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Tuberous Sclerosis or Angiomyolipoma? A Case Report

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Abstract: Tuberous sclerosis complex (TSC) is a multisystem disorder, with significant renal cystic and solid tumour disease. It is caused by mutations in either TSC1 or TSC2 gene, which regulate cell growth and proliferation by inhibition of mTORC1 signaling. It is characterized by affecting multiple organs and it is associated with glial tumours, adenoma sebaceum, rhabdomyoma and hamartomatous tumours of liver, lung, thyroid, retina, pancreas, adrenal glands and ovaries which determine the clinical manifestations. Its neurological manifestations include epilepsy, autism, cognitive and behavioural dysfunction. We report a case of a 39year old women in which the diagnosis is uncertain due to the lack of symptoms presented during the last 10 years and probably due to incomplete investigations. The diagnosis of TSC is primarily made clinically based on Tuberous sclerosis complex diagnostic criteria. Genetic testing is not required in every individual with TSC, though it may be helpful in patients suspected to have TSC but does not have enough signs of the disease to meet the full diagnostic criteria. Early diagnosis of TSC is very important in order to offer appropriate care and long-term surveillance especially when a new therapy is available. The present study reports a high probability case of Tuberous sclerosis complex.

Keywords: tuberous sclerosis; angiomyolipoma; kidney

1. Introduction

Tuberous sclerosis complex (TSC) is a multisystem disorder, with significant renal cystic and solid tumour disease. It is caused by mutations in either TSC1 or TSC2 gene, which regulate cell growth and proliferation by inhibition of mTORC1 signaling. It is characterized by affecting multiple organs and it is associated with glial tumours, adenoma sebaceum, rhabdomyoma and hamartomatous tumours of liver, lung, thyroid, retina, pancreas, andrenals and ovaries which determine the clinical manifestations. Its neurological manifestations include epilepsy, autism, cognitive and behavioural dysfunction,

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2. Case Presentation

A 39year old woman with a chief complaint of bilateral lumbar pain of one week duration was admitted to Emergency Clinical County Hospital Constanta in July 2011. No relevant medical or family history was reported. Laboratory examinations yielded moderate anemia and leukocyturia. CT scan demonstrated one liver cyst (8th segment), bilateral renal angiomyolipomas, with a larger expression on the right side accompanied by kidney capsule rupture and a perirenal collection. It was determined that the patient required surgical treatment. During the surgery, abscission of the tumoral masses is performed. The patient recovered well, and no postoperative complications were observed. Histological examination indicated angiomyolipoma consisting in dominant leiomyoma and minimal adipose cells representation. Immunohistochemical staining came in support of the histological diagnosis.

Due to the lack of symptoms, further investigations were not performed, until 2017 when the patient returns with bilateral lumbar pain and frontal and occipital headache and reports a 3 months old surgery for a periungual fibrous mass with no histological tests performed.

Figure 1 Periungual fibrous mass

Ultrasonography of the genitourinary system was performed, which revealed multiple solid lesions in the right kidney, the largest one located mediorenal and at the upper pole (26/34mm, 20/22mm) and fibromatous uterus. In addition, the physical examinations revealed tenderness on percussion pain over the both kidney region. The abdominal palpation revealed pain in the hypogastrium. Inspection of the skin and mucous membranes revealed a hypomelanotic skin lesion in the bilateral lumbosacral region. No other dermatologic or dental features of tuberous sclerosis were seen.

The suspicion of tuberous sclerosis complex arises and further investigations are performed. A contrast enhanced CT scan of the abdomen revealed two liver cysts (the largest 15/13mm in the 7th segment subcapsular), right kidney with multiple nodular lesions with lipid content (~35HU) with extensive local spreading, the larger one located in the lower pole with mixt content, tissue and lipid (44/30mm) which does not overcome the renal capsule.

Additionally, magnetic resonance imaging of the brain, ophthalmologic check, pulmonary radiography and ECG were performed, with no pathological findings. Echocardiography was not performed. Genetic screening could not be done due to unavailability of the service.

According to the recommendations of the 2012 International Tuberous Sclerosis Complex Consensus (ITSCC) our patient would meet 3 major criteria to confirm the diagnosis of TSC: >2 angiomyolipomas, shagreen patch and ungual fibroma, IF a histological test of the ungual fibroma would have been performed.

The patient had only complained of lumbar pain and no abnormal laboratory examination results have been noted. At this moment, conservatory treatment is preferred. Although guidance towards a specialized Center in Romania was performed, the patient did not follow it.

In February 2019, the patient returns to our Clinic accusing gross hematuria and right flank pain of two days. Emergency ultrasonography of the urinary system and a CT scan of the abdomen were performed which revealed no cause of bleeding and angiomyolipomas stationary, numerical and dimensional.

