematology		
Haemoglobin	118	115 - 165 g/L
Mean Corpuscular Volume	90	82 - 100 fL
White Cell Count	9.9	4.0 - 11.0 x 10 /L
Platelets	423	140 - 400 x 10 /L
Neutrophils	6.9	2.0 - 7.5 x 10 /L
ESR	81	0 - 30mm/hr
Biochemistry		
Sodium	133	135 - 145 mmol/L
Urea	3.8	2.5 -7.5 mmol/L
Creatinine	54	65 - 140 µmol/L
EGFR	>60ml/min	
Bilirubin	11	0 -21 µmol/L
Alkaline Phosphate	197	35 -130 iu/L
Alanine Aminotransferase	32	0 - 50iu/L
Albumin	42	35 -53 g/L
Corrected Calcium	2.33	2.12 - 2.62mmol/L
C-Reactive Protein	51	0 - 10mg/L

Table 1: Initial Blood Investigations taken demonstrating raised platelets, raised erythrocyte sedimentation rate and raised C-reactive protein.

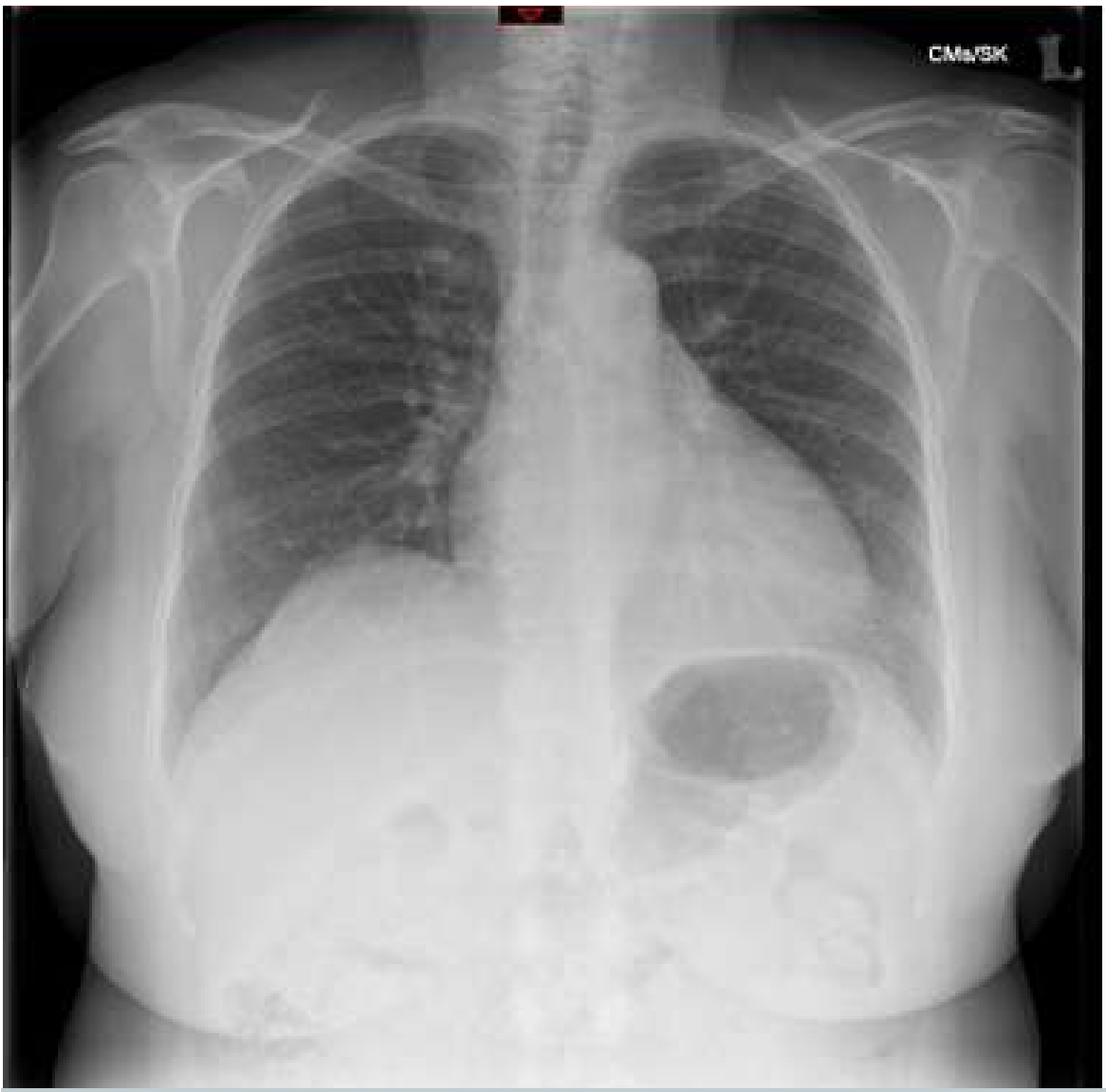
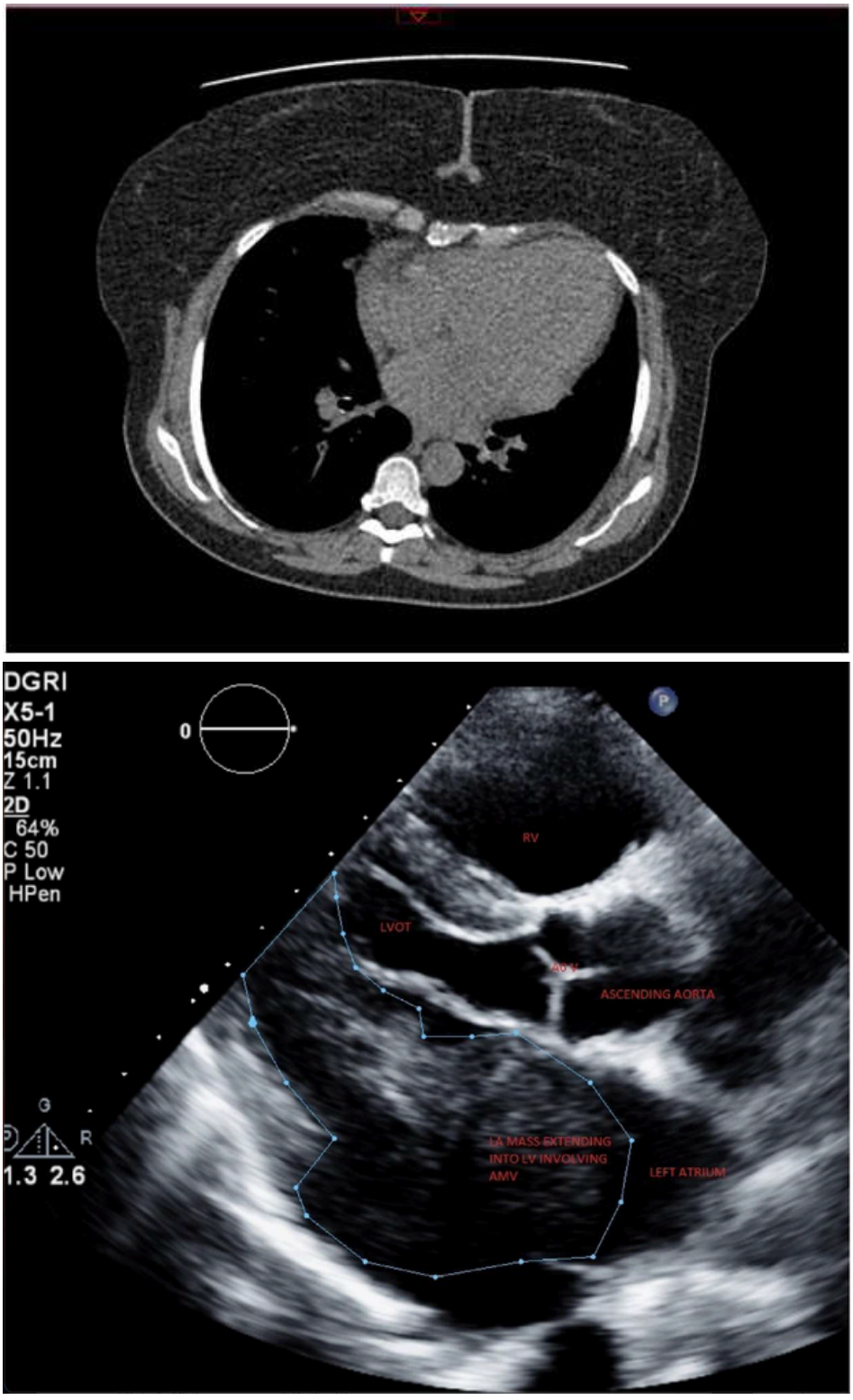


Fig. 1: Case 1. (A) Chest radiograph showing the AICD device and right ventricular lead in situ. (B) Zoomed view of the chest radiograph showing damage (white arrow) in the AICD lead. (C) Device interrogation showing high pacing impedance suggestive of lead conductor fracture. (D) Fluoroscopy post lead revision showing device with capped old lead and functional new lead.



