Primary adrenal angiosarcoma. A case report

ABSTRACT

Primary adrenal angiosarcoma is a rare vascular malignancy with fewer than fifty cases reported in the literature, with a preference for middle-aged men and a poor prognosis with a median survival of around eighteen months and a five-year overall survival of 30%. A case of a 61-year-old male patient who consulted for pain in the left renal fossa radiating to the ipsilateral flank and constitutional syndrome is reported. Diagnostic imaging tests show a large solid left adrenal mass with no signs of local tumor extension or in other organs; Laboratory studies confirm autoproduction of cortisol and association with probable paraneoplastic consumptive coagulopathy. Open left adrenalectomy was performed with an anatomopathological diagnosis of primary epithelioid angiosarcoma of the adrenal gland and liver metastases. During the immediate postoperative period, hematoma of the surgical site was evidenced, which was treated conservatively with favorable evolution. Subsequently, adjuvant chemotherapy treatment with paclitaxel was administered, presenting metastatic progression in diagnostic imaging tests five weeks after surgery. Exitus letalis, presented three months after surgery.

Keywords: Primary adrenal epithelioid angiosarcoma, adrenal, immunohistochemistry, poor prognosis.
RESUMEN
El angiosarcoma suprarrenal primario es una neoplasia vascular maligna rara con menos de cincuenta casos reportados en la literatura, con preferencia por hombres de mediana edad y mal pronóstico con una mediana de supervivencia de alrededor de dieciocho meses y una supervivencia global a los cinco años del 30%.
Se reporta un caso de un paciente varón de 61 años que consulta por dolor en fosa renal izquierda irradiado a flanco ipsilateral y síndrome constitucional. Las pruebas diagnósticas por imagen muestran una gran masa sólida suprarrenal izquierda sin signos de extensión tumoral local ni en otros órganos; estudios de laboratorio confirman autoproducción de cortisol y asociación con probable coagulopatía de consumo paraneoplásica. Se realizó suprarrenalectomía izquierda abierta con diagnóstico anatomopatológico de angiosarcoma epitelioide primario de la suprarrenal y metástasis hepáticas. Durante el postoperatorio inmediato se evidenció hematomatología del sitio quirúrgico, que fue tratado de forma conservadora con evolución favorable. Posteriormente se administró tratamiento quimioterápico adyuvante con paclitaxel, presentando progresión metastásica en exámenes de diagnóstico por imagen a las cinco semanas de la cirugía. Exitus letal, presentado tres meses después de la cirugía.

Palabras clave: Angiosarcoma epitelioide suprarrenal primario, suprarrenal, inmunohistoquímica, mal pronóstico.

1. Introduction
Primary adrenal angiosarcoma is a rare malignant vascular neoplasm with less than fifty cases reported in the literature, with preference for middle-aged men and a poor prognosis with a median survival of about eighteen months and overall survival at five years at 30%.

2. Case report
A 61-year-old male patient who consulted for pain in the left renal fossa radiating to the ipsilateral flank and constitutional syndrome. Diagnostic imaging tests show a large solid left adrenal mass without signs of local tumor extension or in other organs; laboratory studies confirm cortisol self-production and association with probable paraneoplastic consumption coagulopathy. Open left adrenalectomy was performed with a pathological diagnosis of primary epithelioid angiosarcoma of the adrenal and liver metastases. During the immediate postoperative period, hematoma of the surgical site was evident, that was treated conservatively with a favorable evolution. Subsequently adjuvant chemotherapy treatment with paclitaxel was administered, presenting metastatic progression in diagnostic imaging exams five weeks after surgery. Exitus letalís, presented three months after the surgery.

3. Clinical Case
A 61-year-old male patient with a personal history of allergy to latex, habitual consumption of 3-4 Standard Drinking Units (SDU), arterial hypertension, mild tricuspid regurgitation and an appendectomy, was evaluated by Internal Medicine for pain in the left lumbar region irradiating to the ipsilateral flank and presenting constitutional syndrome of one month of evolution reporting a loose of 8kg, without other associated urological symptoms. During physical examination, the patient presented pain on palpation in the left hypochondrium with a palpable mass.

A thoracic-abdominal CT (Figure 1) performed shows a solid left adrenal mass of up to 10 cm, oval, with defined contours, linear calcifications on its wall and a necrotic center without locoregional or distant involvement (Figure 1.1), with peripheral increase in metabolic activity on PET-CT (Figure 2) and cortisol production in hormonal study. The blood analysis revealed normocytic anemia Hb 8.1 g/dl, Hematocrit 25% & MCV 88, with the rest of the series normal, alteration in coagulation parameters with decreased prothrombin (PT) activity, prolonged prothrombin time (PT) and international normalized ratio (INR) 1.52, together with, Ferritin 1837ng/ml, elevated derived fibrinogen 813mg/dl, in relation to consumption coagulopathy of probable paraneoplastic origin. Cortisol and Dehydroepiandrosterone are normal for suprarenal studies. Tumor markers (Alpha-1-fetoprotein, Ca 125 Ag., Ca 15-3 Ag., Ca 19-9 Ag., Carcinoembryonic Ag and specific neuronal enolase) were negative.

