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TUBEROUS SCLEROSIS COMPLEX. FORTY-YEARS OF FOLLOW-UP OF A PATIENT AFFECTED.

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Summary.- **OBJECTIVES:** To report the case of a patient diagnosed with tuberous sclerosis complex (TSC), describe its clinical features, diagnosis, and to attract attention on the fact that after 40 years of follow-up, the patient has presented practically all the manifestations described in the literature.

METHODS: A 42 year-old man diagnosed with TSC presented the emergency department due to left lumbar pain and self-limited gross hematuria. On clinical examination patient was haemodynamically stable, but with decrease in haemoglobin (6.8g/ dL). Abdominal CT scan showed a 20 cm diameter heterogeneous mass in the left kidney suggesting hemorrhage of an angiomyolipoma.

RESULTS: Left radical nephrectomy was performed and the pathological study of the surgical specimen confirmed the diagnosis of angiomyolipoma. Immunohistochemical staining was positive with HMB-45.

CONCLUSIONS: To recommend that patients with TSC be evaluated by a multidisciplinary group of clinicians, including urologists, neurologists and dermatologists. As patients with TSC survive into adulthood they will require more intervention by the urologist. CT scan is usually enough for the diagnosis of angiomyolipomas. Complete nephrectomy is appropriate when the whole kidney has been replaced by angiomyolipoma. The identification of molecular markers (HMB-45) facilitates histopathological diagnosis.

Keywords: Tuberous sclerosis complex. Angiomyolipoma. Kidney.

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Resumen.- **OBJETIVOS:** Presentar un caso singular de un paciente diagnosticado de esclerosis tuberosa, describir sus manifestaciones clínicas, diagnóstico, y llamar la atención sobre el hecho que, tras 40 años de seguimiento el paciente ha presentado prácticamente todas las manifestaciones descritas en la literatura.

MÉTODOS: Hombre de 42 años de edad diagnosticado de esclerosis tuberosa que acude a urgencias por dolor lumbar izquierdo y hematuria macroscópica auto-limitada. A la exploración física el paciente se presentaba hemodinámicamente estable, pero con disminución de la hemoglobina (6.8g/ dL). El TAC abdominal mostraba una masa heterogénea de 20 cm. de diámetro en el riñón izquierdo que sugirió hemorragia de angiomiolipoma.

RESULTADOS: Se realizó nefrectomía radical izquierda y el estudio patológico de la pieza quirúrgica confirmó el diagnóstico de angiomiolipoma. El estudio inmunohistoquímico fue positivo para HMB-45.

CONCLUSIONES: Recomendamos que los pacientes con esclerosis tuberosa sean evaluados por un grupo clínico multidisciplinar, que incluyan urólogos, neurólogos y dermatólogos. Como los pacientes con esclerosis tuberosa llegan a la edad adulta requerirán más intervención por los urólogos. El TAC es normalmente suficiente para diagnosticar el angiomiolipoma. La nefrectomía total es apropiada cuando todo el riñón está reemplazado por el angiomiolipoma. La identificación de marcadores moleculares (HMB-45) facilita el diagnóstico histopatológico.

Palabras clave: Esclerosis tuberosa. Angiomiolipoma. Riñón.

INTRODUCTION

Tuberous sclerosis complex (TSC) is characterized by important neurological involvement, cutaneous manifestations and visceral abnormalities.

The prevalence is estimated to be between 1/5000 and 1/15000 individuals. Tuberous sclerosis is still a clinical diagnosis. Clinical manifestations have been divided into major and minor criteria.

The singularity of the case presented is based on the fact that after 40 years of follow-up (from six months of age), the patient has presented practically all the manifestations described in the literature - having met up to 8 major diagnostic criteria for the disease.

CLINICAL CASE

Male diagnosed with tuberous sclerosis complex (TSC) after the appearance of seizures at six months of age (1962), hypomelanotic macules and facial angiofibromas after three years of age. Slight mental retardation and periungual fibromas presented during development. (Figure 1)

At sixteen years of age (1978), frontal craniotomy was performed due to obstructive hydrocephalus secondary to a periventricular tumor. A ventricular derivation valve was inserted and the tumor was removed surgically. Histopathological evaluation: giant cell astrocytoma.

Radiographic follow-up studies revealed multiple cortical hamartomas and periventricular bilateral subependymal nodules. (Figure 2)

At 42 years of age (2004), the patient presented to emergency department due to left lumbar pain and self-limited gross hematuria. Haemodynamically stable. Physical exam: palpable mass in the whole left hemiabdomen. Analytically: Creatinine 1.6 mg/dL, Haemoglobin 6.8 g/dL, leucocytosis of 13500/ μ L. No alterations in the remaining biochemical parameters.

Abdominal CT Scan: 20 cm diameter mass, liquid, with various densities, in the left upper pole of the kidney and in a subcapsular position, displacing the renal parenchyma ventrally. Multiple low-attenuation nodular elements in both kidneys with some cortical cystic elements and multiple low-attenuation images in the right perirenal fat, suggesting small hemorrhages in the right kidney (Figure 3). The MRI corroborated these findings and revealed an important displacement of the abdominal aorta towards the right side.

