Case Reports

Alveolar rhabdomyosarcoma originating from the uterine cervix

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Summary

Cervical alveolar rhabdomyosarcoma is a rare condition associated with poor prognosis. An 18-year-old patient presented with vaginal bleeding and a protruding mass from the vagina. Biopsy of the mass revealed alveoler rhabdomyosarcoma (ARMS), and radiological evaluation demonstrated that it originated from the uterine cervix. First, Wertheim's operation was carried out followed by four cycles of vincristine, actinomycine-D, ifosfamide (VAI) chemotherapy. However, the disease relapsed within three months, and the patient died of disease progression. Despite combination treatment, we could not achieve a desirable survival advantage in ARMS. Future studies may unveil the genomic profile of this rare condition, leading to invention of targeted therapies, which is the emerging trend in the treatment of sarcomas.

Key words: Alveolar rhabdomyosarcoma; Cervix; Treatment.

Introduction

Rhabdomyosarcoma (RMS) is a common soft tissue tumor predominantly seen in children and adolescents. RMS has been classified into four subtypes: embryonal, alveolar, pleomorphic and botryoid. Alveolar RMS (ARMS) accounts for 20-30% of all RMS tumors, most of which occur in children and adolescents, often occurs in the skeletal muscle of the extremities. Although the major histologic appearance is muscle differentiation the tumor is believed to originate from incomplete myogenic differentiation in embryonal and fetal development. RMS can also occur in visceral organs. A rare case of alveolar RMS originating from the uterine cervix is presented.

Case Report

An 18-year-old nulliparous female patient was admitted to a state hospital in Izmir with vaginal bleeding and a mass protruding from the vagina in January 2006. Physical examination revealed a necrotic, red-purple colored mass 3 x 4 cm in dimension protruding from the vagina. Blood biochemistry and total blood count tests were normal. Abdominal magnetic resonance imaging (MRI) was performed for diagnosis which revealed a solid mass at the mid-pelvis appearing to originate from the uterine cervix and protruding from the vagina with necrotic components. The biopsy from the vaginal mass demonstrated ARMS. No evidence of distant metastasis was detected and Wertheim's operation (total hysterectomy and pelvic-paraaotic lymph node dissection) was performed. Intraoperative observation showed that the mass originated from the uterine cervix, filled the vagina, and was enlarged to the pelvic region. There was a tumoral implant at the right parametrium 3 cm in dimension, and at the right obturator space 2 cm in dimension which were both excised. Peritonel biopsy also showed tumoral infiltration. Postoperative pathological evaluation revealed a mass 11 cm in dimension that invaded the serosa of the uterine cervix with tumoral implants including cells with rhabdoid morphology and alveolar pattern. Immunocytochemical staining analysis showed that the tumor was positive for desmin and Myo D1 and negative for S100 and cytokeratin, thus making the diagnosis clear for ARMS (Figures 1-3).

Postoperatively, the patient was admitted to our university hospital for systemic chemotherapy. For evaluation of distant metastasis, an abdominal MRI, thorax computerized tomography (CT), bone marrow aspiration and biopsy, and bone scintigraphy were performed. There were no signs of distant metastatic disease. The patient received four cycles of vincristine (1.4 g/m^2 D1-5), actinomycine-D (1.4 g/m^2 D1-5), and ifosfamide (1800 mg/m^2 D1-5), since the patient was accepted as being in an intermediate risk group, according to the Intergroup Rhabdomyosarcoma Study Group. After termination of chemotherapy with no treatment related complications, a 50.4 Gy dose of radiotherapy was also performed to the pelvic region. During the follow-up period, the patient remained disease-free for only three months time. After that period, she presented with a huge intraabdominal mass that had grown very rapidly and which was accompanied by massive ascites. Unfortunately, she died within three days after hospitalization due to ascites infection and septicemia.

Discussion

ARMS of the cervix is a very rare condition in oncology. To the best our knowledge, only three patients have been reported in the literature [1-3]. The first case, reported by Emerich *et al*. in 1996, was a 45-year-old woman who had only 3.5 months survival although surgical resection and postoperative radiotherapy were performed [1]. Ng *et al*. and Case *et al*. also reported cervix RMS patients that achieved complete remission after surgery,

