Pleomorphic Leiomyosarcoma of the Adrenal Gland with Osteoclast-like Giant Cells

Fernando A. Candanedo-González, MD,1 Teresa Vela Chávez, MD,1 and Arturo Cérbulo-Vázquez, MD, PHD2

Abstract

Pleomorphic leiomyosarcoma (PLMS) of the adrenal gland is a rare tumor in an unusual location. A primary PLMS of the left adrenal gland is reported in a 59-yr-old Mexican woman who presented progressive flank pain and weight loss. The tumor measured 16 cm in diameter, showed markedly pleomorphic and osteoclast-like giant cells, necrosis, and high mitotic activity (average 15 per 10 high-power fields). The phenotype was supported by light microscopy and corroborated by immunohistochemistry. The neoplastic cells were strongly positive for muscle-specific actin, desmin, vimentin, and p53. They were negative for CD34, HMB45, estrogen receptors, and S-100 protein. The percentage of Ki-67 positive neoplastic cells was 7.6%. DNA content analysis by flow cytometry showed that tumor was diploid, with a high level of apoptosis. Extra-adrenal primary sites of origin were clinically excluded. The patient developed local recurrence and liver metastases 12 mo after initial treatment. She then received adjuvant chemotherapy and radiotherapy and the metastasis was resected. Twenty-four months later, she is alive with no evidence of disease. This is the second case of adrenal PLMS reported. This case exhibited a high histologic grade, aggressive behavior, and p53 overexpression, but diploid DNA content. 

Key Words: Pleomorphic leiomyosarcoma; osteoclast-like giant cells; adrenal gland; Ki-67; p53; DNA content; flow cytometry.

Introduction

Leiomyosarcomas (LMS) are relatively rare tumors occurring in adults and arise mainly in the retroperitoneal space and abdominal cavity [1]. Only a few cases of primary adrenal leiomyosarcoma have been reported. The tumors most likely arise from smooth muscle of the central adrenal vein of its tributaries [2–6]. Some cases have been associated with acquired immunodeficiency syndrome.

Primary pleomorphic leiomyosarcomas (PLMS) of the adrenal gland are exceedingly rare, with only one case reported [6]. Pleomorphic areas in leiomyosarcomas resemble storiform–pleomorphic variant of malignant fibrous histiocytoma (MFH). In extra-adrenal sites, the differential diagnosis of pleomorphic MFH vs PLMS is important, because the prognosis and therapy are different [7]. However, the characteristics and biologic behavior of adrenal PLMS have remained unknown.

A correlation between cellular DNA content and prognosis has been reported in extra-adrenal LMS. Patients with aneuploid tumors had a poor prognosis, whereas patients with diploid and tetraploid tumors had a better prognosis [1]. LMS are characterized by overexpression of p53, a tumor-suppressor protein and by high Ki-67 labelling indices, which correlate...
with a poor prognosis [8,9]. No reports have established a relationship between p53 and DNA content in PLMS of adrenal gland. We report the clinicomorphological features of a primary adrenal PLMS in a Mexican woman. The proliferative activity and p53 expression were examined by immunohistochemical methods, and DNA content by flow cytometry.

**Case Report**

A 59-yr-old woman with a history of leiomyomas of the uterus previously treated with radical hysterectomy was admitted to the Oncology Hospital in the National Medical Center, Century XXI, in July, 2001. She presented with left upper quadrant abdominal pain and 4 kg weight loss over 3 mo. An asymptomatic abdominal mass was found by physical examination. Blood pressure was 120/80 mmHg. Abdominal ultrasonography and computed tomography (CT) scan showed a large mass in the retroperitoneal space. Excretory urography showed no abnormality in the left kidney. There was no evidence of neoplasia in other abdominal organs of lymph nodes. CT of the chest and brain, chest X-ray, and bone scintigraphy were negative. Laboratory tests, including adrenal hormone levels in serum and urine, were within normal limits. A laparotomy showed a left adrenal tumor with invasion of the adjacent tissue. The tumor was removed completely with negative margins. A histologic diagnosis of PLMS was corroborated by immunohistochemistry findings. The patient developed local recurrence and liver metastases at 12 mo after initial treatment. She then received adjuvant chemotherapy (adriamycin and ifosfamide) and radiotherapy followed by resection of the metastasis. Twenty-four months later, the patient is alive with no evidence of disease.

**Materials and Methods**

The specimen was fixed in 10% formalin and paraffin-embedded. Hematoxylin and eosin-stained sections were used for diagnosis. Immunohistochemistry was performed on 5-µm sections from a representative block using the avidin–biotin–peroxidase complex method. Appropriate negative and positive controls from normal tissues were also examined. The following antibodies were used: muscle-specific actin (1:150; Dako, Carpinteria, CA, USA); desmin (1:10, Dako, Carpinteria, CA, USA); vimentin (1:20, Dako, Carpinteria, CA, USA); S-100 protein (polyclonal; 1:400, Dako, Carpinteria, CA, USA); CD34 (1:300, Dako, Carpinteria, CA, USA); HMB-45 (1:150, Dako, Carpinteria, CA, USA); and estrogen receptor (1:100, Dako, Carpinteria, CA, USA). Immunoreactivity for p53 (1:100, Dako, Carpinteria, CA, USA) was evaluated by the distribution pattern of positive nuclei. Proliferative activity was examined using anti-Ki-67 monoclonal antibody MIB-1 (1:100, Dako, Carpinteria, CA, USA). A labeling index, expressed as percentage of nuclei positive for Ki-67, was determined by counting 5000 neoplastic cells with oil-immersion objective (magnification ×1000) randomly in hot spots of reactivity.

**Tissue Preparation and DNA Staining**

Measurement of DNA content was performed as previously described [10]. One block with leiomyosarcoma was selected for ploidy analysis. Tissue sections 50 µm thick from a representative block were obtained, co-incubated in xylene (Merck Art: 21586) for 10 min and hydrated with decreasing concentrations of ethanol (Omnichem 17019). Tissue sections were cut in small fragments, and incubated for 30 min at 37°C in pepsin solution 0.5% (pH 1.5). Samples were cen-