CLINICAL CASE - TEST YOURSELF Musculoskeletal imaging

# A rare diagnosis in a patient presenting with back pain

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## PART A

A 43-year-old female with a known history of hypertension presents with back pain, predominantly in the lower back. She also reports intermittent palpitations and a chronic uninvestigated cough. On further questioning she reports a family history of seizures regarding her sister and maternal aunt. On physical examination her skin appears to have multiple small circular papular lesions on her face and extensor surfaces (right elbow and left knee). She appears to have lumbar spinal tenderness on palpation of the area and bilateral crepitations are heard on auscultation of the chest. On cardiac auscultation a low pitch systolic murmur is heard in the 5th intercostal space, at the level of the left midclavicular line. Urea and Electrolyte blood results, Full Blood Count and urine dip test were unremarkable. Abdominal Ultrasound revealed renal cystic lesions with hypoechoic centers bilaterally, as well as two hyperechoic circular, well defined lesions in the left renal cortex, the largest with a diameter measuring at about 2.3 cm. Cardiac echo showed a small (1.5 cm in diameter) well demarcated hyperechoic circular lesion attached to the myocardium of the left atrial wall. MRI imaging of the lumbar spine without IV contrast, due to the allergy status of the patient, was performed, in T1, T2 and STIR sequences.

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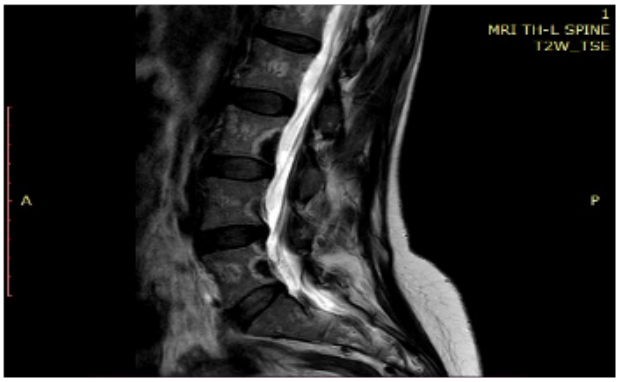