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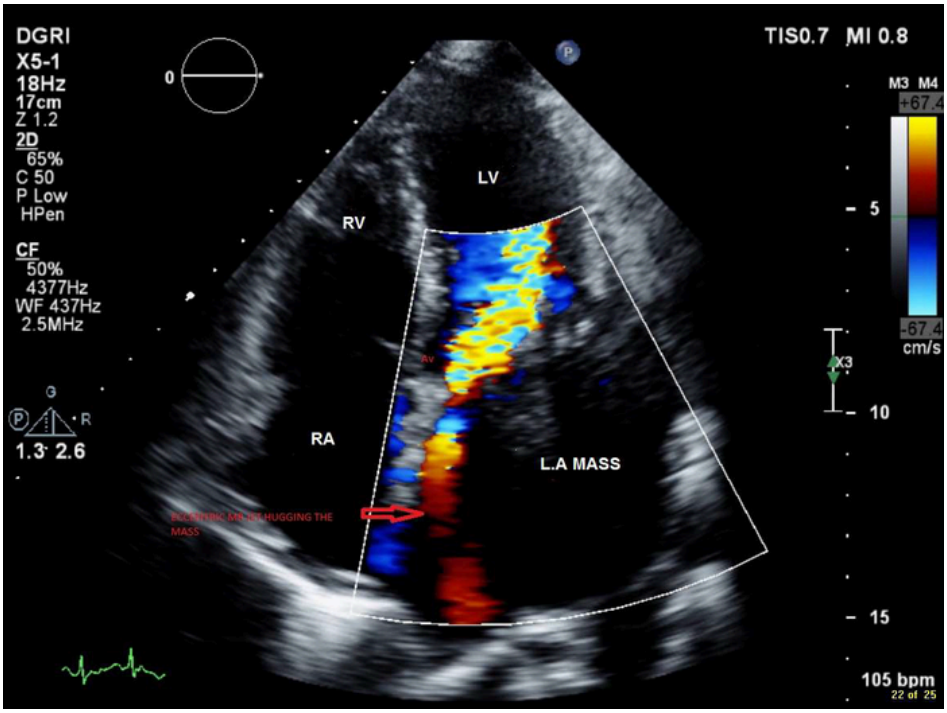

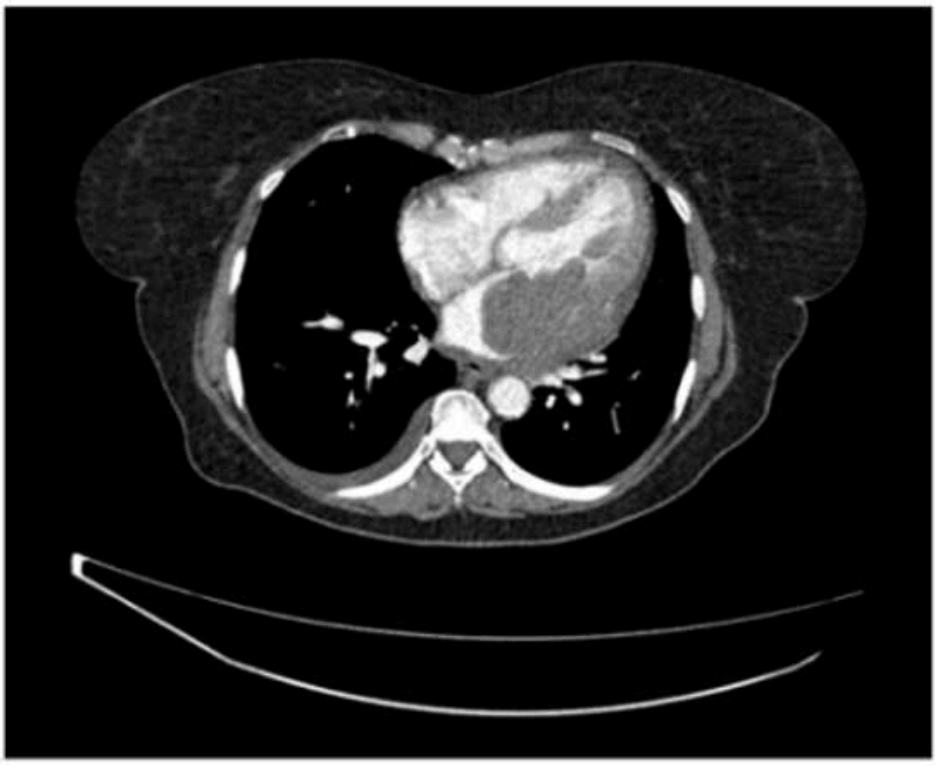

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