RADIOLOGICAL ROAD MAP TO TUBEROUS SCLEROSIS COMPLEX (TSC)

Khurram Khaliq Bhinder, Samreen Aslam, Sana Sayeed, Humaira Bashir

Department of Radiology, Shifa International Hospital, Islamabad, Pakistan.

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ABSTRACT

OBJECTIVE: The objective of this article is to present imaging findings in tuberous sclerosis complex (TSC), which will eventually help in imaging based diagnosis. **STUDY DESIGN:** Retrospective study **PLACE AND DURATION OF STUDY:** Radiology Department, Shifa International Hospital, from 2010 to 2021. **METHODOLOGY:** Total of 20 patients were selected from the radiology database retrospectively from 2010 to 2021. These patients were diagnosed with Tuberous Sclerosis by radiology department and their scans were performed and reviewed at CT and MRI machines of Shifa International Hospital. CT scan was performed on Toshiba 640 slices, Siemens 128 slices and Siemens 16 slices, and MRI was performed on Siemens 3 tesla, Toshiba-titan 1.5 tesla and Hitachi 0.4 tesla. The literature review was also done to identify different organ system involvement of this disease. **RESULT:** Different organ system involvement by this disease and imaging features of them are reported. **CONCLUSION:** TSC has wide range of radiological imaging findings. Recognition of various organ manifestations on imaging is necessary for making the accurate diagnosis and is helpful in the treatment plan.

Keywords: Tuberous sclerosis, Cortical tubers, Subependymal nodule, Rhabdomyoma, Lymphangioleiomyomatosis, Renal angiomyolipoma, Radiology.

Introduction

Tuberous Sclerosis complex (TSC) is a rare autosomal dominantly inherited genetic neurocutaneous disorder. It occurs due to inactivating mutation in TSC 1 or TSC 2 gene which has vital role in regulation of cell growth and proliferation.[1] TSC incidence is 1:600 - 1:10,000 live births in general population. It is characterised by development of benign or rarely malignant tumors in many tissues and organs especially brain, skin, retina, kidneys, heart and lungs.[2] The classical picture of TSC consists of facial adenoma sabeceum, epilepsy and mental retardation. However, common presentation include cortical tubers, subependymal nodule, white matter abnormalities, renal abnormalities, cardiac rhabdo-myoma, lymphangioleiomyomatosis, renal angiomyo-lipoma and skin lesions.[3] TSC manifestations are seen after years. TSC lasts lifelong thus it requires regular monitoring of TSC patients to identify new symptoms.[4] Most common cause of mortality in TSC is due to neurological manifestations, therefore neuroimaging is important in early diagnosis. Computed tomography and MRI are used as first line investigations in TSC.[5] Thus, TSC is a multisystem disorder characterized by a broad and extensive spectrum of imaging features. Timely identification of particular radiologic findings of various organ manifestations may help in early diagnosis and prompt management and improve end results in TSC patients.[6]

Correspondence : Dr. Khurram Khaliq Bhinder
Department of Radiology,
Shifa International Hospital,
Islamabad, Pakistan.
Email: kkbhinder@yahoo.com

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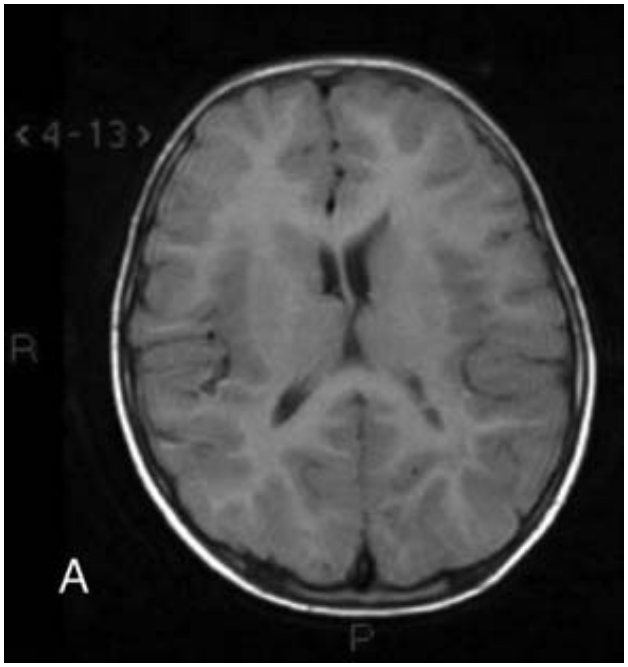
Methodology

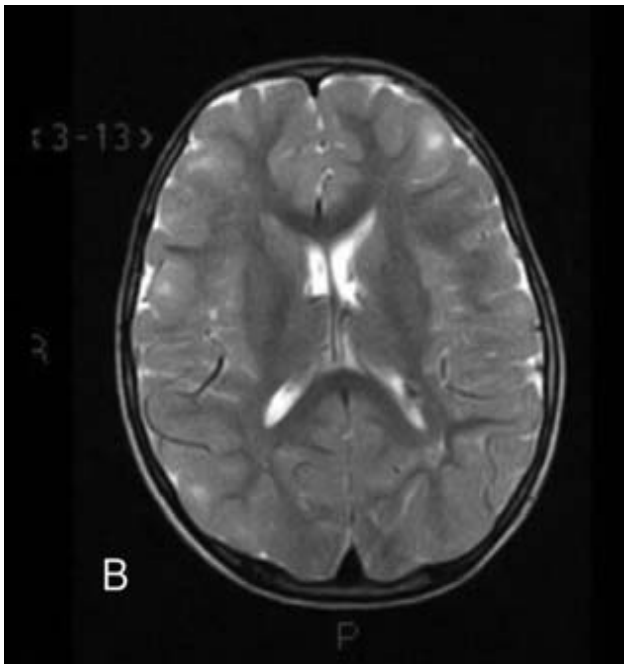
This study was performed retrospectively after Institutional Review Board s approval. In this study, patients diagnosed with tuberous sclerosis were included. Involvement of different organs by this disease is studied by radiological modalities. We compiled 20 cases over the year 2010-2021 with involvement of organs by this disease. CT scan was performed on three machines namely Toshiba 640 slices, Siemens 128 slices and Siemens 16 slices. MRI was performed on Siemens 3 tesla, Toshiba-titan 1.5 tesla and Hitachi 0.4 tesla.