***Figure 1:*** *Sagittal T2 weighted of lumbar spine image*

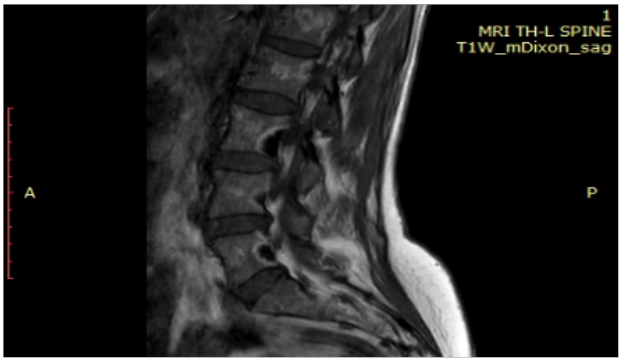


***Figure 2:*** *Sagittal T1 weighted image*

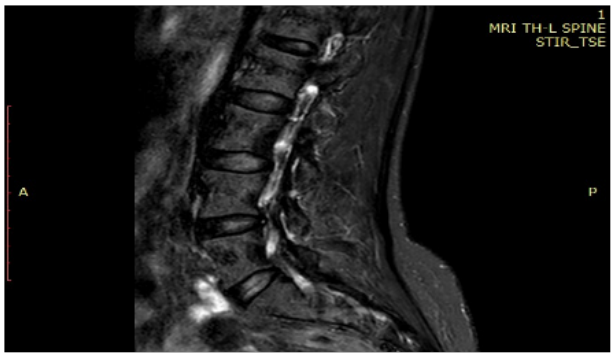


***Figure 3:*** *Sagittal STIR weighted image of the lumbar spine*

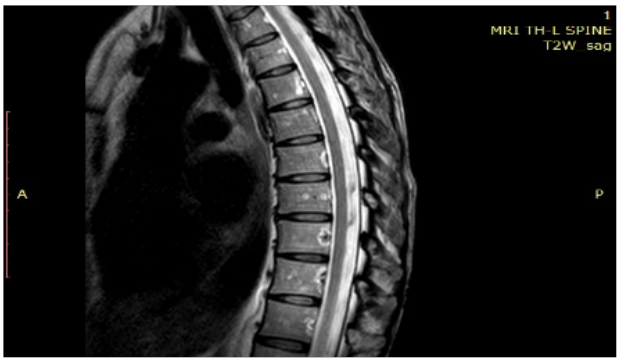


***Figure 4:*** *Sagittal T2 weighted image of the thoracic spine*

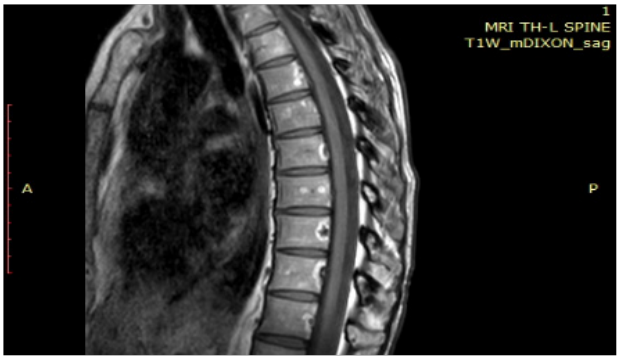


***Figure 5:*** *Sagittal T1 weighted image of thoracic spine.*

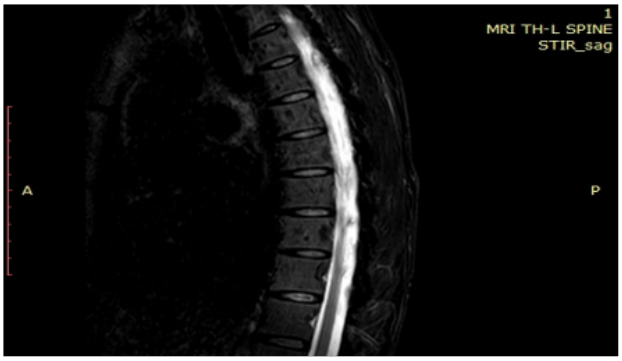


***Figure 6:*** *Sagittal STIR weighted image of the thoracic spine*

# PART B

### *Diagnosis: Sclerotic thoracic and lumbar spinal lesions in the context of Tuberous Sclerosis*

MRI showed multiple focal lesions in the lumbar and thoracic vertebral bodies, measuring up to 3 cm in diameter. These lesions were mainly seen in the T9, T10, T11, T12, L3, L4 and L5 vertebral bodies. The scan revealed low signal intensity on both T1 and T2 weighted sequences, suggesting sclerotic texture of the lesions. In both T1 and T2 weighted sequences the lesions were surrounded by fatty halo. These lesions maintained their hypointensity in the STIR sequence imaging. No accompanying bone marrow oedema was seen. Given the patient's history and imaging of Sclerotic Bone Lesions (SBLs), following an in-depth multidisciplinary team meeting including the clinical team caring for the patient, the diagnosis of Tuberous Sclerosis was made.

Tuberous sclerosis (TS) or tuberous sclerosis complex (TSC) is a rare multisystem genetic condition that is inherited in an autosomal dominant manner, but *de novo* pathogenesis is not seldom. There are two main genes that have been identified to be linked to the condition, TSC1 and TSC2. The condition is thought to affect 1 in 6'000-10'000 births.[1,2] The diagnosis of the condition relies mainly on the history of the patient, with emphasis on the family history, the patient's clinical manifestations, as well as multiple tests and imaging of the different body systems pathologically involved, in order to confirm the diagnosis. Genetic testing may be done too; however, it is not always reliable.[2,5]

TS usually causes disorganized non-malignant growth development, such as the formations of hamartia and hamartomas, affecting various systems of the body. One of the main systems affected is the central nervous system. A common finding is the development of cortical tubers, which are benign epileptogenic hamartomatous lesions, usually affecting brain cortex and underlying white matter. Other neurological lesions that may be seen include subependymal nodules in the ventricular walls, and in rarer occasions giant cell astrocytomas. The subependymal nodules typically present as small (< 1cm in diameter) intraventricular masses with calcifications and may cause secondary hydrocephalus. On CT imaging these lesions have variable contrast enhancement, whereas on MRI imaging, they appear to be hyperintense, compared to gray matter, but sometimes may have hypointense areas, findings suggesting interlesional calcification. If appearing larger, the differential diagnosis of progression of the lesion to a giant cell astrocytoma should be considered. The above neurological lesions often develop at an early age and are usually seen in brain imaging, following presentation with infantile epileptic episodes or developmental delay and mental retardation. In such cases, the diagnosis of TS occurs in early childhood.[6] Given the plethora of signs and symptoms and spectrum of severity of the condition, paediatric presentation and diagnosis do not always occur. Our patient's family history of seizures hinted at a genetic disorder affecting the central nervous system.