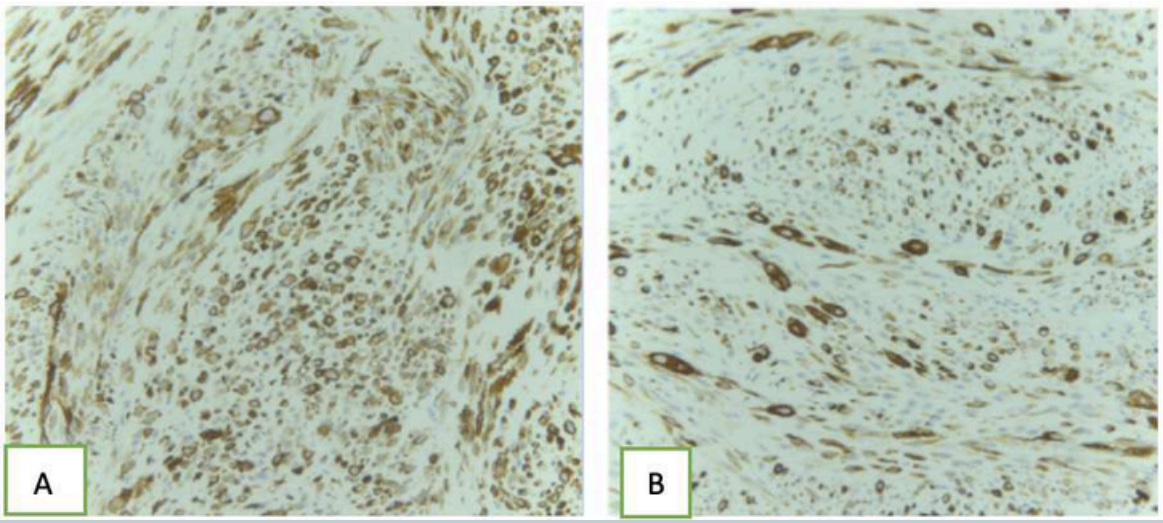
Figure 2.4: Sagittal section of Contrast-enhanced CT chest-abdomen-pelvis demonstrates metastatic deposits at T12 and L3. The blue arrows indicate the metastatic deposits.



