Malignant rhabdoid tumor of the clitoris in an elderly patient: report of a case

D. Haidopoulos, *M.D.*; **A. Elsheikh,** *M.D.*; **G. Vlahos,** *M.D.*; **M. Sotiropoulou**[1], *M.D.*; **A. Rodolakis,** *M.D.*; **Z. Voulgaris,** *M.D.*; **S. Milingos,** *M.D.*; **E. Diakomanolis,** *M.D., Ph.D.*

1st Department of Obstetrics and Gynecology, University of Athens, [1]Department of Pathology, "Alexandra" Hospital, Athens (Greece)

Summary

Malignant rhabdoid tumors of the vulva are rare neoplasms which most of the time show aggressive behavior and a dismal prognosis. We report a case of malignant rhabdoid tumor of the clitoris occurring in an elderly patient. Due to the similarities that these neoplasms show with other low-differentiated tumors, immunohistochemical and ultrastructural assessment should always be conducted so that accurate diagnosis is achieved. Individualized extensive surgical treatment might decrease relapsing disease.

Key words: Malignant rhabdoid tumor; Vulva; Immunohistochemistry; Clinical management.

Introduction

Malignant rhabdoid tumors (MRTs) of the vulva are very rare with only eight cases reported in the English literature. They represent neoplasms exhibiting very aggressive behavior, showing multimodal therapy resistance and most of the time a dismal prognosis [1].

Although, rhabdoid tumors are often confused with and may be diagnosed as other malignant neoplasms, a number of pathological and immunohistochemical characteristics distinguish them from the latter. Hall reported in 1980 a case of epithelioid sarcoma of the vulva which according to Perrone's reclassification, nine years later, was the first MRT of the vulva reported [2, 3].

Most of the papers published so far regarding MRTs of the vulva reported the labia majora as the primary location of the tumors and all reports concerned women less than 50 years old. We report the case of a 70-year old woman with primary rhabdoid tumor of the clitoris.

Case Report

A 70-year-old woman, gravida 4, para 3, presented at the Colposcopy Division complaining of severe vulvar pruritus for the last two years. Her past medical and surgical history were free apart from a mild diabetes mellitus under diet. The patient mentioned loss of appetite, loss of weight and tiredness for the previous six months and a malodorous vaginal discharge lasting two months. She was otherwise asymptomatic. On examination a 5 cm solid lump of the clitoris extending to both labia majora was noted. The neoplasm was firm, nodular and tender to palpation. A block of partially mobile inguinal nodes was also confirmed on the right inguinofemoral area. The mass was biopsied and histology showed undifferentiated carcinoma of the vulva. The patient was admitted to the Gynecologic Oncology Unit. Further laboratory evaluation included a full blood count, which indicated anemia (HCT: 21.9) and leukocytosis (WBC: 22,800), and a urine swab showing bacteriuria. A chest X-ray and a C/T scan of the upper and lower abdomen were found to be normal. The patient was placed under intravenous antibiotics (ceftazidime 3g/d and metronidazole 1.5g/d) and received preoperatively four units of blood. She underwent a radical vulvectomy with bilateral groin node dissection (3-incisions technique) [4]. Her recovery was satisfactory and she was discharged nine days later. The patient was admitted again 14 days later suffering from a bilateral wound breakdown. She was treated conservatively and was released 12 days later. The surgical specimen from a radical vulvectomy with bilateral inguinofemoral lymphadenectomy was examined. The tumor was located on the clitoris with extension to the left and right labia majora and it measured 6 x 6 x 2 cm in size. The neoplasm was protruded, had a lobulated appearance and almost circumscribed margins. The tumor's cut surface was solid, tanned and glistening focally. The resection margins were free of tumor. Microscopically the neoplastic cells were arranged in nests and cords and had an epithelioid or plasmatocytoid appearance with loss of tight cohesiveness. The cells were round or polygonal with vesicular nuclei, prominent nucleoli and abundant cytoplasm containing acidophilic and PAS-positive hyaline inclusions of globules. Mitotic figures were frequent (30 per HFP) (Figure 1). There were areas with myxoid changes and neoplastic emboli in the lymph vessels. A total of 27 inguinofemoral nodes – 14 from the right side and 13 from the left – were free of disease, showing inflammation. Following this diagnosis, a C/T scan of the chest and an MRI of the head were performed and were negative for metastatic disease. No adjuvant therapy was administerd. Seventeen months later, the patient was alive and well with no sign of local or distant metastasis.