Discussion

1. Central Nervous System

Tuberous sclerosis is identified as causing many neurological manifestations. Commonly seen neurological abnormalities are subependymal nodules, cortical tubers, subependymal giant cell astrocytomas (SEGA), and white matter abnormalities. Cortical tubers are hamartamatous benign lesions at the grey white matter junction. MR is the modality of choice for detecting lesions on which these are hypo-intense on T1 weighted sequences and hyper-intense on T2 weighted sequences.[7] Exception on this imaging is in infants and neonates where enhancement is seen





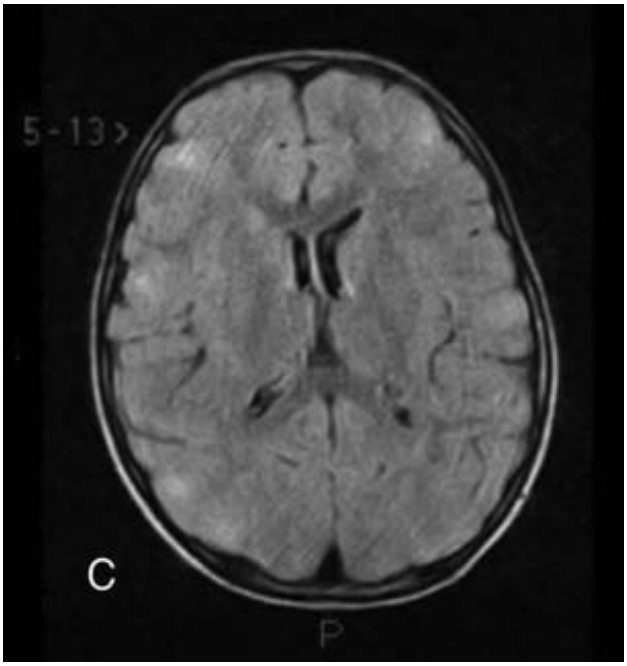


Figure 1: Cortical Tubers MRI (A: T1, B: T2, C: Flair)

on T1 weighted images due to the unmyelinated brain and similar relaxation time of T1.[8] Only 10% of cortical tubers enhance on post-contrast images.[8] Cortical tubers occur in almost 90% of patients while subependymal nodules are seen in 80% of patients associated with tuberous sclerosis complex.[9]

SENs on non-contrast CT demonstrate small calcified foci along the wall of the lateral and third ventricle while MR imaging will show hyperintense signals on T1-weighted sequences and isointense to hyperintense on T2 weighted sequences.[10]

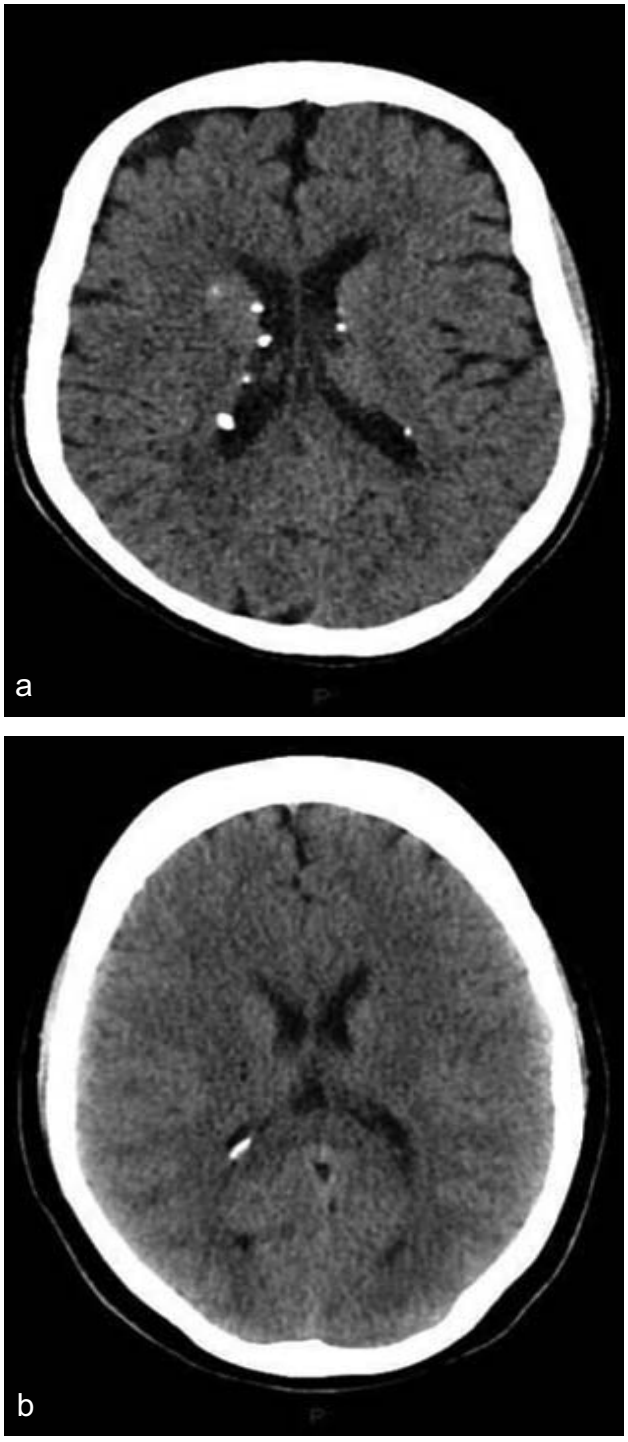
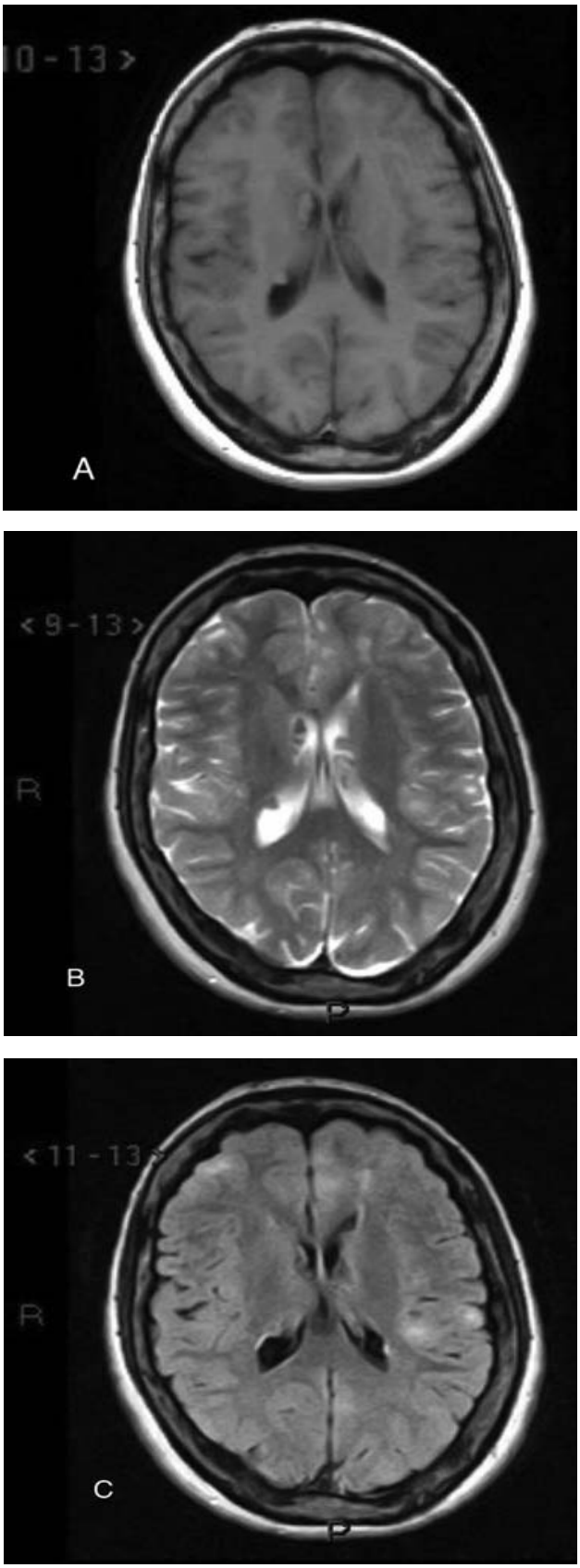


