A rare case of malignant epithelioid angiomyolipoma in multiple locations: multifocal disease or metastases?

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BACKGROUND: Perivascular epithelioid cell tumors (PEComas), make up a family of extremely rare mesenchymal neo-
plasms, with characteristic morphological, immunohistochemical and molecular findings. Malignant PEComas and gas-
trointestinal epithelioid angiomyolipoma (E-AML) are especially rare. To the best of our knowledge E-AML have not
been found in the breast. The difficulty in determining what constitutes optimal therapy for PEComas, owing to the
sparse literature available, led us to report this rare case.

METHODS: We report a case of a 44-year-old woman, with a family history of multiple endocrine neoplasia syndrome
(MEN) (gastrinoma, medullary thyroid cancer and parathyroid hyperplasia), affected by PEComa located in the kidney,
stomach, ileum, liver and breast.

RESULTS: The renal, gastric, ileal and mammarian tumors were completely resected, with no evidence of local disease.
Liver lesions were biopsied. The morphological and immunohistochemical findings confirm the diagnosis of PEComa.

CONCLUSION: On this basis it is difficult to determine if some E-AML are multifocal tumors or metastatic disease.

KEY WORDS: Breast Gastrointestinal; Malignant epithelioid angiomyolipoma; PEComas

Introduction

Angiomyelolipoma (AML) is a benign mesenchymal tumor with abnormal blood vessels, smooth muscle and adipose tissue as key histological features. AML belongs to the family of perivascular epithelioid cell tumors (PEComas) \(^1,2\). These tumors are found most often in

the kidney, are very difficult to interpret histologically, and are often associated with tuberous sclerosis \(^2,3\). AML of the gastrointestinal tract is very uncommon \(^4,6\). The epithelioid type (epithelioid angiomylolipoma;E-AML) is extremely rare and is characterized by a predominance of epithelioid smooth muscle cells \(^1,4\). Malignant E-AML is equally rare, and very aggressive \(^3,5\). In the case reported here, due to the presence of the tumor in the kidney and subsequently in the stomach, ileum and breast, and liver, we were faced with the question of whether the patient had multiple primary tumors or metastatic disease.

Case report

D.R., a 48-year-old female, was admitted to our unit because of an episode of hematemesis and severe anemia (Hb:6g/dl). She had a family history of multiple
endocrine neoplasia II (MEN II) (her father had gastrinoma, medullary thyroid cancer and parathyroid hyperplasia) She had undergone left nephrectomy due to an expanding lesion in the lower part of the middle third of her left kidney involving the renal pelvis and infiltrating the capsule. Definitive histology and immunohistochemical analysis, which excluded leiomyosarcoma and sarcomatoid renal cell carcinoma, identified E-AML (PEComa) without lymph node involvement. [Nese et al, Am J Surg Pathol, 2011]. The patient underwent esophagogastroduodenoscopy as an inpatient. The findings were a sessile, polypoid neoformation approximately 3cm in diameter, located just below the cardias, which bled upon contact with the scope. A computed tomography (CT) scan was therefore performed. The scan revealed a vascularized neoformation of the small curvature of the stomach, approximately 5cm in diameter, that protruded into the lumen and penetrated the full thickness of the gastric wall, emerging from the serosa (Fig. 1) as well as multiple vascularized lesions in the liver parenchyma (segments IV and VII) with signs of internal necrosis (Fig. 1-2). An richly vascularized expanding neoformation, approximately 20 cm in diameter was seen in the lumen of the ileum, at the level of the pelvic cavity (Fig. 3), and nodules (maximum diameter 6 mm) in the lungs (Fig. 4).

Due to the patient’s severe anemia and the results of diagnostic imaging, an atypical gastric resection was performed (Fig. 5) liver lesions were biopsied, and the ileum

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**Fig. 1:** Computed tomography scan showing gastric and hepatic neoplasms.