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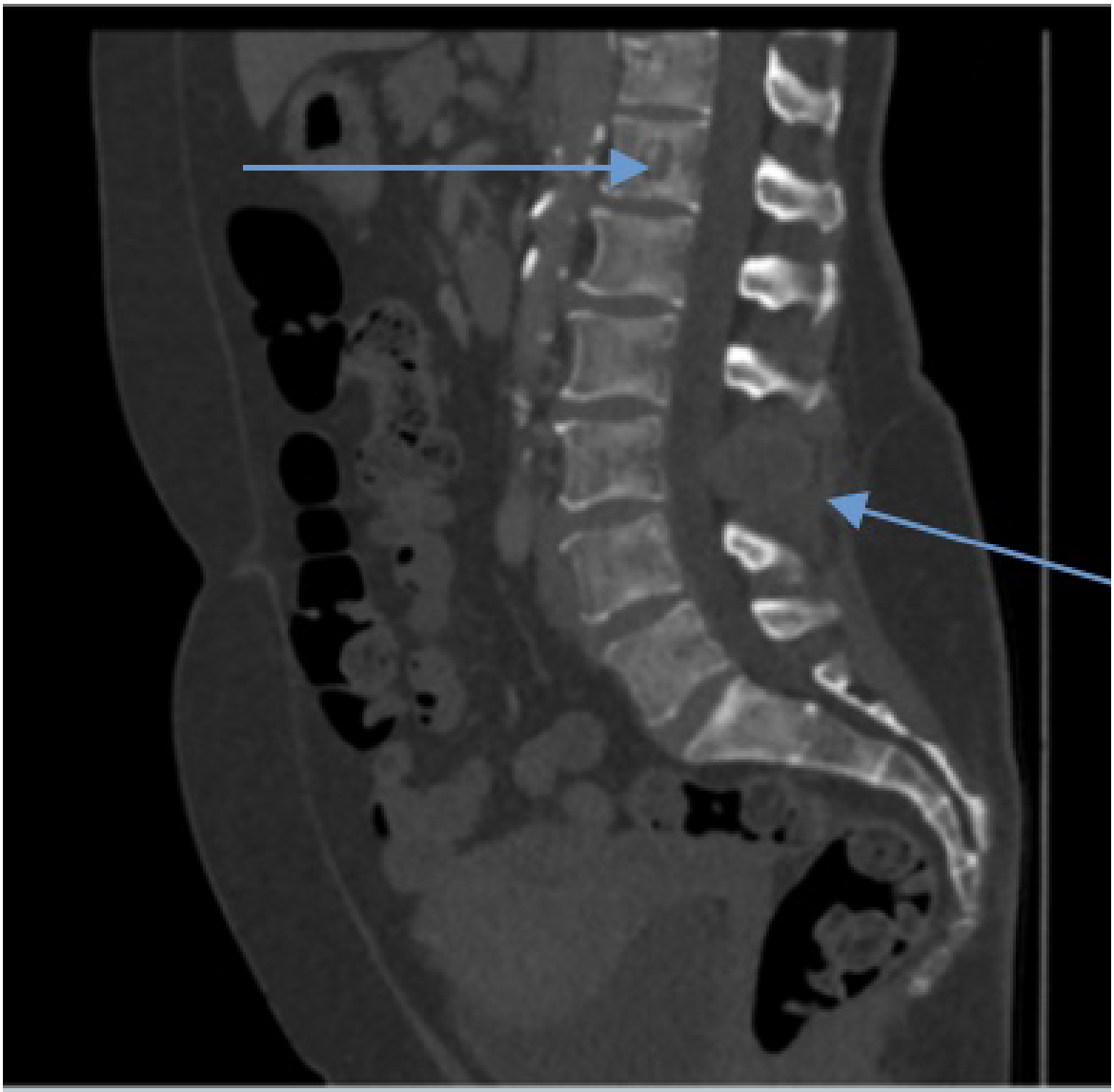
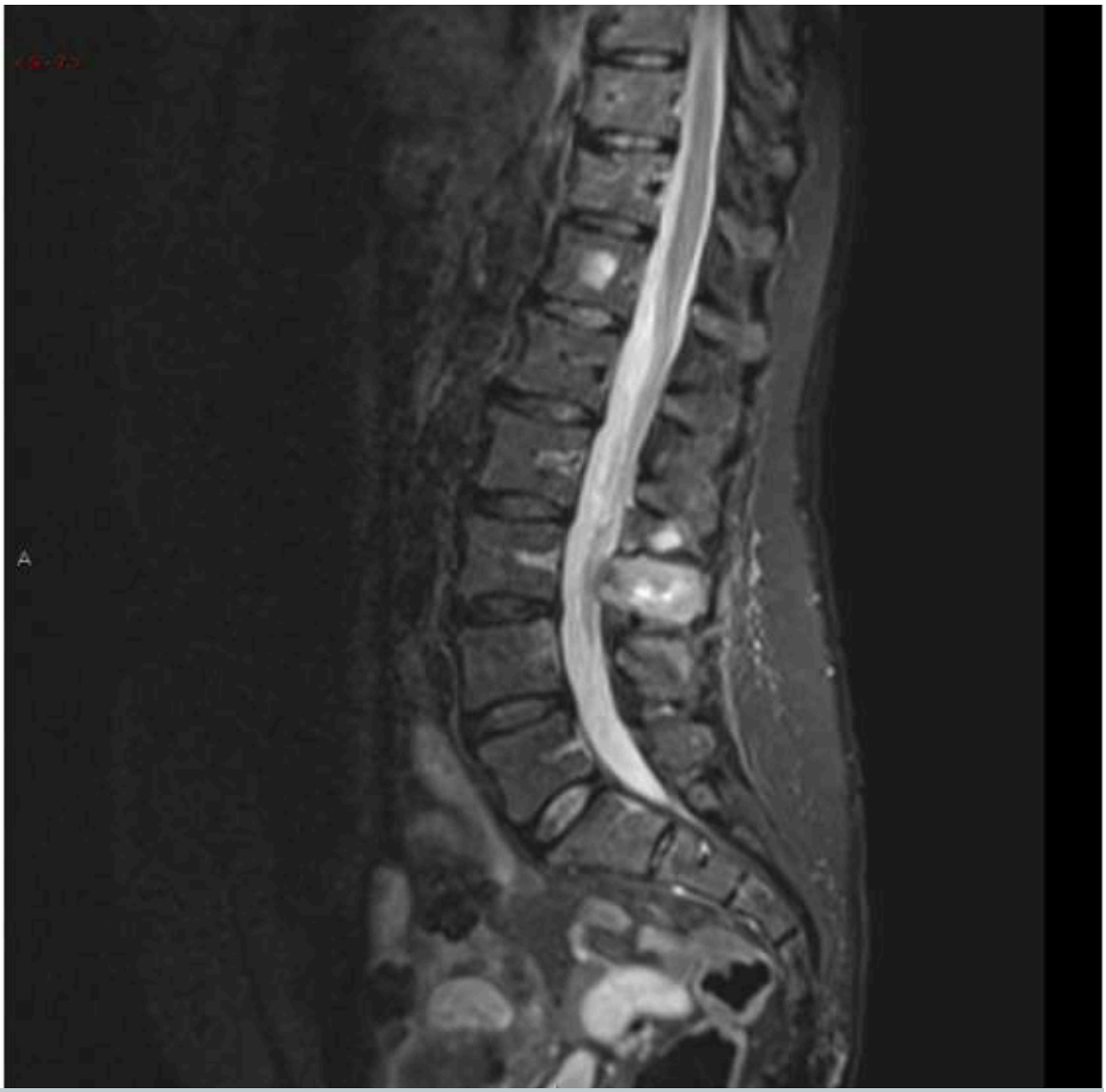


Figure 4: MRI Spine: Sagittal T1, T2, STIR and axial T2 sequences were obtained. This STIR images demonstrate the bone metastases at T12 and L3 levels. No clear signs of cauda compression, spinal stenosis and myelopathy were noted on it.



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