Figure 2: Non Contrast CT Brain showing hyperdense foci in the body of lateral ventricle



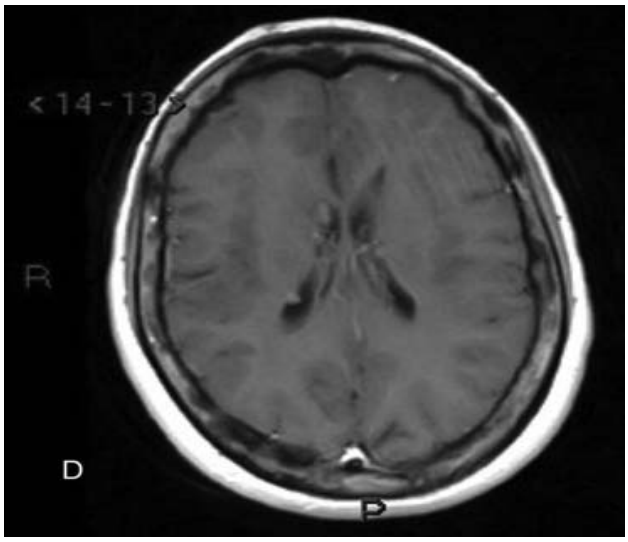
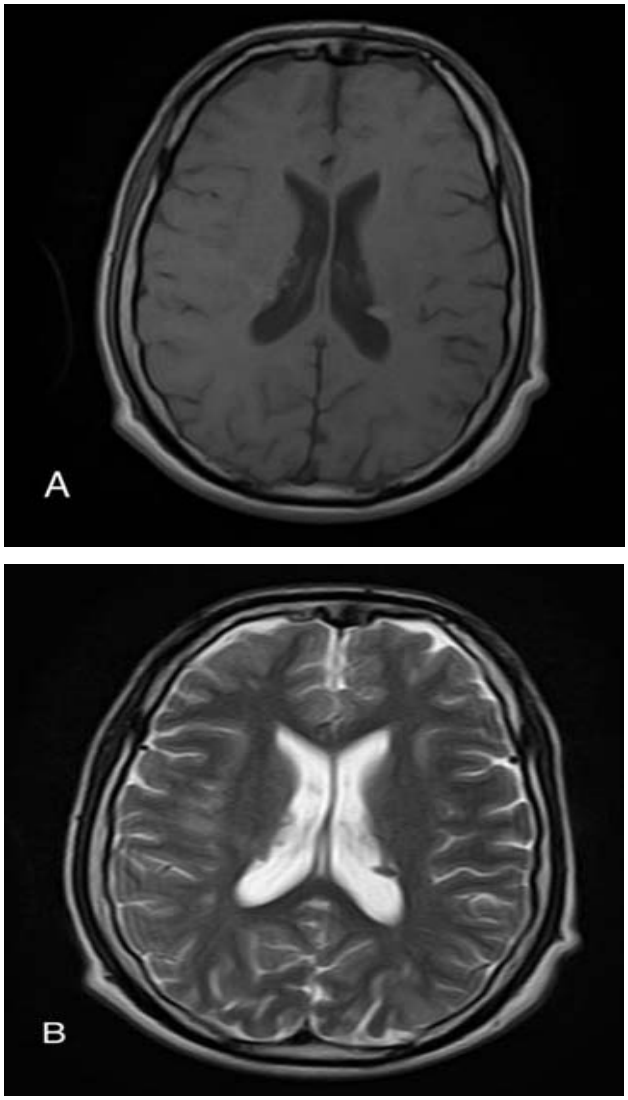
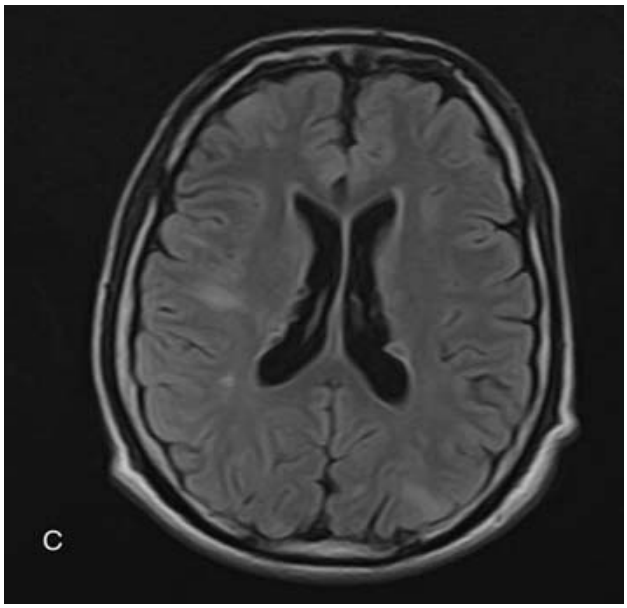


Figure 3: SEN MRI (A: T1, B: T2, C: Flair, D: T1 Post-contrast)





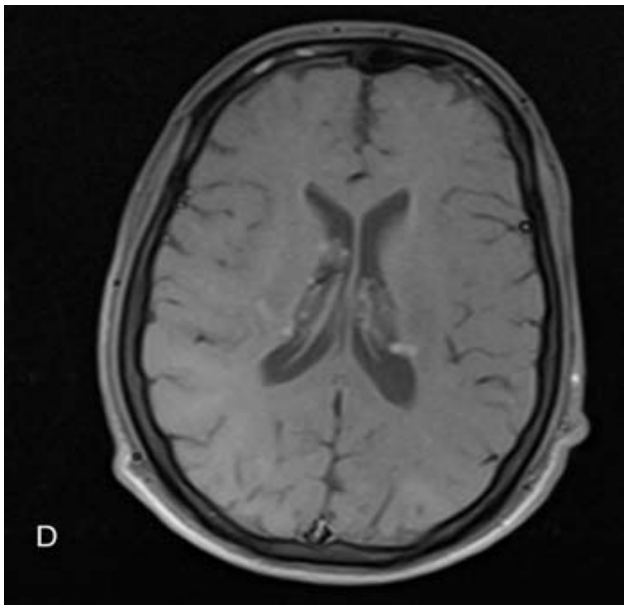


Figure 4: SEN MRI (A: T1, B: T2, C: Flair, D: T1 Post-contrast)

SEN can progress and transform into SEGA and both are histologically identical.