**Fig. 2:** Computed tomography scan showing liver lesions.

**Fig. 3:** Computed tomography scan showing an intraluminal ileal neoformation.

**Fig. 4:** Computed tomography scan showing lung lesions.

**Fig. 5:** Intraoperative image: gastric neoplasm extending into the lumen.
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was resected (Fig. 6-8). On definitive histology a rare form of malignant E-AML of the stomach and ileum with liver metastases was identified. Microscopic examination revealed cellular proliferation with some bands of spindle cells and some solid nests of epithelioid cells separated by thin-walled blood vessels. There was pronounced nuclear polymorphism with multinucleated cells and abundant eosinophilic, at times granular, cytoplasm. There were a few cells with vacuoles and a peripheral nucleus, morphologically much like adipocytes. In some areas there were numerous branching thick-walled blood vessels. Many mitotic figures, including atypical ones, were seen, as well as microfoci of necrosis. In one of the samples there was a small focus of neoplastic cells in the peritumoral tissue that was partly surrounded by smooth muscle tissue (but it was not possible to rule out blood vessel invasion). Immunohistochemical analysis of the
tumor cells showed intensely positive immunoreactivity for both smooth muscle actin and epithelial membrane antigen (EMA), and local immunoreactivity for CD 117 [Kit] and bcl2. Moreover, the tumor cells were positive for the melanocyte markers HMB-45 and A-103 (melA), as well as for desmin, S-100, and pan-cytokeratin.

The patient's postoperative course was uneventful, but approximately 2 months after discharge she returned to our institution because there was a nodule in her left breast (Fig. 9-10). Suspicion of a primary breast tumor led us to perform an excisional biopsy. However, on intraoperative histological assessment revealed the same morphological characteristics as those of the gastric, ileal, and hepatic tumors. Immunohistochemical analysis confirmed the diagnosis of E-AML of the breast.

Discussion

PEComas are defined by the World Health Organization (WHO) as mesenchymal tumors composed of perivascular epithelioid cells with special morphological and immunohistochemical characteristics. They belong to a family of heterogeneous tumors which have been genetically linked to the tuberous sclerosis complex (TSC) 1. The differential diagnosis includes gastrointestinal stromal tumors (GIST), smooth muscle tumors, metastatic melanoma, and endocrine tumors. PEComa can mimic GIST when it has a spindle cell morphology or expresses CD117. Moreover, the morphology of leiomyomas or leiomyosarcomas can be very similar to that of PEComas. Only immunohistochemical analysis can provide a definitive diagnosis of PEComa, a metastatic melanoma must be ruled out especially when there is immunoreactivity for melanocytic markers. The ultrastructural characteristics such as the presence of glycogen in the cytoplasm, premelanosomes, thin filaments, occasional dense bodies, hemidesmosomes, and incomplete intracellular junctions, can help to determine the origin of these tumors. However, ultrastructural analysis cannot be routinely performed 1,2. Some authors state that E-AML with cellular atypia may be malignant. It has been shown that approximately one third of PEComas with these morphological characteristics produce local recurrence and/or distant metastases 2-5. Recent metanalyses of 69 and 40 cases of E-AML, report that 38% and 26% of the tumors respectively were malignant 6,3. The second study also expressed CD117. Moreover, the tumor cells were positive for the tumor cells showed intensely positive immunoreactivity for both smooth muscle actin and epithelial membrane antigen (EMA), and local immunoreactivity for CD 117 [Kit] and bcl2. Moreover, the tumor cells were positive for the melanocyte markers HMB-45 and A-103 (melA), as well as for desmin, S-100, and pan-cytokeratin.

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è estremamente rara come quella maligna, soprattutto nel tratto gastrointestinal. Riportiamo un raro caso di E-AML maligno con localizzazione renale, gastrica, ileale, epatica e mammaria trattata con chirurgia resettiva. Risulta spesso complicato definire preoperatoriamente il comportamento biologico dei PEComi: attualmente la chirurgia è il trattamento di scelta per i tumori primi-
tivi, per le recidive locali e per le metastasi.

Reference


