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CASE REPORT

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An unusual renal angiomyolipoma with morphological lymphangioleiomyomatosis features and coexpression of oestrogen and progesterone receptors

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Abstract Angiomyolipoma is the most common mesenchymal renal tumour, the clonal origin of which has recently been demonstrated. It is composed of varying amounts of blood vessels, smooth muscle and fat. In this report, we describe a renal angiomyolipoma, which is unusual owing to the presence of a lymphangioleiomyomatosis-like component, occurring in a 41-year-old woman suffering from sporadic lymphangioleiomyomatosis. The diagnosis was based on histopathological and immunohistochemical findings. The tumour consisted of an intimate admixture of two components: one was typical of a classical angiomyolipoma and the other was reminiscent of lymphangioleiomyomatosis. HMB45 positivity was found on 5% of the cells of the angiomyolipoma component. Ten percent of the nuclei of the lymphangioleiomyomatosis and angiomyolipoma components expressed oestrogen receptors and 5% progesterone receptors. This case illustrates a very unusual pattern of a renal angiomyolipoma containing a lymphangioleiomyomatosis-like component. The oestrogen and progesterone immunoreactivity suggests that angiomyolipoma could be hormonally dependent. Therefore, we have emphasised the morphological and immunohistochemical similarities between angiomyolipoma and lymphangioleiomyomatosis.

Keywords Kidney · Angiomyolipoma · Lymphangioleiomyomatosis

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Introduction

Angiomyolipoma (AML) is a mesenchymal renal tumour, the clonal origin of which has been reported recently [11]. AML is composed of blood vessels, smooth muscle and mature fat cells. We report a case of renal AML that is unusual in that the tumour, occurring in a 41-year-old woman suffering from sporadic lymphangioleiomyomatosis (LAM), contains a LAM-like component. In this report, we discuss the relationship between AML and LAM.

Case report

A 41-year-old woman was referred to hospital because of recent dyspnoea. She had no particular previous medical history. The chest radiograph showed a left pleural effusion and bilateral reticular opacities. The computed tomography (CT) scan of the thorax revealed multiple thin-walled cysts evenly distributed throughout the lung fields. At thoracocentesis the pleural fluid was chylous. The patient was treated by pleurectomy. The open-lung biopsy obtained at that time showed changes characterised by a haphazard proliferation of smooth muscle cells around bronchioles, in alveolar septa, around arteries, veins, lymphatic spaces and in the pleura. There was no interstitial fibrosis. The diagnosis of LAM was thereby confirmed. No anomaly was detected at the clinical cutaneous and neurological examination. A cerebral CT scan was normal. The abdominal CT scan detected a right renal tumour without fat density located on the posterior side of the kidney. The patient underwent a complete nephrectomy.

Materials and methods

The surgical specimen was fixed with 10% formaldehyde and embedded in paraffin. Sections (3-µm thick) were stained with haematoxylin and eosin. Immunohistochemical analysis was performed using an indirect immunoperoxidase technique with diaminobenzidine (DAB) revelation and the following primary antibodies: anti-smooth muscle actin (Dako, 1A4, 1/200), anti-desmin (Dako, D33, 1/100), anti-HMB 45 (Biogenex, HMB 45, 1/100), anti-oestrogen receptors (Tebu, CC4–5, 1/20) and anti-progesterone receptors (Tebu, 1A6, 1/20).

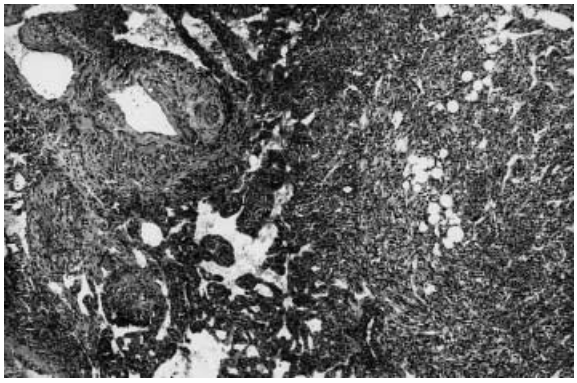

Fig. 1 The tumour is composed of smooth muscle cells, thick-walled blood vessels, areas indistinguishable from lymphangioleiomyomatosis and fat cells (haematoxylin and eosin, original magnification ×10)

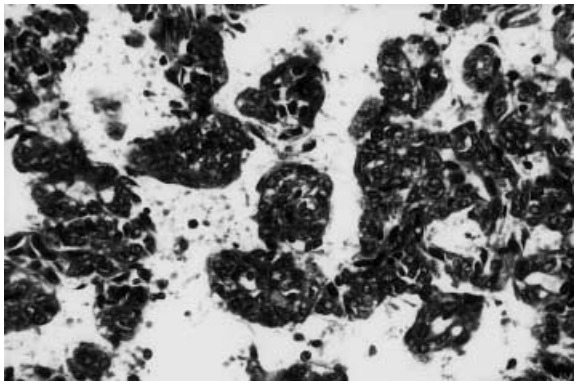

Fig. 2 Morphological pattern indistinguishable from lymphangioleiomyomatosis (haematoxylin and eosin, original magnification ×20)

Pathological findings

The tumour measured 3×2×2 cm. The sectioned surface was whitish with areas of haemorrhage. No lymph node was found. Microscopically, it was not sharply delimited, and it extended into the perirenal fat. It was composed of spindle and epithelioid smooth muscle cells arranged in interlacing bundles and sheets (Fig. 1). The tumour contained, in some areas (20% of the tumour), thin-walled branching vessels surrounded by a thick layer of smooth muscle that had an architecture similar to that of the pulmonary lesions (Fig. 1, Fig. 2). A few cells had enlarged irregular nuclei with prominent nucleoli. Numerous fibrous thick-walled vessels were present (Fig. 1). There were a few isolated mature fat cells (Fig. 1).