SEGA is a growing tumor with a diameter greater than 1cm occurring mostly near the foramen of Monro. Sega incidence in tuberous sclerosis is 5-15% and is notorious for causing complications like hydrocephalus.[11] SEGA show more intense enhancement than SEN on CT imaging and MR shows heterogenous enhancement with iso to hypointense signals on T1 weighted images while iso to hyper-intense signal on T2/FLAIR weighted images.[10]

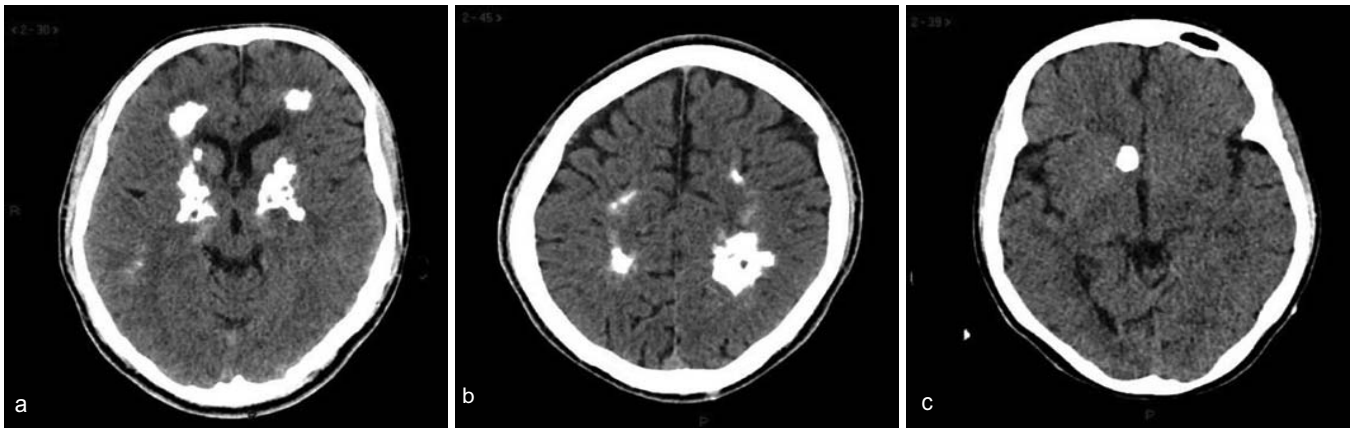


Figure 5: Non Contrast CT brain showing giant SEGA

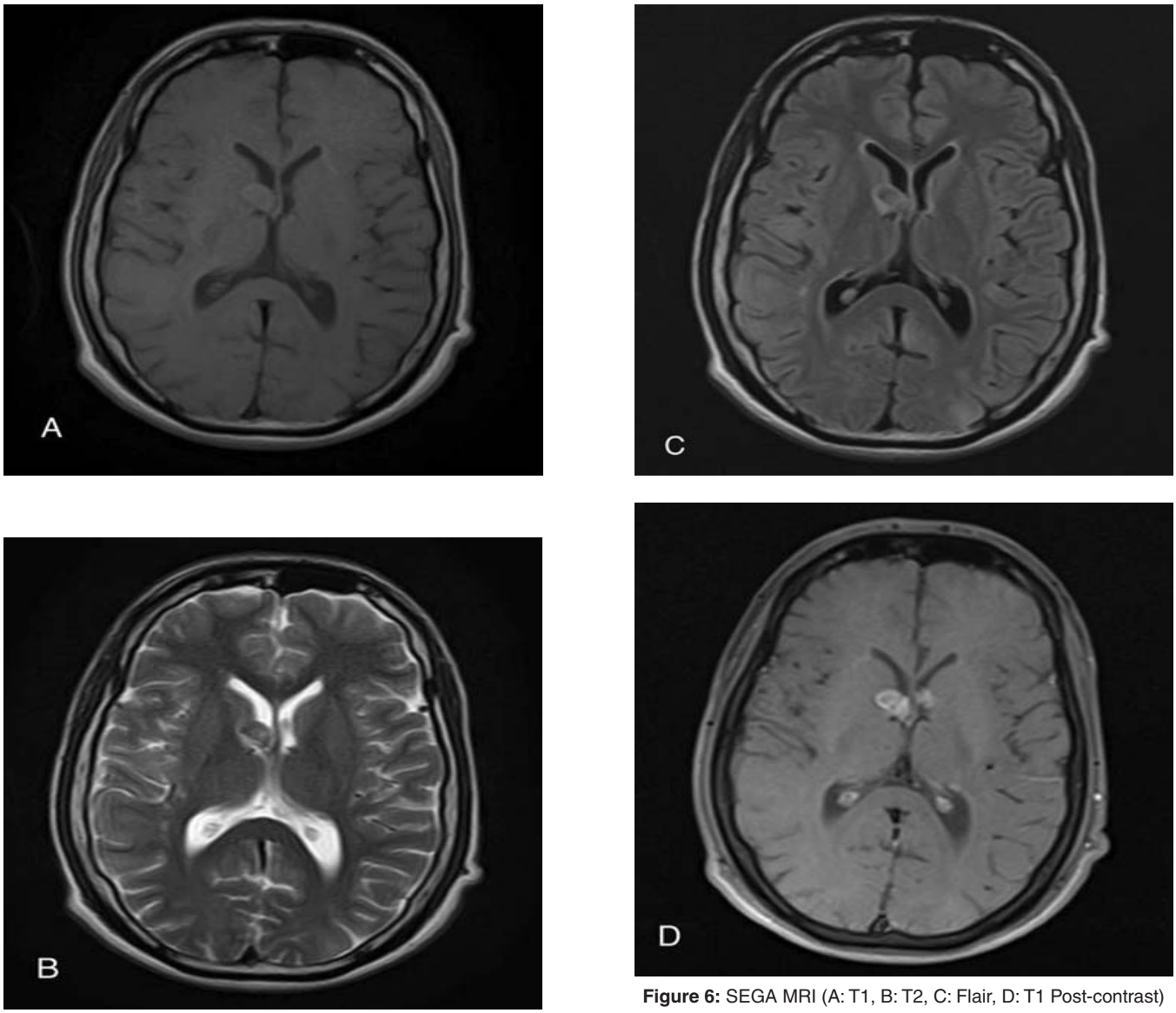
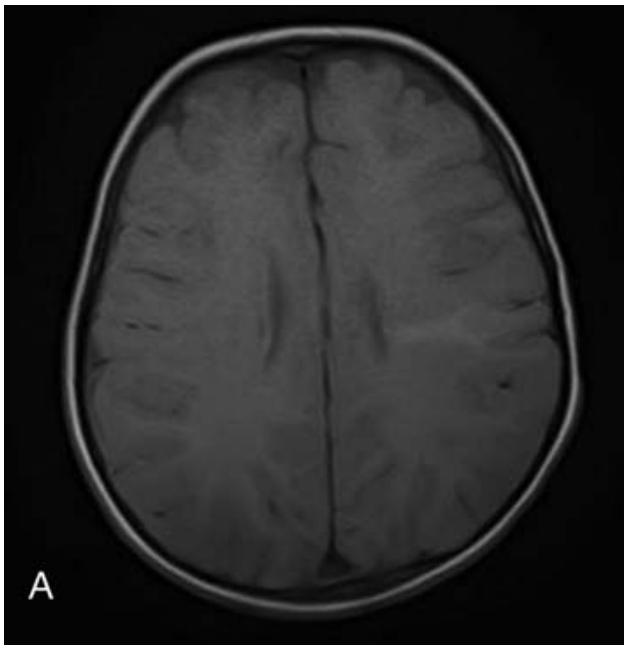
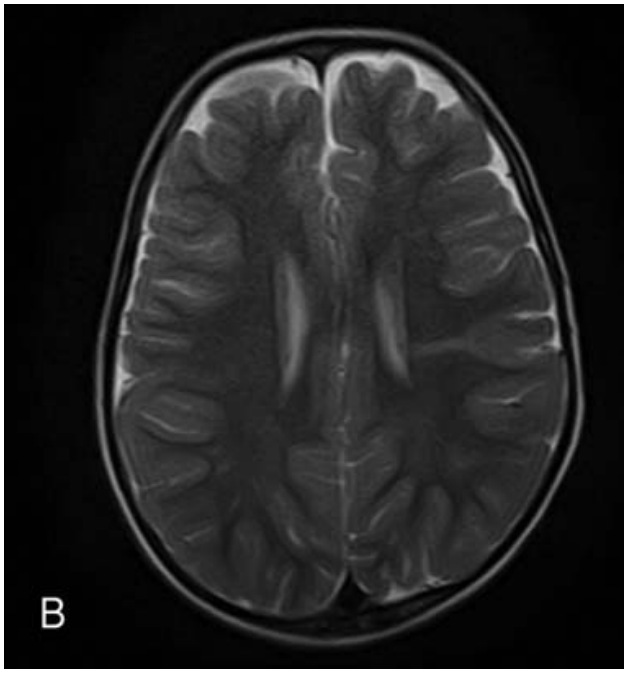
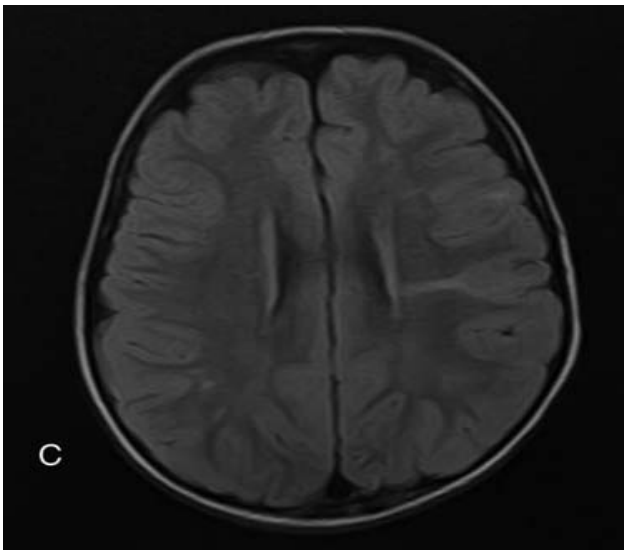