Revised manuscript accepted for publication April 8, 2010

Fig. 1

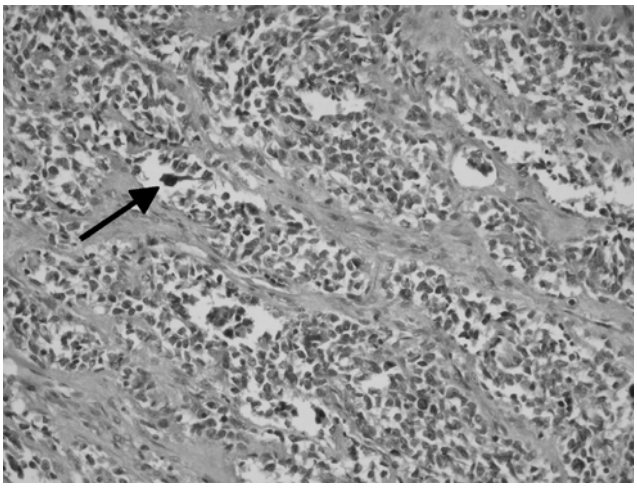

Fig. 2

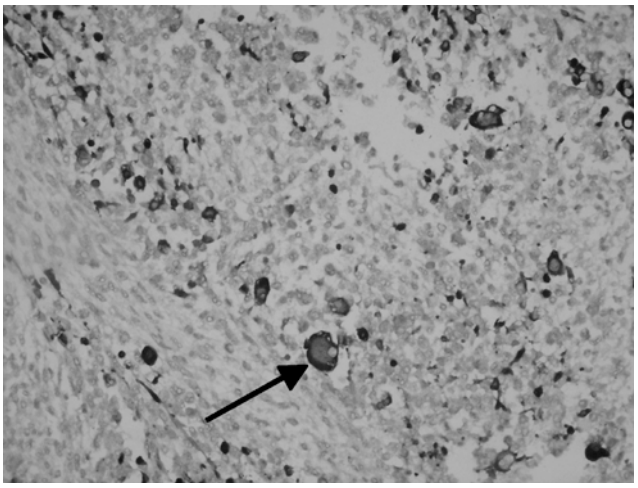

Fig. 3

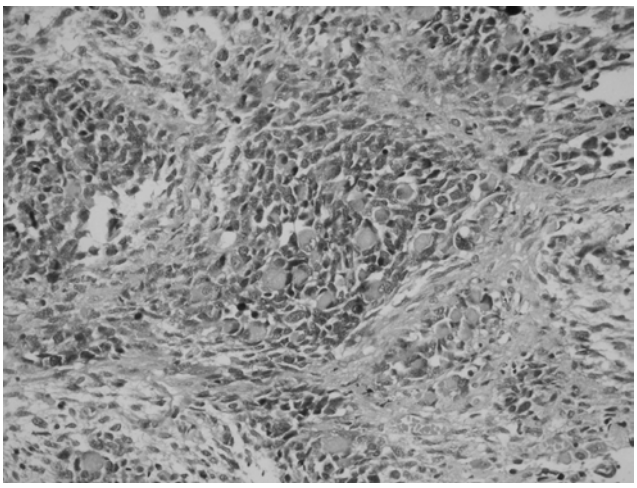

Figure 1. — Myo D1 positivity in smooth muscle nucleus (arrow). Typical alveoler pattern of growth of the tumor. Tumoral implants including cells with rhabdoid morphology in fibrotic stroma are present.

Figure 2. — Desmin positivity in smooth muscle cytoplasm.

Figure 3. — Tumor cells with large eosinophilic cytoplasm and an eccentric settled nucleus is shown. The nucleus is pleomorphic with significant nucleolus.

chemotherapy and radiotherapy at 36 months and 20 months follow-up, respectively [2, 3]. Although treatment strategies have improved survival in the last 30 years, the disease still has a very poor prognosis, especially in advanced stage. Our case also had a very short survival due to tumoral spread to the abdomen at the time of the diagnosis. Although she was treated by a combination of surgery, chemotherapy and radiotherapy, the disease-free survival period was very short with tumor relapse after three months time.

RMS is the most common soft tissue sarcoma seen in children and adolescents [4]. In recent years due to new treatment modalities survival rates have reached more than 70% [5]. The most common and also most favorable form of the disease is embryonal subtype with head-neck and genitourinary localization. Alveolar forms have a poorer outcome, often occur in skeletal muscle of the extremities, and genitourinary localization is very rare. Cytologically, alveolar RMS cells have large cells with Ewing-tumor like nuclei with centrally or peripherally placed nucleoli [6]. The differential diagnosis should be made with poorly differentiated adenocarcinoma, other types of sarcomas, melanoma and lymphoma.

As the case series have few numbers, the largest trials

Table 1. — *IRSG postsurgical grouping classification*.

Group 1 – Localized disease, completely excised with no microscopic residual
A) Confined to site of origin, completely resected
B) Infiltrating beyond site of origin, completely resected
Group 2 – Total gross resection
A) Gross resection with evidence of microscopic residual
B) Regional disease with involved lymph nodes, completely resected with no microscopic residual
C) Microscopic local and/or nodal residual
Group 3 – Incomplete resection or biopsy with gross residual
Group 4 – Distant metastasis.

Table 2. — *IRSG staging system*.

Stage	Sites of primary tumor	Tumor size (cm)	Regional lymph nodes	Distant metastases
1	Orbit, non-PM head/neck; GUS nonbladder/prostate; biliary tract	Any size	N0, N1	M0
2	All other sites	≤ 5	N0	M0
3	All other sites	≤ 5	N1	
		> 5	N0 or N1	M0
4	Any site	Any size	N0 or N1	M1

PM, Parameningeal; GUS, genitourinary system; N0, regional nodes not involved; N1, regional nodes involved by tumor; M0, no distant metastases; M1, distant metastases at diagnosis.

have been performed by the Intergroup Rhabdomyosarcoma Study Group (IRSG). IRSG has suggested a post-surgical grouping classification and staging system (Tables 1 and 2) [7]. Raney *et al*. summarized the IRS-I to IV and suggested the optimal therapeutic strategies [8]. IRS-V combines the group, stage and histologic subtype to determine the risk profile and divides the patients into three risk groups (low-intermediate-high). To our knowledge from IRSG, the standard approach should include a multimodal therapy approach, containing surgery, chemotherapy and radiotherapy [7]. IRS-IV has reported that VAC (vincristine, actinomycin, cyclophosphamide), VAI (vincristin, actinomycin, ifosfamide) and VIE (vincristine, ifosfamide, etoposide) chemotherapies are equally effective in RMS patients and showed that embryonel subtypes are obtaining the best benefit from chemotherapy.

In our case, although the primary tumor was excised totally as peritonel biopsy was positive for tumor, the patient regarded as Stage 1 and Group 2a (intermediate risk) received chemotherapy according to IRSG recommendations. However, due to the aggressive nature of the disease, despite the combination treatment, the patient died of disease in a very short period.

Thus, new treatment strategies are clearly needed to be defined because despite developments in treatment modalities in recent years, ARMS still has a very poor outcome. Also, future studies may unveil the genomic profile of the disease, leading to invention of targeted therapies, which is the emerging trend in the treatment of sarcomas.

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