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Classic Kaposi Sarcoma: An Exceptional Cause of Adrenal Incidentaloma

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Context: Classic Kaposi sarcoma (KS), also known as Mediterranean KS, affects immunocompetent patients and is usually limited to the skin, without profound organ involvement. We report an exceptional case of a primary adrenal classic KS.

Case Description: A left adrenal incidentaloma was fortuitously discovered on a computed tomography scan performed for chest pain in a 60-year-old man. Magnetic resonance imaging showed a heterogeneous left adrenal nodule enhanced by gadolinium injection. Adrenalectomy revealed a massive spindle cell infiltrate of the adrenal gland that was positive for CD31, CD34, and herpes virus 8 (HHV8) on immunohistochemistry, allowing for the diagnosis of KS. The explorations revealed no immunodeficiency or other involvement of KS. Four months later, another nodular lesion appeared on the right adrenal gland, and 2.5 years later, two nodular angiomatous KS lesions had appeared on the right foot. The evolution was indolent, and no complementary treatment of KS was required at 3 years after the diagnosis.

Conclusions: Adrenal involvement of KS is rare, eventually observed in AIDS-KS. The present case is, to the best of our knowledge, the first report of primary isolated adrenal classic KS. KS should be considered in the etiology of adrenal incidentaloma, especially if the patient has epidemiological risk factors for HHV8 infection, mainly, but not exclusively, in the context of immunodeficiency.

Freeform/Key Words: adrenal incidentaloma, Kaposi sarcoma

Kaposi sarcoma (KS) is a herpes virus 8 (HHV8) related chronic disease, presenting in four different epidemiological forms: the classic (or Mediterranean), the endemic (in Africa), the iatrogenic, and the epidemic KS related to HIV (AIDS-KS). Classic KS usually affects the skin, rarely mucous membranes and lymph nodes, and exceptionally profound organs. We report the exceptional case of a primary adrenal classic KS in an immunocompetent patient.

1. Case Report

A man aged 60 years had undergone thoracic computed tomography (CT) for chest pain, which revealed an isolated lesion of the left adrenal gland [Fig. 1(a)]. Magnetic resonance imaging (MRI) was performed. The MRI scan showed a nodular heterogeneous lesion of the left adrenal gland that measured 30 × 22 × 23 mm, without any fatty component, and enhanced

Abbreviations: ACTH, adrenocorticotropic hormone; AIDS-KS, epidemic Kaposi sarcoma associated with HIV; CT, computed tomography; HHV8, herpes virus 8; KS, Kaposi sarcoma; MRI, magnetic resonance imaging; RRID, Research Resource Identification.