Figure 6: SEGA MRI (A: T1, B: T2, C: Flair, D: T1 Post-contrast)

Radial migration lines are seen in association with TSC, which are thin and slender, linear or curvilinear bands of white matter which are hyperintense on T2 and hypo to iso-intense on T1 weighted images.[12]







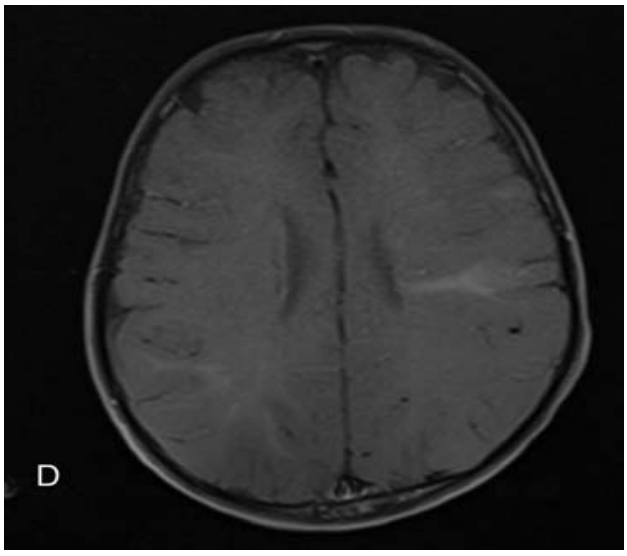


Figure 7: Radial bands MRI (A: T1, B: T2, C: Flair, D: T1 Post-contrast)

TSC is associated with epilepsy and TAND (tuberous sclerosis complex associated neuropsychiatric disorders), in which this disease is responsible for causing neuropsychiatric disorders like aggressive behavior, intellectual disability, autism, and psychiatric disorders.[13]

2. Cardiac System

Cardiac rhabdomyomas and arrhythmias are commonly known complication of TSC in cardiac system.[14] Around 50% of the children diagnosed with TSC have rhabdomyomas.[15] Studies show that it has been estimated that 70-90% of children with rhabdomyomas

have TSC.[15,16] Various modalities are known to diagnose rhadbomyomas like echocardiography and cardiac MR. Myocardial fatty foci (MFF) are highly specific for TSC and can be diagnosed on CT chest as low attenuating areas in myocardium.[17]