TS often presents with cardiological manifestations and accompanying symptoms. As with our patient, cardiac rhabdomyomata, shown as hyperechoic circular myocardium attached lesion, are often seen. Similarly, sporadic cardiac tissue growths, affecting papillary muscle and valvular function may be seen, manifesting as mitral regurgitation. [3,4]. The kidneys of the affected individual may also be affected. Renal angiomyolipomas and cyst development are often seen, but are usually only diagnosed incidentally, unless renal function is affected, and specific imaging investigations are requested (kidney and urinary tract ultrasound). Dermatological signs are frequent. Ash-leaf spots, shagreen patches and angiofibromas are some examples that may result mostly in cosmetic disturbances. Such findings were seen in our patient as well, increasing our suspicion of a multisystem condition such as TS.[7]

Until recent years, TS was not thought to majorly affect the musculoskeletal system.[8-10] It has, however, been noted that more and more patients with TS have presented with non-specific bone pain, which appears to be linked to focal sclerotic bone lesions. Specifically, a study published in 2018 suggested that SBLs may assist in the diagnosis of TSC a potential imaging biomarker.[8] MRI T1-weighted, T2-weighted, and STIR sequences, of our patient showed the typical focal hypointense lesions, most compatible with the diagnosis of SBLs. The absence of contrast enhancement following administration of IV contrast (gadolinium) is seen in imaging of such patients and would be expected in our case as well.

Given the non-specific manifestation and subsequent presentation of the condition, in the case of sclerotic bone lesions (SBLs), certain differential diagnoses should be kept in mind. These include haemangiomas, infarcts,

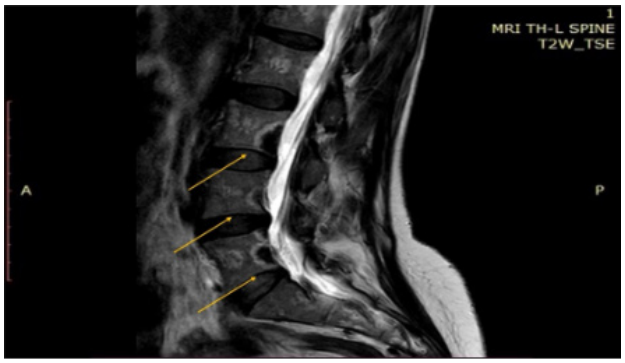


***Figure 7:*** *Sagittal T2 weighted image reveals hypointense lesions surrounded by a halo of fat in the lumbar vertebral bodies (L3, L4, L5)*

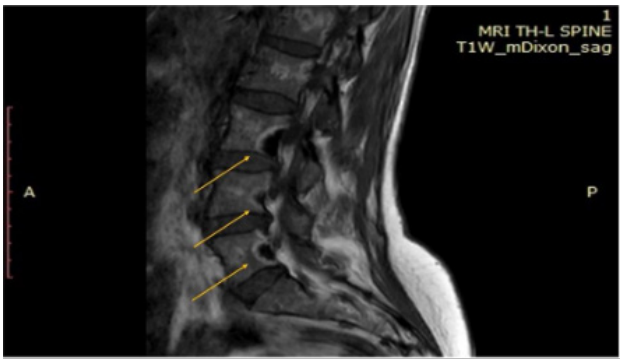


***Figure 8:*** *Sagittal T1 weighted image reveals hypointense lesions surrounded by a halo of fat in the lumbar vertebral bodies (L3, L4, L5)*