Subsequent left radical nephrectomy only identified the kidney's lower pole, multiple renal angiomyolipomas, multiple lipomas and renal cysts. HMB-45 immunohistochemical staining was positive.

After six months of follow-up, the patient is asymptomatic and his renal function within normal limits.

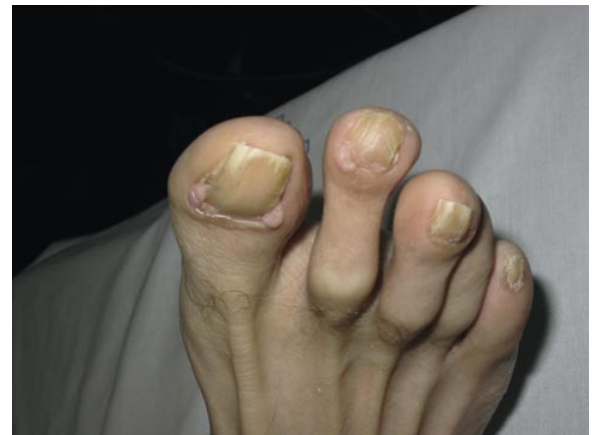


FIGURE 1. Periungual fibromas, which typically appear after puberty, as in our patient.

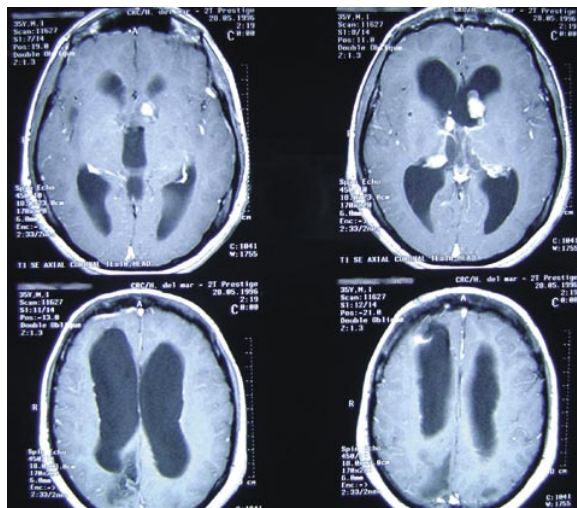


FIGURE 2. Hydrocephalus and periventricular tumor.

DISCUSSION

Tuberous sclerosis complex is an organogenesis defect that causes the formation of hamartomas in ectodermal and mesodermal tissues. Autosomal dominant disease originating from a defect on chromosome 9q and 16p (1).

Multisystemic manifestations:

-Dermatological: hypomelanotic macules, angiofibromas in a malar distribution on the face and non-traumatic ungual or periungual fibromas (Koenen tumors). Shagreen patches and café-au-lait macules are other dermatological manifestations (2).

-Neurological: the primary cause of morbidity and mortality (2). Appearance of seizures and mental retardation. There are two types of hamartomas in the central nervous system: cortical tubers which are multiple nodules in the frontal and parietal lobes, and glial subependymal hamartomas, which are also multiple, bilateral, periventricular and can cause obstructive hydrocephalus. This typically happens in the first two decades of life (3). 7-15% of subependymal nodules are a giant cell type astrocytoma.

-Renal: Second leading cause of morbidity and mortality (2). Almost 50% of the patients have angiomyolipomas. Although considered to be hamartomas in the past, angiomyolipomas are now known to be clonal neoplasms (4). Angiomyolipomas in patients with TSC tend to present earlier with larger tumors and greater multiplicity than the sporadic type and require surgical intervention more often (1).

The renal cysts are multiple and bilateral (2).

-Other: lymphangiomyomatosis, which also has HMB-45 immunoreactivity (5). Cardiac rhabdomyoma, retinal glial hamartomas and rectal polyps are other manifestations observed (2).

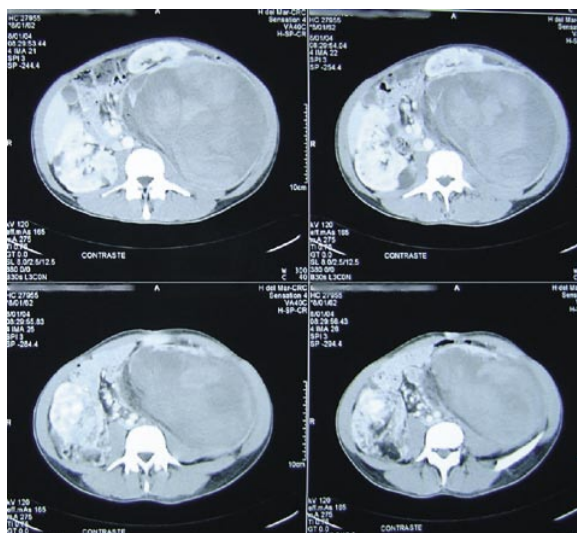


FIGURE 3. Computerized tomography scan of the abdomen showing the large mass and multiple cysts, lipomas and angiomyolipomas in the right kidney.

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(*of special interest, **of outstanding interest)

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