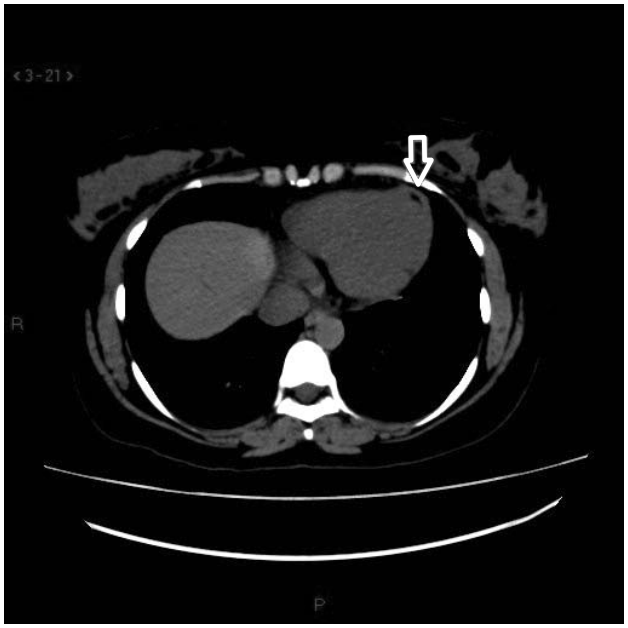
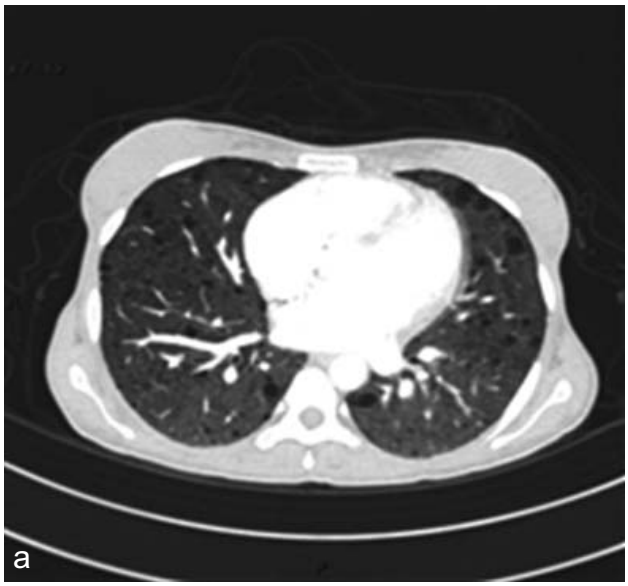
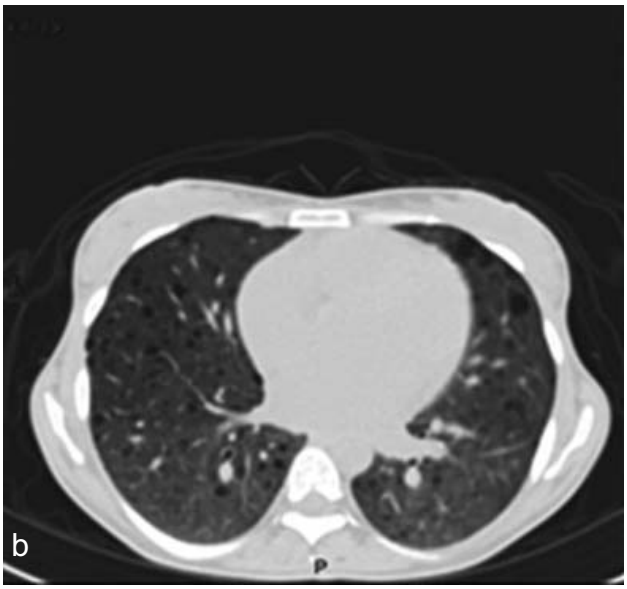


Figure 8: Myocardial fatty foci (MFF) on axial CT chest

3. Pulmonary System

Commonly seen TSC manifestation in pulmonary system are lymphangioleiomyomatosis (LAM) and multifocal micronodularpneumocyte hyperplasia (MMPH).[18] On CT chest, LAM appears as thin walled rounded cysts.





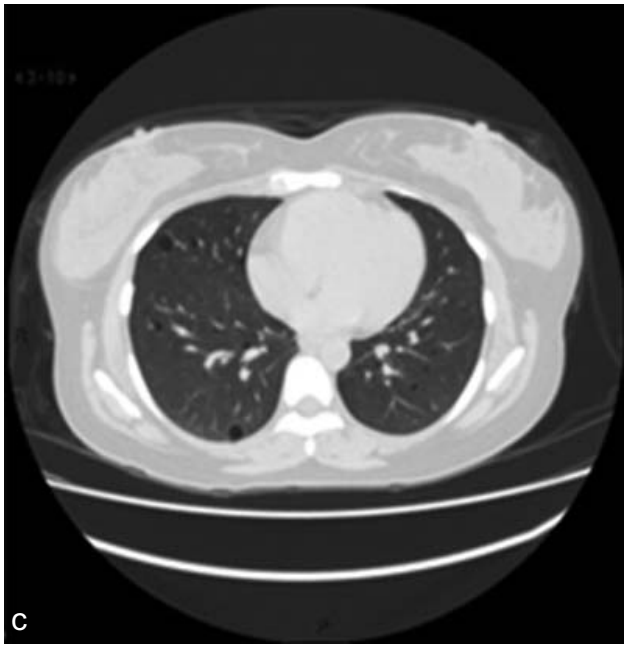


Figure 9: Axial slices of CT chest on lung window showing multiple LAM

Patients with LAM are at high risk of developing spontaneous pneumothorax.[19] Thus, LAM is a crucial cause of morbidity and mortality among TSC patients. Obstruction of thoracic duct is pulmonary lymphatic manifestation of LAM leading to chylothorax (seen in 20-30% of patients)[20] or chyloptysis.[21] MMPH is the proliferation of type II pneumocytes which radiologically present as ground glass nodules.[22]

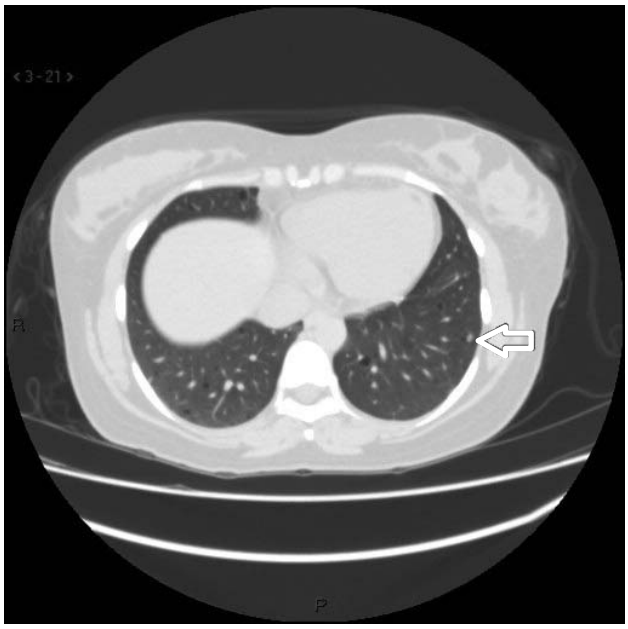


Figure 10: Multifocal micronodularpneumocyte hyperplasia (MMPH) on lung window of CT chest

4. Renal System

Angiomyolipoma, renal cysts, renal cell carcinoma and oncocytomas are the renal manifestation of TSC. Renal AML are seen in 75-85% of the patients with TSC.[23] These AML are at high risk for hemorrhage and cause expose the patients to chronic kidney disease and evenly to end stage renal disease.

