

Case Report
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Sporadic Association of the Carcinoma Gall Bladder in A Patient with Tuberos Sclerosis Complex

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ABSTRACT

Tuberous sclerosis complex (TSC) is the rare autosomal dominant neurocutaneous disorder that affects the individual by causing various benign lesions. However, in recent studies, few cases of TSC in which a novel malignancy is also observed. TSC has mutations in two suppressor genes, i.e. TSC1 & TSC2, responsible for developing a wide range of hamartomatous lesions [1]. Recent evidence suggests that the TSC genes play an important role in the pathway whose dysregulation leads to an array of epithelial malignancies. TSC 1 mutation is mainly identified in sporadic tumours of epithelial cells that indicate important phenotypic changes resulting from modulation of the hamartin expression. Here we present a case diagnosed with carcinoma gall bladder and having tuberous sclerosis complex defining the co-relation.

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Clinical Presentation

A 35 years old female patient came to our hospital with complaints of pain abdomen and feeling of fullness in both flanks for the last three months. The patient had a history of occasional seizures. On physical examination, the patient had multiple papules and nodules on her face since childhood suggestive of sebaceous adenoma (angiofibroma) [Figure 1A]. She had a yellowish discoloration of the sclera and lumps in her bilateral lumbar regions. On the routine blood investigations, the patient was found to have a raised direct bilirubin level signifying an obstructed jaundice. On ultrasonography of the abdomen, an ill-defined heteroechoic lesion was observed in the segment IVb of the liver with thickening of the adjacent gall bladder wall and bilateral enlarged kidney with multiple hyperechoic lesions as renal parenchyma seen suggestive of fatty content. A CECT abdomen was advised for further evaluation, which revealed multiple sclerotic bony lesions seen in vertebral bodies (a feature of TSC which is also due to pathogenic variants in TSC1 or TSC2 genes resulting in hyperactivation of the mTOR pathway). [Figure 1C] There was a bilateral enlarged kidney with multiple lobulated mixed densities lesions, showing -55 to 45 Hounsfield Unit (HU). The majority of renal cortex was replaced by these lesions (signifies renal fat-rich angiomyolipoma) [Figure 1B] and there is an ill-defined heterogeneous enhancing mass lesion in the gall bladder fossa with direct hepatic plate infiltration. The lesion was also involving the upper common bile duct resulting in intrahepatic biliary dilatation. This lesion, on an imaging basis, was diagnosed as carcinoma gall bladder [Figure 2A,2B,2C & 2D]. The histopathological examination from the gall bladder confirmed the diagnosis of carcinoma. The prognosis was explained to the patient, and she was referred for chemotherapy.

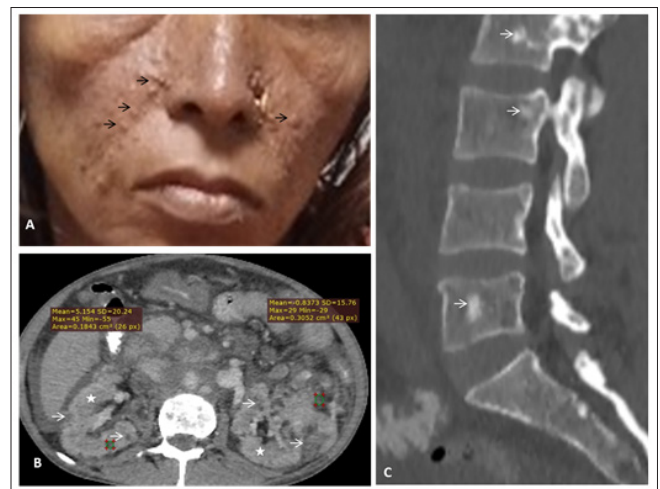


Figure 1: Images Illustrating features of tuberous sclerosis complex (TSC). (A) Clinical picture of the patient illustrates the multiple papules and nodules on her face suggestive of sebaceous adenoma (black arrows). (B) Contrast enhanced computed tomography of abdomen in axial plane showing bilateral enlarged kidney with altered CT attenuation and multiple lobulated mixed densities, irregular lesions (white arrows), showing -55 to 45 Hounsfield Unit (HU) signifies renal fat-rich angiomyolipomas. Normal renal tissue is marked by stars. (C) Contrast enhanced CT scan abdomen at the region of lumbar spine in bone window, sagittal plane demonstrating multiple, discrete sclerotic lesions in vertebral bodies (white arrows).

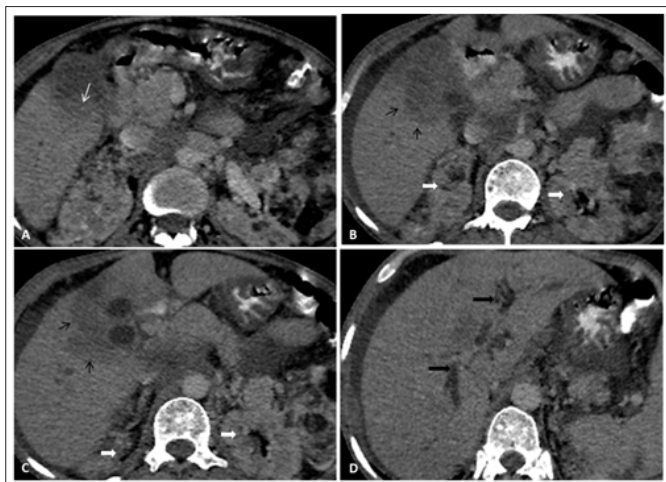


Figure 2: Contrast enhanced computed tomography of abdomen at the level of gall bladder fossa in axial plane illustrating findings of gall bladder carcinoma. (A) Heterogeneously enhancing lesion arising from wall of the gall bladder (white arrow). (B,C) The lesion is directly infiltrating the adjacent liver parenchyma (black arrows). Also note the renal angiomyolipomas in the kidneys (thick white arrows). (D) Dilated intra hepatic biliary radicals are marked by thick black arrows.

Discussion

The literature on genetic changes in various other sporadic epithelial cancers divulges the deletion or mutation in the region of the TSC genes [2]. The various genetic studies have explained the sporadic association of gall bladder carcinoma in a patient with TSC. One study stresses over the loss of heterozygosity (LOH) an association of LOH in TSC genes with various tumours types. The study states that ovarian and gall bladder carcinomas are associated with chromosome 9q LOH mapped to two discrete regions approx. >50% and >88%, respectively, one of which contains TSC1 [3]. According to another genetic study, significantly high-frequency deletions in 9q34 and 16p13 are associated with non-small-cell carcinoma, gall bladder, and ovarian carcinoma [4,5].

Learning Points

- Tuberous sclerosis is associated with benign lesions and may be associated with various malignant tumours.
- In the case of tuberous sclerosis, the presence of sclerotic lesions in vertebral bodies or other bones is the catching point suggestive hyperactivation of the mTOR pathway, which signifies TSC1 variant and may lead to the malignant lesion.
- Renal angiomyolipoma is more frequently associated with TSC, and the fat-rich subtype of AML requires no histopathological confirmation, whereas poor fat type requires confirmation to differentiate it from any renal cell carcinoma.

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