After pre-surgical hematological preparation with fresh frozen plasma and phytomenadione to optimize coagulation, left adrenalectomy was performed using an open approach and a biopsy was taken of suspicious sub-centimetric liver lesions not observed in preoperative imaging studies. Anatomopathological studies were consistent with adrenal epithelioid angiosarcoma with free surgical margins and liver metastases of angiosarcoma.

At the early postoperative phase, the patient presented with hemodynamic instability and decreased hemoglobin levels accompanied by persistent coagulopathy, for which an urgent abdominal CT was performed, revealing a large hematoma in the surgical bed without identifying a clear active bleeding; It was decided to perform expectant management, transfusion of 6 packed red blood cells, fresh frozen plasma, and tranexamic acid, with favorable evolution and discharge fourteen days after the intervention.

Readmission is done at five weeks postoperatively, due to suspicion of active bleeding in previous postoperative hematoma seen on the control abdominal CT (Figure 3), with a slight decrease in hemoglobin.
levels without associated hemodynamic repercussions. Conservative management was performed with a new transfusion of 2 packed red blood cells and fresh frozen plasma, requiring third-step analgesia due to the reappearance of pain at the left renal fossa radiating to the ipsilateral lower limb during admission. After a favorable evolution with radiological and analytical stability the patient was discharged after fifteen days.

Figure 1. PRE-SURGICAL ABDOMEN-PELVIS CT:
Axial (a and b) and coronal (c) CT slice with contrast in the portal phase.
A large left adrenal mass measuring 13cm in greatest diameter was observed. It has a rounded morphology with well-defined edges and heterogeneous density and enhancement. The periphery of the lesion presents linear calcifications and an area of greater density that may correspond to bleeding or greater enhancement. It presents a hypodense central area related to necrosis. No dominant vessel is seen that is nourishing the mass. There is a small amount of perisplenic fluid and a slight increase in fat density around the mass. Anteriorly displaces the splenic artery, pancreatic body, and tail. Laterally the spleen and caudally the left kidney.

Figure 1.1. Coronal CT section.
Large left retroperitoneal solid mass located in the adrenal bed with a 10 cm sagittal axis, defined slightly ragged contours presenting linear calcifications on its wall and a necrotic center that displaces adjacent structures.
Metastatic progression was found in the liver, lung, bone, abdominal wall, and omentum by CT (Figure 4) on the fifth postoperative week an CT follow up is performed (Figure 5) and subsequent chemotherapy treatment started with paclitaxel.

Ultimately, the patient presented with Exitus Letalis at three 3 months after the intervention due to decline on his general state, anemia and acute confusional syndrome.

Figure 2. PET/CT with 18F-FDG.
Left adrenal mass with peripheral metabolic activity augmented, with a high probability of malignancy (SUV max 21.7) in the adrenal mass. This documented uptake, corresponds to the areas of greatest enhancement on the CT. Additionally, a small hypermetabolic focus was documented in segment (6) of the liver, suggestive of metastasis (SUV max 7).

Figure 3. Coronal CT section.
Signs of active bleeding in the left adrenal surgical bed with progression of the left subphrenic hematoma and the presence of hemoperitoneum. New-onset pulmonary, omental, and bone metastases.
4. Discussion

Adrenal gland masses may develop from the cortex (cortical adenoma or adrenal carcinoma) or from the medulla (pheochromocytoma, ganglioglioma, neuroblastoma, ganglioneuroma). The adrenal gland can also be compromised secondarily (metastasis). Other tumors that can compromise it are myelolipomas, teratomas, leiomyomas, schwannomas and angiosarcomas.

Angiosarcoma is a malignant vascular neoplasm that accounts for less than 1% of all sarcomas (1), with a predilection for highly vascularized organs such as skin, lungs, or liver, with hardly fifty reported cases of primary adrenal involvement (2). Primary adrenal epithelioid angiosarcoma PAEA, is an uncommon disease originally described by Kareti and his colleagues in 1988. Thirteen other cases have been reported in a recent five-year span.

Risk factors related to its development like radiotherapy, exposure to thorium dioxide, vinyl chloride or arsenic, chronic lymphedema, and possibly genetic alterations stand out (1).