The immunohistochemical study indicated diffuse smooth-muscle actin and desmin positivity and smooth-muscle HMB45 positivity on 5% of the cells of the AML component (Fig. 3). Ten percent of the nuclei of the LAM and AML component expressed oestrogen receptors and 5% progesterone receptors.

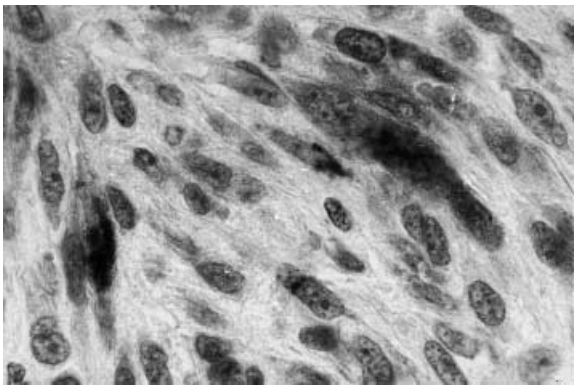

Fig. 3 Focal HMB 45 positivity on the smooth-muscle component (original magnification ×100)

Despite progesterone administration (as intramuscular depot of medroxyprogesterone 500 mg/month), the patient had been developing severe respiratory failure for 9 years. At present pulmonary transplantation is planned, and there has been no recurrence of the renal tumour.

Discussion

LAM is a rare pulmonary disease that affects primarily women. Microscopically, LAM is characterised by a proliferation of benign-appearing smooth muscle cells in the interstitium, around bronchioles, arteries, veins and lymphatic spaces, in alveolar septa and in the pleura. The clinical course is marked by progressive respiratory failure leading to death [7].

In about 50% of cases, LAM is associated with renal AML [2], which is primarily unilateral, small and asymptomatic [7, 11]. There do not appear to be any histological differences between AML that is or is not associated with LAM. The tumours are composed of varying amounts of abnormal thick-walled blood vessels, smooth muscle and mature adipose tissue [4]. A confident radiological diagnosis can be made in almost all cases on the detection of fat in the tumour [4]. Our case is unusual because of the LAM-like component and the low proportion of fat that did not allow its preoperative distinction from a renal cell carcinoma.

Cases in which renal tumours are morphologically indistinguishable from LAM are uncommon. We have found only three cases, which were differently named by the authors in the literature: a renal lymphangiomyoma replacing the kidney of a 79-year-old man (Jacobs et al.) [6], a LAM with pulmonary, retroperitoneal and left renal lesions in a 58-year-old woman (Saegusa et al.) [12] and a renal AML in a 45-year-old woman (L'Hostis et al.) [8]. It is difficult to establish whether these tumours are true lymphangiomyomas (localised lesion) or whether renal involvement occurs by LAM (extensive lesions) or simply AML, because clinical and radiologi-

cal information is generally incomplete. Furthermore, inadequate sampling of the tumour may cause the presence of adipose tissue being missed. Ansari et al. [1] described areas reminiscent of LAM in regional lymph nodes of a 46-year-old woman with renal AML extending into the lymph nodes, and McIntosh et al. [10] reported a case of multiple renal AML occurring with LAM of the regional lymph nodes in a 55-year-old woman. The presence of LAM-like foci in renal AML was also documented by Chan et al. [3].

In LAM and AML, the smooth muscle cells are smooth-muscle actin, desmin (less reliable) and, in variable proportions, HMB45 positive [3, 4, 7, 11]. The nuclei express oestrogen and progesterone receptors in about 50% of cases of LAM and apparently in more than 25% of cases of AML with coexpression in 10% of cases [8, 11]. Tawfik et al. [14] and Uzzo et al. [15] studied the hormonal receptors in two cases in which renal AML was associated with LAM: hormonal receptors were negative in the renal tumours. Recently Logginidou et al. [9] examined 12 specimens of AML from women with sporadic LAM; in 83% of the AML there was oestrogen receptor immunoreactivity with progesterone receptor immunoreactivity in 100%. LAM and AML are thought to be hormonally dependent because of their occurrence primarily in women during their reproductive years and the risk of deterioration during pregnancy [4, 7, 11]. The hypothesis that smooth muscle cells of LAM and AML are closely related is supported by all these data. In our case, the peculiar histological pattern with morphological features of both entities in the same tumour reinforces this concept.

AML and LAM occur in association with tuberous sclerosis complex (TSC) or sporadically [4, 7, 11]. TSC is an autosomal dominant disorder. The diagnosis is made using the criteria described by Gomez [5] and the National Tuberous Sclerosis Association. The diagnosis of TSC requires at least two "presumptive or secondary features among others" [14, 15]. Although AML and LAM are both presumptive criteria, it seems that the association of AML and LAM does not permit a diagnosis of TSC because none of the women with LAM (with or without renal AML) has borne a child with TSC [11]. Two genes are implicated in TSC: these are *TSC 1* on chromosome 9 and *TSC 2* on chromosome 16. A germline mutation of one of these two genes requires a second somatic mutation (loss of heterozygosity). Smoralek et al. [13] found loss of heterozygosity of the *TSC 2* gene in 54% of AML from patients with LAM and in lymph nodes from a woman with retroperitoneal LAM. Although loss of heterozygosity has been found in sporadic AML, the relatively high frequency of *TSC 2* abnormalities suggests that these findings are linked to LAM. Loss of heterozygosity of TSC genes in lung tissue has yet to be evaluated.

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