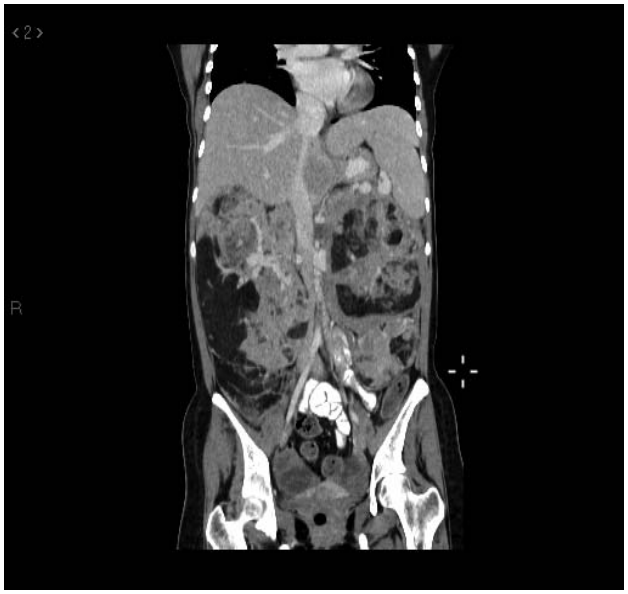
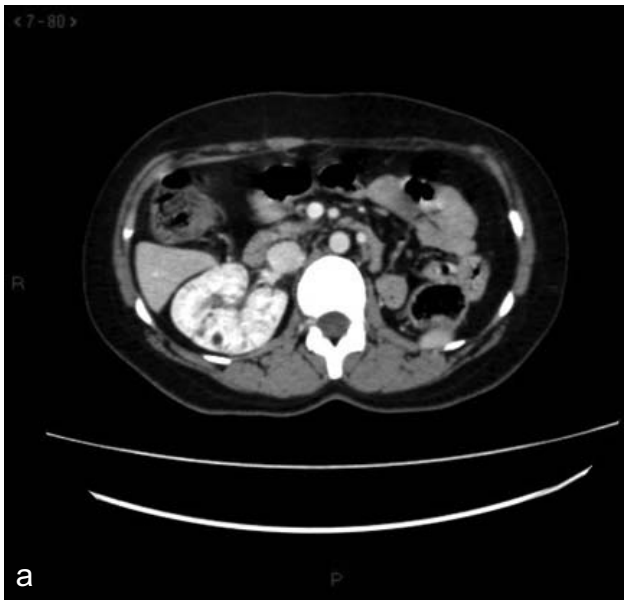


Figure 11: Massive AML



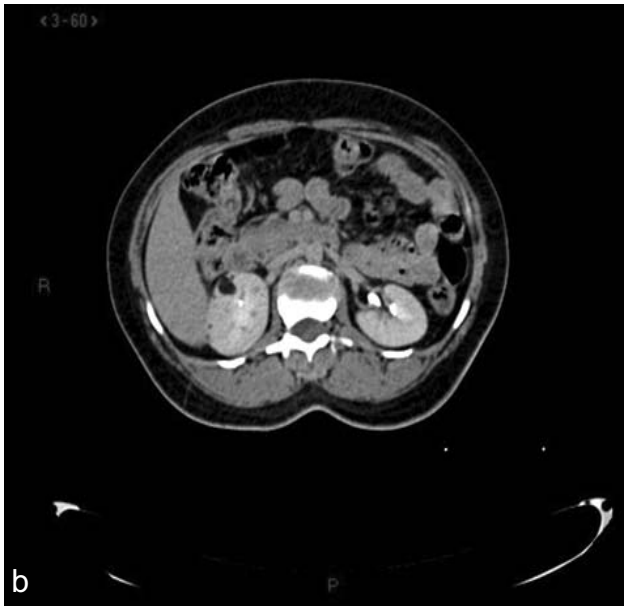


Figure 12: AML visible

Multiple interlobar and distal renal artery aneurysms are also seen in some cases which also lead to life threatening bleed. This renal bleeding can be fatal and can cost the life of patient. Thus, prompt imaging must be done to specify bleeding aetiology and site.Interventional Radiology has a pivotal role in treatment of renal bleeding by coiling and embolization. About 50% of the patients with TSC have cystic disease.[23]

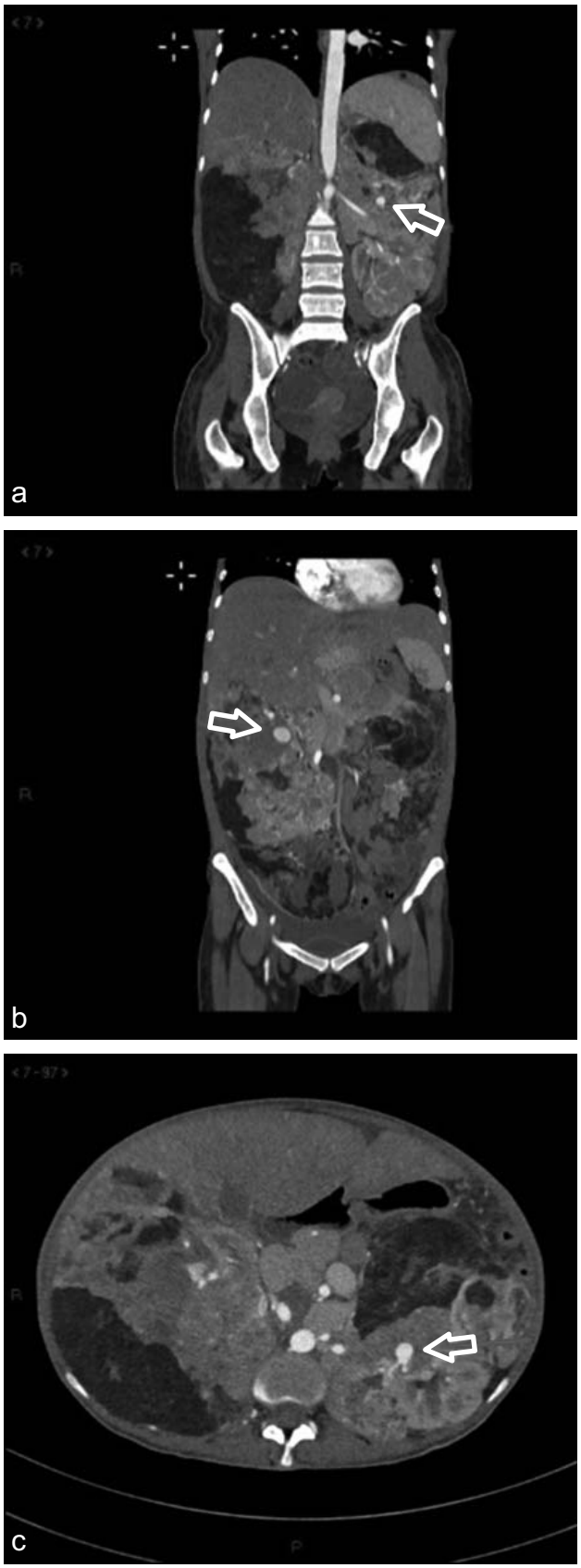
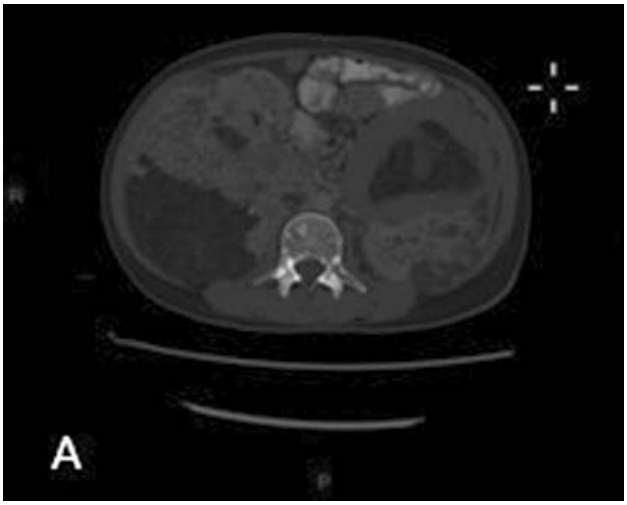