With a higher prevalence on middle-aged men (around the sixth decade of life) and its aggressive nature dims the prognosis, with a median survival of eighteen months and overall survival of 30% at five years (1).

Clinically these masses in the adrenal glands may arise due to:

- Hormone hyperproduction observed in tumors originating in the cortical and medullary adrenal gland (glucocorticoids, mineralocorticoids, catecholamines, sex hormones and steroid precursors. Due to the above, patients consult with Cushing syndrome, virilization,
diagnosis of adrenal mass despite its scant incidence (3).

• Constitutional symptoms in malignant processes: Fever or weight loss
• Hypoglycemia as a paraneoplastic syndrome
• In the case of angiosarcomas or myelolipomas, it can present with
  • spontaneous bleeding

The usual clinical presentation incorporates the appearance of pain jointly with a palpable abdominal mass; however, in many cases it is diagnosed in asymptomatic patients as an incidental radiological finding of a large solid and heterogeneous adrenal mass with areas of necrosis. In this way, its diagnosis prior to the histological study is a real challenge since it affects the adrenal gland, so it should be included in the differential diagnosis of adrenal mass despite its scant incidence (3).

Primary adrenal epithelioid angiosarcoma (PAEA) is a very rare tumor, but it is the angiosarcoma variant that prevails in the adrenal gland (6,7). Angiosarcoma has a broad morphologic appearance, ranging from lesions that are cytologically soft and vasoformative, to solid sheets of highly pleomorphic cells without definitive angiogenesis (6). PAEA is characterized by vascular proliferation that often forms anastomosed channels lined by atypical endothelial cells and sheets of epithelial-like endothelial cells with abundant eosinophilic cytoplasm, a large nucleus with a prominent nucleolus. Areas of necrosis and hemorrhages are very frequent and, in some cases, prevailing. Atypical mitoses are common (12/mm2). Neoplastic cells are positive for CD31, CD34, Fli-1, ERG, Vimentin, PanCK and negative for inhibin, Melan A, Calretinin and HMB45.(4,5,7). The Ki-67 proliferation index was 30%.

By imaging we must consider the size and density of the lesion. And we must consider if there is a history of a known primary tumor as well as if there are parameters of hormonal hyperproduction (9).

• Lesions with macroscopic fat suggest mainly myelolipomas or less likely teratomas.
• Lesions smaller than 2cm are probably benign, if they do not have hormonal hyperproduction or a history of previous cancer, a follow-up study can be performed in one year or compare with previous studies to document stability.
• Adrenal CT is recommended for 2cm to 4cm lesions or with a history of previous cancer, which includes a phase without contrast to determine if they correspond to an adenoma (in this case, the density is less than 10 HU), if a study without contrast is not available and the lesion is demonstrated in a study carried out in the portal phase, you can wait 15 minutes and do a new scan and measure the density and obtain the percentage of absolute or relative washing to assess whether the lesion to an adenoma (60% absolute washout and 40% relative washout).
• If there is a history of previous cancer, the performance of PET CT is indicated or biopsy to rule out metastasis
• Lesions larger than 4cm without fat density are generally malignant: neuroblastomas, carcinosarcomas or angiosarcomas, metastasis. PET CT and surgical resection are indicated for these lesions.

Currently, complete surgical resection is the therapeutic approach of choice, evaluating the need for radiotherapy and/or chemotherapy a posteriori due to its high predilection for local and distant recurrence (1,5).

5. Conclusions

Despite being an infrequent pathology, it is essential to include it in the differential diagnosis of adrenal mass due to its aggressiveness and difficulty in making an accurate diagnosis prior to the anatopathological study. The gold standard treatment consists in a complete surgical resection with the possibility of performing adjuvant radiotherapy and/or chemotherapy due to the high risk of local and distant recurrence.

References


Histopathology Images

Figure 6. Macroscopic aspect of adrenal angiosarcoma.
Mass that measures 11.1 x 10cm and weighs 67g, has replaced almost the entire glandular parenchyma. The mass is reddish, somewhat spongy, with extensive areas of hemorrhage and necrosis.

Figure 7. Microscopic features of adrenal epithelioid angiosarcoma.
Low magnification view showing a vascular neoplasm forming anastomosed channels containing red blood cells in the lumen. With this magnification large and hyperchromatic nuclei are recognized (H&E, 4X).

Figure 8. Irregularly shaped anastomosing vascular channels or sheet-like of epithelioid cells with abundant eosinophilic cytoplasm, enlarged nuclei, prominent nucleoli. (H&E 20x).
Figure 9. Intratumorally hemorrhage is common. (H&E 20X).

Figure 10. Immunohistochemical staining.
The epithelioid cells strongly expressed vascular differentiation markers such as CD31.