Immunohistochemical analysis

Fixed tissue from the tumor, margins and lymph nodes were processed in 10% buffered formalin and embedded in parafin. Sections were stained with hematoxylin-eosin and PAS stains. Immunohistochemical investigation with a panel of antibodies was used (method streptavidin-biotin, immunoalkaline-phosphatase technique). The antibodies were PAN-keratin (Zymed), vimentin (Immunon), epithelial membrane antigen-EMA (Immunon), α-smooth muscle actin (Immunon), keratin-7 (Neomarkers), keratin-19 (Neomarkers), Desmin (Immunon), S-100 (Dako), Bc2 (Medical Innovations), a-sarcomeric-actin (Zymed), CEA (Dako), CD 34 (Ylem) and HMB-45 (Dako).

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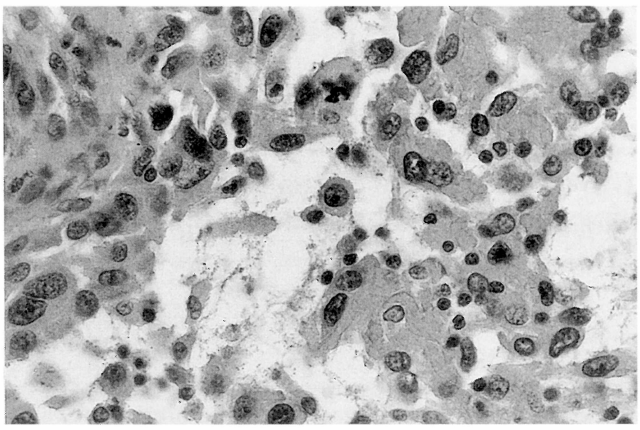

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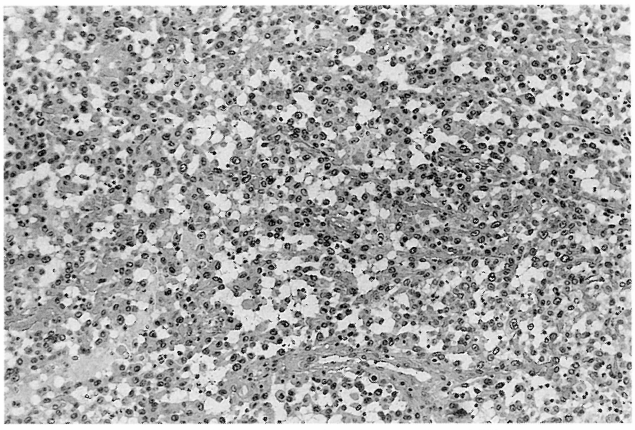

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Figure 1. — Malignant rhabdoid tumor: High magnification showing large polygonal cells with distinctive eosinophilic cytoplasmic inclusions. H-E stain x 400.

Figure 2. — Malignant rhabdoid tumor. Cells arranged in nests and cords. Myxoid stroma. H-E x 100.

Immunohistochemically, the intracellular acidophilic material was positive with antibodies against PAN-keratin. Cytokeratin was localized to the homogeneous eosinophilic zone adjacent to the nucleus. Epithelial membrane antigen and Vimentin were also positive (Figure 2). The SMA and Bc2 were faintly expressed while cytokeratins 7,19, a-sarcomeric actin, desmin, CEA, S-100, CD 34 and HMB 45 were negative. The tumor was interpreted as a highly malignant neoplasm compatible with rhabdoid tumor.

Discussion

The first MRT was reported in 1978, mimicking a Wilms' nephroblastoma. Extra-renal sites where MRTs have been cited to arise are the tongue, the pelvis, the liver, the paravertebral tissues, the soft tissues, the prostate, the brain, the heart, the skin, the prostate and bladder, the adnexa, the uterus, the cervix and the vulva [3, 5, 6].

Although MRT appears to be a dinstinct entity, several poorly differentiated neoplasms may show similar cellular features. Thus, in some cases differential diagnosis may be difficult, often requiring careful microscopic, immunohistochemical and ultrastructural assessment of the tumor [7]. Malignant tumors with rhabdoid and epithelioid features such as epithelioid sarcoma, poorly differentiated carcinoma, rhabdomyosarcoma, synovial sarcoma, epithelioid angiosarcoma, malignant melanoma, mesothelioma and malignant myoepithelioma, may mimic this tumor [8, 9, 10]. A neoplasm should be designated as MRT if it shows large polymorphic cells with prominent nucleoli and abundant acidophilic cytoplasm, intracellular PAS positive acidophilic lobules, loss of tight cohesiveness and lobulated pattern. Perrone *et al.* described the resemblance of epithelioid sarcoma with MRT [11]. The "proximal" type of epithelioid sarcoma presents the same morphological, immunohistochemical and ultrastructural features as the extra-renal MRT [9]. In our case, the majority of cells had intra-cellular globules and cytokeratin was localized to the eosinophilic zone adjacent to the nucleus, a feature that characterizes MRT. Additionally, Bc2, which is positively expressed in some mammary and gynecological tumors, was present in this tumor, a finding that has not been reported by other authors. Differential diagnosis from large cell poorly differentiated carcinoma can also be difficult. In our case, immunohistochemical expression of EMA, cytokeratin and vimentin were the same but cytokeratin 7 and 19 were negative while there was a faint expression of SMA. Although the "monophasic" synovial sarcoma expresses positive vimentin, keratin and EMA, detailed examination usually reveals a biphasic pattern, which can lead to the correct diagnosis [7]. The possibility of malignant melanoma is excluded by the negative immunostaining of