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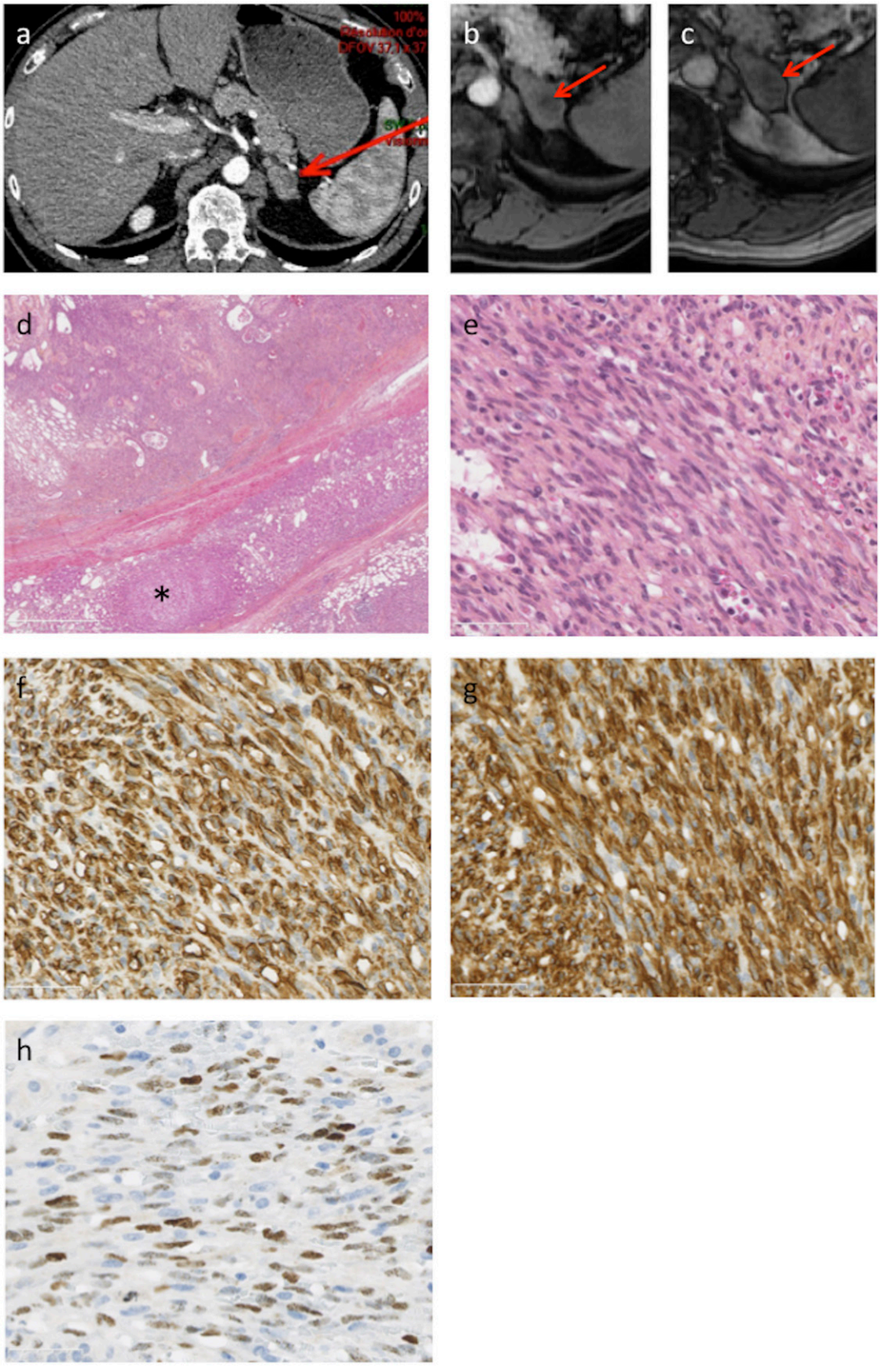
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Figure 1. (a) Axial image of contrast-enhanced CT scan (arterial phase) showing a solid nodule of the left adrenal gland, enhanced after contrast injection. Axial MRI scans: (b) T_1-weighted with gadolinium injection and (c) out-of-phase sequences showing a heterogeneous nodule of the left adrenal body, without loss of signal on the opposed-phase sequence, indicating the absence of fat component and enhanced after gadolinium injection. (d) Infiltration of the adrenal gland by spindle cell proliferation. *Residual nontumoral adrenal gland (hematoxylin and eosin staining). (e) Bland monotonous spindle cells (hematoxylin and eosin staining). (f) Diffuse and intense staining with CD31 antibody. (g) Diffuse and intense staining with CD34 antibody. (h) Nuclear staining of variable intensity with HHV8 antibody.

with gadolinium injection [Fig. 1(b) and 1(c)]. A repeat MRI scan performed 6 months later showed a discrete increase in size of the lesion, peripheral enhancement with gadolinium injection, and probable central necrosis. The findings for the right adrenal gland were normal. An 18-fludeoxyglucose positron emission tomography scan revealed increased uptake of the left adrenal gland (maximum standardized uptake value, 9.5). The clinical examination findings were normal. One month later, a diagnostic left adrenalectomy was performed. The histological analysis revealed a massive infiltration of the adrenal gland and the surrounding fat by multinodular spindle cell proliferation with infiltrative margins [Fig. 1(d)]. The spindle cells were arranged in intersecting fascicles. They showed little atypia. Numerous extravasated red blood cells were observed between the spindle cells [Fig. 1(e)]. The number of mitoses was 11 per 10 high-power field. Immunohistochemistry showed intense positivity for CD31 [Research Resource Identification [RRID], AB_2114471; Fig. 1(f)] and CD34 [RRID, AB_2063006; Fig. 1(g)] confirming the endothelial nature of the proliferation. Immunohistochemistry with a monoclonal antibody targeting the latent nuclear antigen 1 of HHV8 (RRID, AB_2637095) [1] was positive, with nuclear staining of many spindle cells [Fig. 1(h)]. This histological image is typical for KS. The diagnosis of a left adrenal incidentaloma due to KS affecting the adrenal was confirmed.