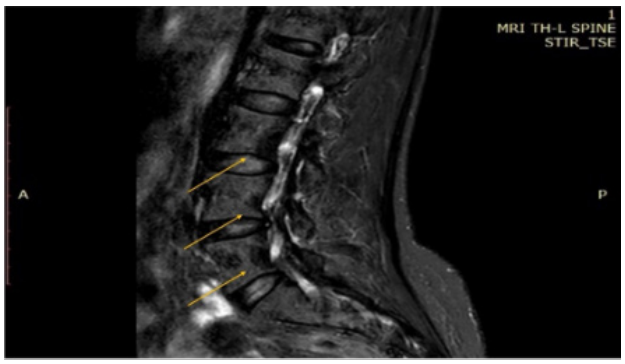


***Figure 9:*** *STIR weighted image of the lumbar spine, reveals hypointense lesions. No bone marrow edema is seen*

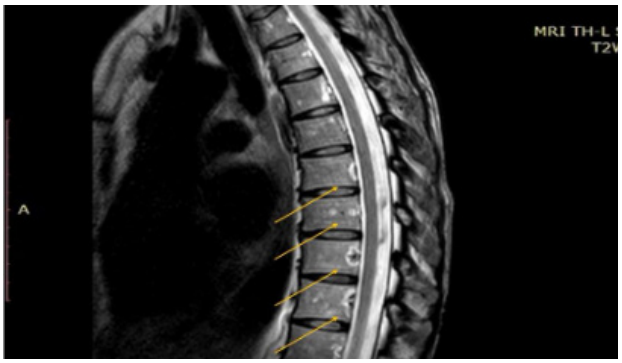


***Figure 10:*** *T2 weighted image reveals hypointense lesions surrounded by a halo of fat in the thoracic vertebral bodies (mainly T9, T10, T11, T12)*

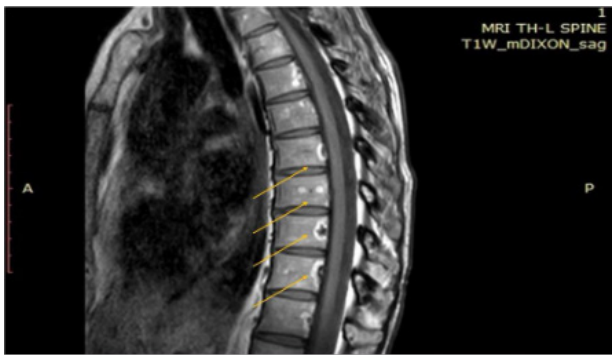


***Figure 11:*** *T1 weighted image reveals hypointense lesions surrounded by a halo of fat in the thoracic vertebral bodies.*

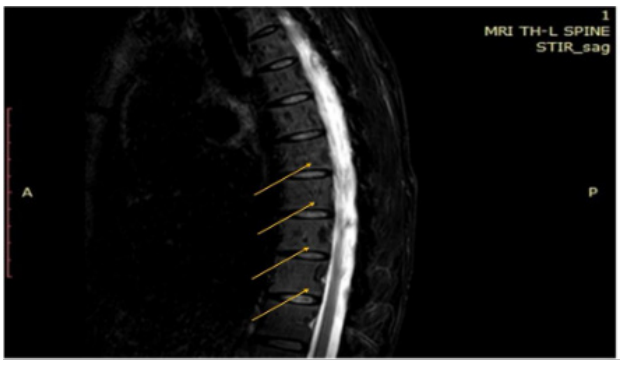


***Figure 12:*** *STIR weighted image of the thoracic spine reveals hypointense lesions. No bone marrow edema is seen*

chronic osteomyelitis, neoplastic disease (metastatic or primary), endocrine causes including Paget's disease and parathyroid disturbances, as well as other congenital or genetic bone-genesis disorders. While haemangiomas may be easier to differentiate as they usually present with their typical "jail bar" appearance with thickened vertebral trabeculae and high signal intensity on T1 and T2 MRI sequencing and their vascular characters with contrast uptake, or Paget's disease which presents with alternating, irregularly patterned sclerotic and lytic lesions, other differentials such as early neoplastic disease or metabolic disturbances, which appear to resemble SBLs seen in TSC may be harder to rule out. It is important to remember that unlike other types of bone lesions, SBLs in TSC are not coupled to osteoporotic fractures. This underlines the need for acquiring a good history from the patient and coupling the clinical picture to the radiological findings.

Following the diagnosis of the patient, she was offered genetic counseling. Genetic testing was also offered, however, she politely declined. Benign lesions such as our patient's renal angiomyolipomas and SBL are followed up in a timely manner, and she is currently also cared for by the cardiologists who until now recommend conservative treatment of her rhabdomyoma.

Conclusion: SBL are commonly seen in TS and when seen should trigger the differential of TS, given that such a diagnosis fits the history of the patient. **R**

***Conflict of interest***

None declared

***Ethical consideration***

Written informed consent was taken from the patient, regarding their inclusion in the study and its subsequent publication. Patient identity was anonymized.

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KEY WORDS musculoskeletal, bone lesions, tuberous sclerosis, genetic, back pain

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