Table 1. — *Differential diagnosis based on immunohistochemistry.*

Antibody/ Tumor	Present case	Rhabdomyo-sarcoma	Epithelial sarcoma	Synovial sarcoma	Malignant mesothelioma	Poorly differentiated carcinoma	Malignant myoepithelioma
Cytokeratin	+	-	+	+	+	+	+
Vimentin	+	+	+	+	+	+	+
EMA	+	-	+	+	±	+	±
SMA	±	±	-	-	-	-	+
Sarcomeric	-	+	-	-	-	-	-
Desmin	-	+	+	-	-	-	-
S-100	-	-	-	±	?	±	+

antibodies S-100 and HMB 45 and positive for cytokeratin. The differential diagnosis of MRT and malignant myoepithelioma and epithelioid angiosarcoma is based on strongly positive SMA and S-100 for the first one and CD 34 for the second one [7, 10]. The differential diagnosis based upon immunohistochemical characteristics is shown in Table 1.

MRTs can be either of mesenchymal or epithelial origin. The typical rhabdoid cells are not the hallmark of a specific single entity. It is a nonspecific phenotype shared by a heterogeneous group of poorly differentiated neoplasms marked by an overproduction of intermediate filaments. If any conclusion can be drawn from our immunohistochemical investigation it is that the exact nature of malignant rhabdoid tumors remains uncertain.

Although there are no large series of MRTs, clinically they are considered extremely aggressive tumors, usually exhibiting a high rate of local or distant recurrence. The lungs and the liver seem to be the commonest sites of distant metastases [1, 3, 12].

Eight cases of vulvar malignant rhabdoid tumors have been reported in the English literature, all in women of reproductive age with the labia majora being the most usual site of occurrence. Six out of these patients developed local recurrence, four of them within two months from the initial surgical treatment (three had undergone a wide local excision of the tumor and one a radical right hemivulvectomy). Of those six women, four subsequently developed subsequently widespread metastases and died despite the different therapeutic approaches that were applied to each patient. Three of the eight women remain alive although two of them have had local recurrence (one had two local recurrences) while for the third one who has not shown any signs of relapse, the disease-free period is too short. In our case, the age of the woman, the clear surgical margins and the disease-free lymph nodes supported the decision for no further treatment. Despite the fact that the patient is alive and well with no signs of recurrence 17 months after initial therapy, we are sceptical about the course of the disease. Due to the rarity of the neoplasm, different therapeutic approaches were advocated following surgery in all the cases reported so far in the literature. From this data, there is no evidence that aggressive postoperative therapy in the form of adjuvant chemotherapy or radiotherapy is of any efficacy. Additionally, previous reports in MRTs of the vulva and other parts of the body showed no benefit from chemotherapy, radiotherapy or hormone therapy when these were administered as second-line treatments [3, 12]. It seems reasonable to believe that more radical routes in terms of initial surgery in order to ascertain local control could be offered to patients with vulvar MRT, given the fact that the majority of these women develop quite shortly local recurrence and subsequently, if ever, distant metastases. Each case should be individualized and age of the patient should always be taken into consideration. We believe that radical local surgery with lymphadenectomy in accordance with the site of the tumor would be a more conservative way of treating this neoplasm in women of reproductive age, whereas in older women, radical vulvectomy with bilateral groin dissection would be the right approach.

Rhabdoid tumors of the vulva represent aggressive malignant neoplasms of unknown origin. Immunohistochemical investigation should be conducted whenever differential diagnosis from other low-differentiated malignancies that show similar features is difficult. Predictions regarding the course of the disease and guidelines for management cannot be made due to the small number of cases. Nevertheless, these authors believe that extensive initial surgical treatment might decrease the number of cases of relapsing disease.

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Address reprint requests to:
D. HAIDOPOULOS, M.D.
7 Vasiliou str.,
152 37, Philothei, Athens (Greece)