The patient had no history of immunodeficiency. HIV serology was negative. He had lived in Algeria until the age of 6 and had not lived in any other country with high HHV8 prevalence since then. He had no associated mucocutaneous lesions, no lymphadenopathy, and no hepatosplenomegaly. A thoracic-abdominal and pelvic CT scan was performed and revealed no other lesions. The patient had undergone upper gastrointestinal endoscopy and colonoscopy 3 years earlier for irritable bowel syndrome. These tests showed no abnormalities, and these examinations were not repeated, because he had had experienced no new digestive symptom or anemia. Eighteen months after surgery, HHV8 viremia was highly positive at 8200 copies/mL (3.91 log). HHV8 serology testing (HHV-8 immunofluorescence assay, Biotain, Lyon, France) was also positive. The diagnosis of classic KS with isolated left adrenal involvement was retained.

The patient underwent hormonal evaluation 4 months after adrenalectomy, which showed a possible partial primary adrenal gland deficiency, with high adrenocorticotropic hormone (ACTH; 62.56 pmol/L; normal, <13 pmol/L) and normal plasma morning cortisol (450 nmol/L; normal, 260 to 560 nmol/L). The 1-mg dexamethasone suppression test showed normal inhibition of salivary cortisol (<1 mnol/L). The dehydroepiandrosterone, delta-4 androstenedione, and 17 hydroxy-progesterone levels were low: 0.8 μmol/L (normal, 4 to 13 μmol/L), 2.51 nmol/L (normal, 2.8 to 7.4 nmol/L), and 0.815 nmol/L (normal, 4.5 to 8.5 nmol/L), respectively. The aldosterone and renin levels were normal [114.5 pmol/L (range, 55 to 360 pmol/L) and 31.2 μU/L (normal, 9 to 72 μU/L), respectively]. A repeat abdominal CT scan was performed, showing a 15-mm nodular lesion of the right adrenal gland, atypical for adrenal adenoma (spontaneous density, 25 Hounsfield units; washout, 58%). The nodular lesion was also found on review the postoperative MRI scan and was stable at 6 months. An 18-fludeoxyglucose positron emission tomography scan showed increased uptake of this lesion (maximum standardized uptake value, 5.4), evocative of a possible contralateral adrenal KS. He was treated with a low substitutive dose of 10 mg of hydrocortisone daily. Hydrocortisone treatment was introduced as a precaution,

with the hypothesis that the increased ACTH levels were indicative of subclinical adrenal deficiency. No other treatment was administered for KS.

Three months later, a short synacthen test was normal (morning cortisol, 444 nmol/L; peak serum cortisol, 643 nmol/L). The ACTH level was high (16.9 pmol/L). The aldosterone and renin levels were normal. Testing for adrenal antibodies was negative.

Clinical, biologic, and radiological surveillance was performed every 4 to 6 months and remained stable at 28 months postoperatively. However, 2 months later, two isolated cutaneous angiomatous infracentimetric nodules appeared on the right foot, with an appearance typical for KS (Fig. 2). No associated lymphedema, adenopathy, or abdominal mass was present. One nodule was treated with cryotherapy, and the second was excised. Histologic examination confirmed KS. The HHV8 viremia at this time measured 900 copies/mL (2.95 log). Because no other residual lesions were present, apart from the right adrenal nodule, we decided to continue the surveillance.

2. Discussion

The present case is truly exceptional because the patient presented with a primary and isolated adrenal KS discovered incidentally. This patient was probably infected by HHV8 during his early life because he was born in a high prevalence area. He must be considered as having classic KS because he had no evidence of immunodeficiency.

Classic KS usually affects elderly people from central Europe and the Mediterranean border. The lesions are most often limited to the skin, with angiomatous plaques and papular nodules predominantly on the extremities of the lower limbs, and lymphedema. The evolution is chronic and, in most cases, indolent.

