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CLINICAL CASE

Adrenal gland melanoma without evidence of skin lesion: an unusual presentation. Case report

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Abstract

Adrenal gland melanoma is rare. The diagnostic criteria included involvement of a single adrenal gland, histological exa-mination, no primary melanoma tumor, and no history of resection of pigmented lesions. We present the case of a 76-year-old woman with a history of smoking and hypertension who was admitted because of pain in the right lumbar region, with suspicion of a tumor in the adrenal gland. During surgery, the tumor was removed without complications, and a diagnosis of melanoma was made using immunohistochemical. Diagnostic suspicion and early approach are key due to the high mortality rate of melanoma.

Keywords: *Melanoma. Unknown primary. Immunotherapy. Adrenal gland melanoma. Case report.*

Melanoma de glándula suprarrenal sin evidencia de lesión cutánea: una presentación inusual. Reporte de caso

Resumen

El melanoma de la glándula suprarrenal es raro. Los criterios diagnósticos incluyen afectación de una sola glándula suprarrenal, examen histológico, ausencia de tumor primario de melanoma y ausencia de antecedentes de resección de lesiones pigmentadas. Presentamos el caso de una mujer de 76 años, con antecedentes de tabaquismo e hipertensión, que ingresó por dolor en la región lumbar derecha, con sospecha de tumoración en la glándula suprarrenal. Durante la cirugía se extirpó el tumor sin complicaciones y se realizó el diagnóstico de melanoma mediante inmunohistoquímica. La sospecha diagnóstica y el abordaje precoz son claves por la alta mortalidad del melanoma.

Palabras clave: *Melanoma. Primario desconocido. Inmunoterapia. Melanoma de la glándula suprarrenal. Reporte de caso.*

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Introduction

Melanoma is the most aggressive skin cancer that exists most of the time it usually appears on the skin; however, there are rare occasions that it appears primarily in other places, primary melanoma of the adrenal gland is extremely rare and there are few cases reported in the literature. The accompanying signs and symptoms are non-specific, pain is usually the most common manifestation, and most of the time it appears as an incidental finding, the diagnosis is made by histopathology and immunohistochemical studies.

Clinical findings

A 76-year-old woman with a history of mother who died of lung cancer, a history of smoking with a smoking index of 4.2, and systemic arterial hypertension in irregular control, no other important background to comment.

The endocrinologist referred the patient to the oncology service secondary to pain in the lumbar thoracic region for 1 month (predominantly right) and weight loss of 6 kg in 3 months, asthenia, and adynamic. On physical examination, the patient was found to have an ECOG 0, KARNOSFKY 100%, cardiopulmonary region without any aggregates, abdomen with pain in the right upper quadrant on deep palpation, with the presence of palpable tumor activity, pain in the right thoracolumbar region, and the rest without aggregates.

Diagnostic approach

The initial approach was performed in general laboratories and using abdominal ultrasound. The only altered parameters were hemoglobin 11.2 g/dL, hematocrit 36%, lactate dehydrogenase 642 U/L, alpha-fetoprotein 162 ng/mL, TSH 6.88 μUI/mL. Echocardiography showed a mild-sized pericardial effusion of 95 mL. Abdominal ultrasonography revealed a liver tumor measuring 124 × 80 mm. Abdominal CT confirmed the presence of a retroperitoneal tumor of 91 × 24 × 77 mm with contrast enhancement up to 63 HU, right kidney with displacement, and left kidney simple cyst Bosniak 1, but the possibility of another type of primary retroperitoneal tumor could not be excluded from the study.

Therapeutic intervention

We decided to perform the surgery under general anesthesia. We made a midline supra-and infra-umbilical incision and found a suprarenal and paracaval tumor measuring approximately 10 × 8 cm with increased vascularity, displacement of the right kidney, and extrinsic compression of the inferior vena cava and abdominal aorta without evidence of lymph nodes or suspected tumor activity. The tumor was removed, including the kidney and right adrenal gland and an incidental appendectomy was performed. The patient recovered without post-operative complications.

The histopathological study corresponded to a tumor weighing 375 g and measuring 10.5 × 9.5 × 7.5 cm, the cut surface is heterogeneous with solid areas with scar zone, presence of coagulative necrosis of friable consistency, in the same fragment was identified laminar fragment of hepatic tissue measuring 6 × 5 × 0.7 cm, nodular surface of light brown color: when cut, it is homogeneous, solid and with a smoky consistency. A microscopic study reported high-grade oxyphilic adrenocortical carcinoma of the adrenal cortex.

Immunohistochemical staining revealed that Melan-A and HMB45 were both positive, with negative markers for calretinin, synaptophysin, chromogranin, CD45, and S100. A diagnosis of epithelioid melanoma was made (Fig. 1).

Follow-up and outcomes

After the patient's release from our hospital, some medical test carried out, the altered parameters were androstenedione 3.3 ng/mL, serum cortisol 28 mcg/dL, lactate dehydrogenase 470 U/L, amylase 21 U/L, total proteins 4.7 g/dL, albumin 2.59 g/dL, sodium 134 mmol/L, and glucose 145 mg/dL.