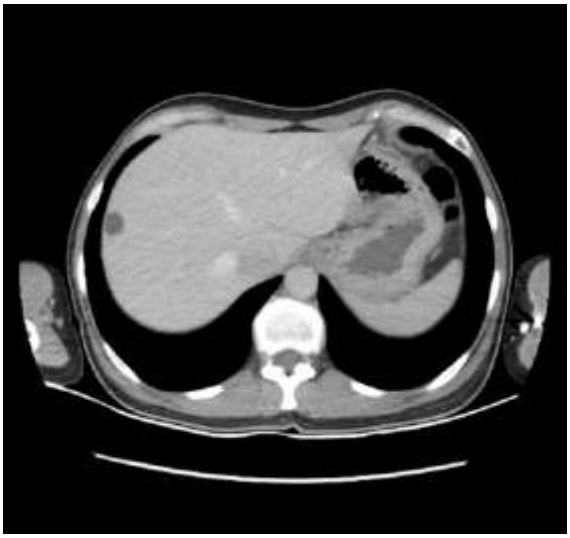

Figure 2. Liver Cysts

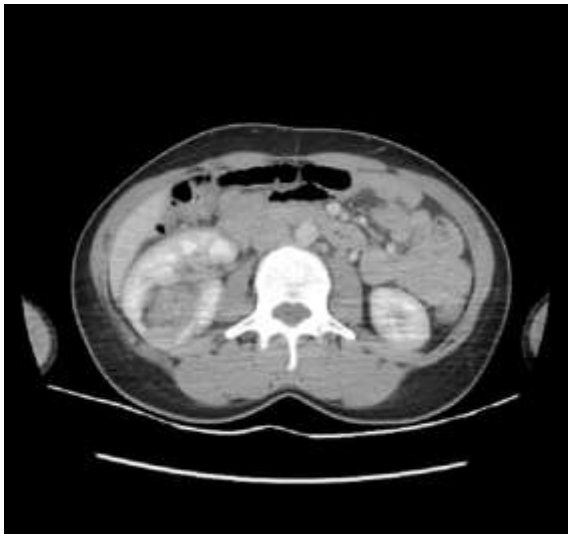

Figure 3. Right Kidney with Multiple Nodular Lesions with Lipid Content

During hospitalization the patient was treated with painkillers and iv infusions with good recovery. We discharged the patient offering her guidance for consulting a urologist.

The patient was lost to follow-up. We assume that in the current pandemic context many patients avoid presenting in large public hospitals.

3. Discussion

Angiomyolipomas occur sporadically in 80% of cases and 20% of cases occur in patients with tuberous sclerosis complex (Parekh et al., 2014). Isolated angiomyolipomas are four times more frequent than in association with tuberous sclerosis(Lin et al., 2017; Parekh et al., 2014; Redkar et al., 2012). Angiomyolipomas associated with tuberous sclerosis are more likely to complications as haemorrhage compared to sporadic renal angiomyolipomas. The treatment strategy depends on the size of the lesion and the symptoms. The main risks of angiomyolipomata, severe bleeding, loss of renal function, and pulmonary lymphangioleiomyomatosis, can be ameliorated by active surveillance and pre-emptive therapy with mTOR inhibitors(Bissler & Christopher Kingswood, 2018). Early diagnosis of TSC is very important in order to offer appropriate care and long-term surveillance especially when a new therapy is available.

The diagnosis of TSC is primarily made clinically based on Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference.

Major features

- Hypomelanotic macules (≥3, at least 5-mm diameter);
- Angiofibromatous (≥3) or fibrous cephalic plaque;
- Ungual fibromas (≥2);
- Shagreen patch;
- Multiple retinal hamartomas;
- Cortical dysplasia;
- Subependymal nodules;
- Subependymal giant cell astrocytoma;
- Cardiac rhabdomyoma;
- Lymphangioleiomyomatosis (LAM);
- Angiomyolipomas (≥2).

Minor features

- Confetti skin lesions;
- Dental enamel pits (>3);
- Retinal achromic patch;
- Intraoral fibromas (≥2);
- Multiple renal cysts;
- Nonrenal hamartomas.

Definite diagnosis: Two major features or one major feature with ≥2 minor features.

4. Conclusions

In the present case, the diagnosis is uncertain for two reasons. First, the lack of patient's symptoms during the last 10 years. Second, in our opinion, the resected ungual fibroma, as a major criterion, should have been histologically confirmation, if performed.

Given the 2017 event with rupture and subcapsular hematoma, the recent haematuria and the fact that bleeding is more common in tuberous sclerosis angiomyolipomas than in isolated ones, has an increased probability for tuberous sclerosis.

Due to the financial condition of the patient and the need to travel in another city, the patient did not follow our instructions and refused guidance to a specialized centre in the management of tuberous sclerosis. We will try to screen our patient in the future for new manifestations and symptoms, and to perform genetic testing.

5. Acknowledgement

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