Adrenal involvement seems very unlikely in the evolution of classic KS. To the best of our knowledge, adrenal involvement of classic KS has only been reported twice before [2, 3]. The first case concerned a Moroccan man who had an asymptomatic adrenal lesion, together with skin, mucosal, and digestive involvement of KS [2]. The second case reported a patient

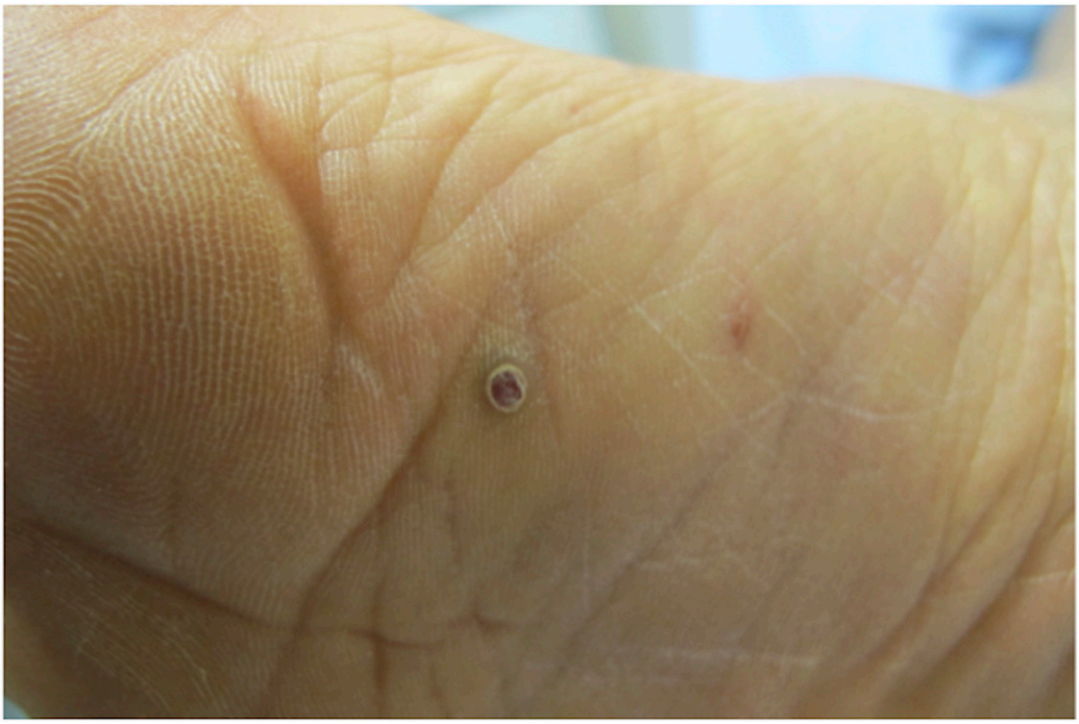

Figure 2. Photograph of purplish nodule of KS on the right sole.

incidentally diagnosed with a primary adrenal KS in its anaplastic form, with an aggressive evolution after surgery that required chemotherapy and radiotherapy [3].

Visceral and especially adrenal involvement is also rare in endemic KS. One case of an immunocompetent Congolese man with a diagnosis of isolated bilateral adrenal KS requiring chemotherapy was reported, with no relapse after 4.5 years of follow-up [4].

Although visceral involvement is frequent in AIDS-KS, adrenal involvement rarely has been reported. We found 29 reported cases of AIDS-KS with adrenal specific lesions [5–8]. However, the diagnosis of adrenal involvement was *post mortem,* on autopsy, in 25 cases.

No specific radiological characteristics indicative of adrenal KS were identified. The entities that should be considered in the differential diagnosis from the present MRI findings include adrenal carcinoma, pheochromocytoma, and metastatic cancer and require a diagnostic adrenalectomy. In the present case, the disease remained indolent; however, the possibility of contralateral localization could not be excluded. The diagnosis was supported by the occurrence of partial primary adrenal insufficiency without another cause and a slight imaging alteration for the contralateral adrenal gland. However, the lack of evolution during 28 months of follow-up and the rather mild severity of these alterations prevented definite conclusions.

3. Conclusions

We report a case of an adrenal incidentaloma revealing a primary and isolated adrenal localization of classic KS. Although adrenal involvement of KS is rarely observed in AIDS-KS, adrenal involvement is exceptional in the other epidemiological forms of the disease. As described in the present report, the disease can begin with adrenal infiltration, and the cutaneous lesions can develop several years later. Therefore, KS should be considered as an etiology of adrenal incidentaloma, especially if the patient has epidemiological risk factors for infection with HHV8, mainly, but not exclusively, in the context of immunodeficiency.

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