Figure13: Pseudoaneurysms

RCC and oncocytoma has also been reported in a number of patients with TSC, although the risk is relatively low and it tends to involve younger age group preferably age 25.[24]

5. Muskuloskeletal System

Frequently seen bony manifestations of TSC include sclerotic bone lesions, hyperostosis of the inner table of the calvaria, osteoblastic changes, new bone formation, bone cysts and scoliosis.[24] These lesions can involve any bony of the body. CT is the ideal modality in detecting the bony lesions and complications.[25]



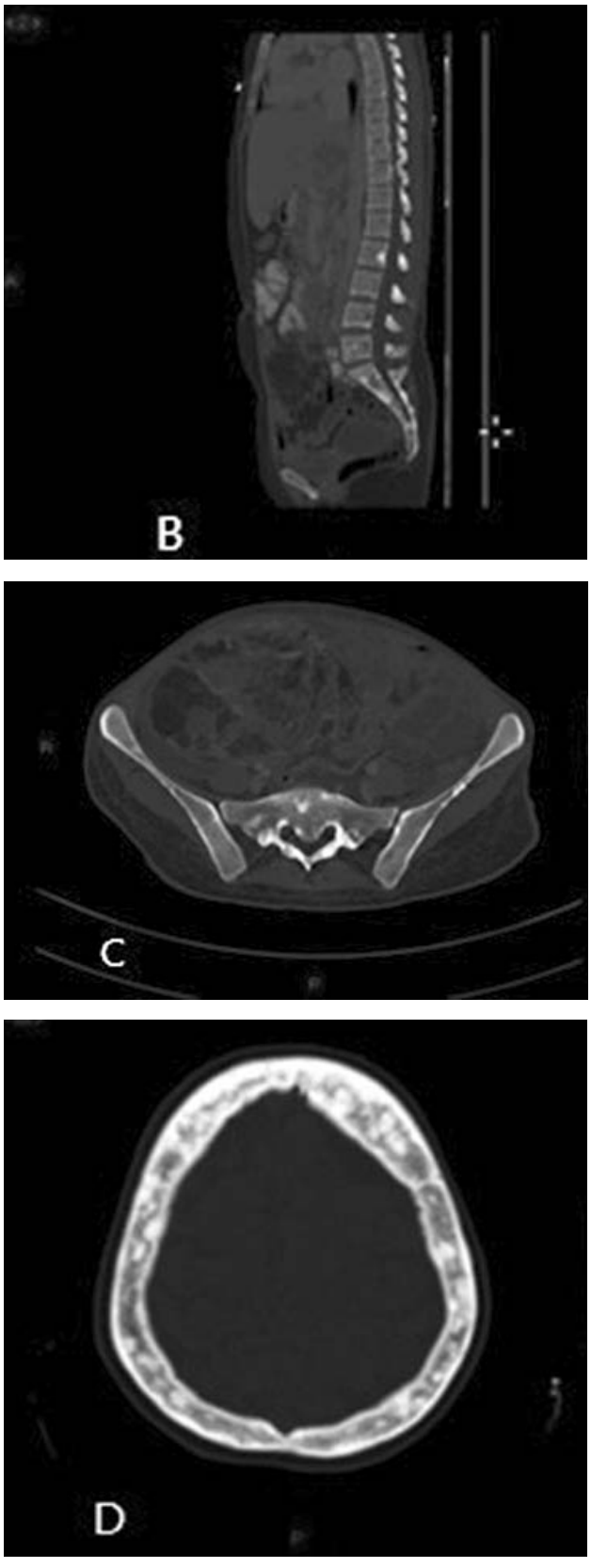


Figure 14: Bony lesions on CT scan

6. Miscellaneous

Various other manifestations of TSC are known till date. It often involves the abdominal digestive organs including the alimentary tract, hepatobiliary system, and pancreas.[24]

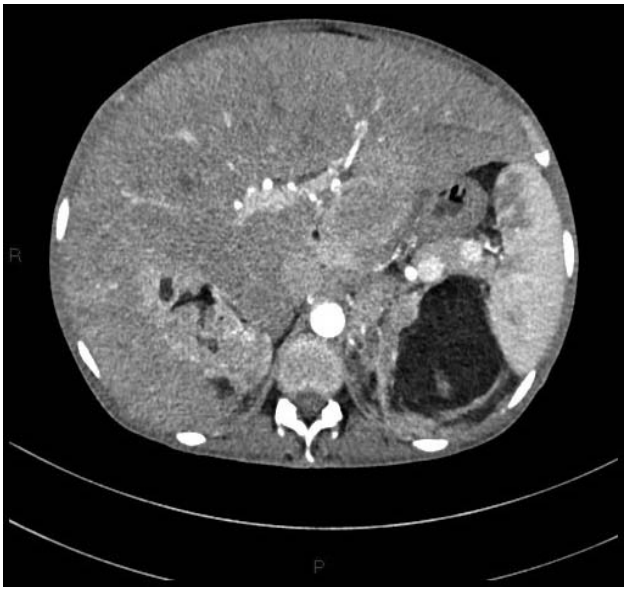


Figure 15: Liver AML

Gastrointestinal polyps are often seen in TSC patients. Adenocarcinoma and vascular malformations are seldom seen with it. Hepatomegaly and hepatic AML are seen when TSC involves the liver. TSC when involves pancreas, it results in hypoplasia, islet-cell tumor, hamartoma, and mucoviscidosis, however it is rarely involved (24). Splenic AML involvement is also seen in some cases.Lymphadenopathy is seen in 40% of cases while in some cases lymphedema of the lower extremities and chylous ascites is seen.[26]

Conclusion

Thus, TSC has various radiological manifestations all over body. It should be kept in differentials when common manifestation like renal AML, CNS SEN and SEGA are seen. Timely identification of these radiological findings are essential in making accurate diagnosis and thus saving the patient from morbidity and mortality.

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