During follow-up, we decided to perform a full-body 18F-FDG PET/CT scan with multiple findings of hypermetabolic tumor activity in multiple peritoneal tumor implants, soft tissues, and cervical, axillary, and mesenteric adenopathy. Subsequently, the patient entered a clinical trial where she was treated with nivolumab, she was treated with 8 cycles of immunotherapy, after 10 months, she was withdrawn from the protocol due to the progression of the disease toward metastasis and systemic toxicity secondary to treatment, which later caused the death of the patient a short time later.

Discussion

Primary cutaneous melanoma is the most aggressive type of skin tumor. In 2020, there was an increase in its incidence with 324 635 thousand new cases and 57 043 thousand deaths per year in both sexes at any age[1]. More than 90% of all melanomas present as primary

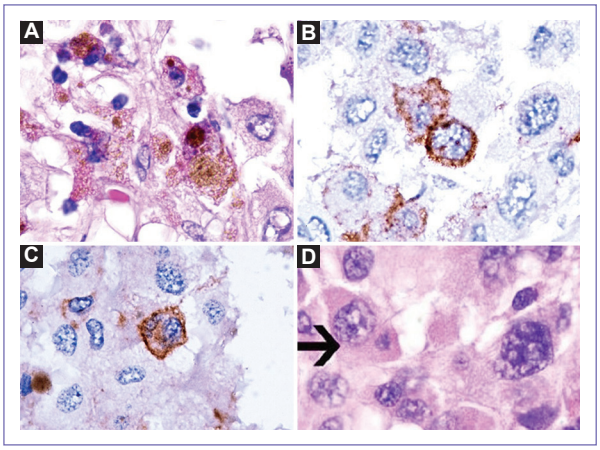


Figure 1. A: representative photomicrographs of anaplastic morphology of epithelioid melanoma. Hematoxylin-eosin staining. **B** and **C:** melanocytes show strong immunoreactivity to the melanoma markers Melan-A and HMB45 respectively. **D:** the tumor cells (arrow) demonstrate marked nuclear pleomorphism with variation in cell size, shape, staining, and increased mitotic activity.

tumors on the skin surface and usually only 1-2% arise on mucosal surfaces or present as an apparent metastatic disease with no history of primary cutaneous lesions[2]. These include the oral cavity, larynx, bronchus, esophagus, rectum, genitourinary system, meninges, ovaries, uterine cervix, vagina, and adrenal glands[3]. The challenge is to determine whether the tumor is truly primary or metastatic[4]. In 1963, Gupta established the definition of melanoma by the presence of subcutaneous tissue, lymph nodes, or melanoma localization in visceral organs in the absence of a cutaneous, ocular, or mucosal site[5].

Adrenal medullary blasts and melanoblasts have a common embryologic origin at the neuroectoderm level[6]. This may result in ectopic melanocytes at this site, causing metaplasia and transformation into malignant cells, leading to melanoma development. In cases of primary melanoma of the adrenal gland, a differential diagnosis should be considered, mainly in cases of metastatic melanoma and pigmented pheochromocytoma[7].

According to the differential diagnosis of pigmented pheochromocytoma, immunohistochemical studies are necessary, essentially neuroendocrine markers, chromogranin, and synaptophysin, in addition to electron microscopy[8]. Pigmented pheochromocytomas showed immunoreactivity for chromogranin, synaptophysin, and enolase. Case series have reported cases of pheochromocytoma with HMB45 positive cells; however, this is not unusual because some adrenal medulla cells or pheochromocytomas are derived from the neural crest, and these are neural crest-derived tumors. In the case of melanoma, the cells do not stain with chromogranin and synaptophysin, nor do they show positivity for ca-te-cholamines, enolase, and opioid peptides, which are typical markers of pheochromocytoma[7].

In one study, the most important clinical predictors for a favorable outcome in cases of metastatic melanoma of the adrenal gland, the presence of isolated adrenal malignancy, and normal lactate dehydrogenase levels represented reasonable primary selection criteria for evaluating patients for surgery versus systemic therapy. Symptoms related to adrenal metastases, di-sease-free interval of ≥ 1 year before the development of metastatic disease, limited extra-adrenal disease that can also be respected, partial response to pre-operative systemic therapy, and tumor burden required for an autologous vaccine were some of the additional criteria that favored surgical resection[9].

Post-operative criteria were used to guide adjuvant therapy and radiotherapy. Inferteron Alfa-2b improves relapse-free survival and has a significant impact on the improvement of these patients[10-12] therapy with it should be considered in selected subjects. On the other hand, radiation to nodular regions reduces the probability of relapse; unfortunately, it does not impact survival, especially in high-risk patients after radical lymphadenectomy[13]. There are insufficient data to predict the frequency of relapses and the prognosis. Of the patient after surgical resection or radiation, therefore, decision-making about the plan and management must be individualized.

The tumor presented in the clinical case only affected the right adrenal gland, and a diagnosis of epithelioid melanoma of unknown primary site was made. Exhaustive tests were performed; none showed a primary site, and there was no significant history that would lead us to think of previous pigmented lesions, so the diagnosis of melanoma of the right adrenal gland with no known primary site was clarified. The patient was treated surgically, and later, she was treated with an immunomodu-lator in a clinical trial; however, the disease spread rapidly, which led to the death of our patient.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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