Angiosarcoma of the ovary in an 11 year old girl: Case report and review of the literature

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Abstract

Sarcomas of the female genital tract in general are rare and ovarian sarcomas comprise less than 1% of ovarian malignancies. In the literature there are 15 reported angiosarcomas of patients 21 year old and younger with no one originated in the ovary. We report a case of ovarian angiosarcoma in an 11 year old girl, presented with left side hip pain. MRI of abdomen and pelvis confirmed expansive solid and cystic mass occupied both ovaries. Imunohistochemistry staining was performed, CD34, Factor VIII, CD31, in order to confirm the diagnosis. Final diagnosis was angiosarcoma. The patient received 6 cycles of chemotherapy, according to the CWS-2002P protocol. 8 months after the diagnosis was established, there were no signs of any tumors according to the ultrasound, CT scan, and MRI. Although, extremely rare, angiosarcoma can also affect children and this diagnosis should be considered carefully in tumor with rich vascular network, necrosis and brisk mitotic activity.

KEY WORDS: primary angiosarcoma, ovary, childhood

INTRODUCTION

Sarcomas of the female genital tract in general are rare and ovarian sarcomas comprise less than 1% of ovarian malignancies. Angiosarcomas (AS) are rare (less than 1%) with most occurrences in non genital regions [1,2]. All angiosarcomas tend to be aggressive, often multicentric with high local recurrence rate and metastasis because of their intrinsic biologic properties [3]. Angiosarcomas are tumors of adults (5-97 year) [4] with a wide range of occurrence. . It is a rare subtype of sarcoma in which malignant cells express the morphological and functional properties of endothelial cells [5, 6] In the literature, there are 15 reported angiosarcomas of patients 21 years old and younger [7] with none originating in the ovary/ovaries. The youngest patient with primary angiosarcoma of the ovary was 19 years old [8]. We report a case of ovarian angiosarcoma in an 11 year old girl, initially presented with left side hip pain.

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CASE REPORT

A previously healthy 11 year old girl presented to the pediatric clinic for an evaluation of left hip pain lasting the previous 15 days with more pronounced pain during the evening. There was no history of trauma. The previous 10 days she urinated more frequently, particularly during the night. She had normal pubertal development (breast and pubic hair changes) Tanner stage 2 [9]. All laboratory data were in referral value. Orthopedic exam indicated slightly limited motion in left hip without the signs of skeletal abnormalities. MRI of abdomen and pelvis confirmed an expansive solid and cystic mass that occupied both ovaries, highly vascularised, with central intratumorous flow 0.36, and ascites on color and pulsing Doppler. A laparotomy was performed with tumorectomy, bilateral salpingo-oophrectomy, and partial omentectomy. No pelvic or para-aortic lymphadenopathy was noticed. There was approximately 500 ml of straw-colored ascites. Early postoperative recovery and general condition of the patient were satisfying. No tumors were found upon control ultrasounds of the abdomen and urotract. The girl was discharged in good condition. The patient was referred to an oncologist.

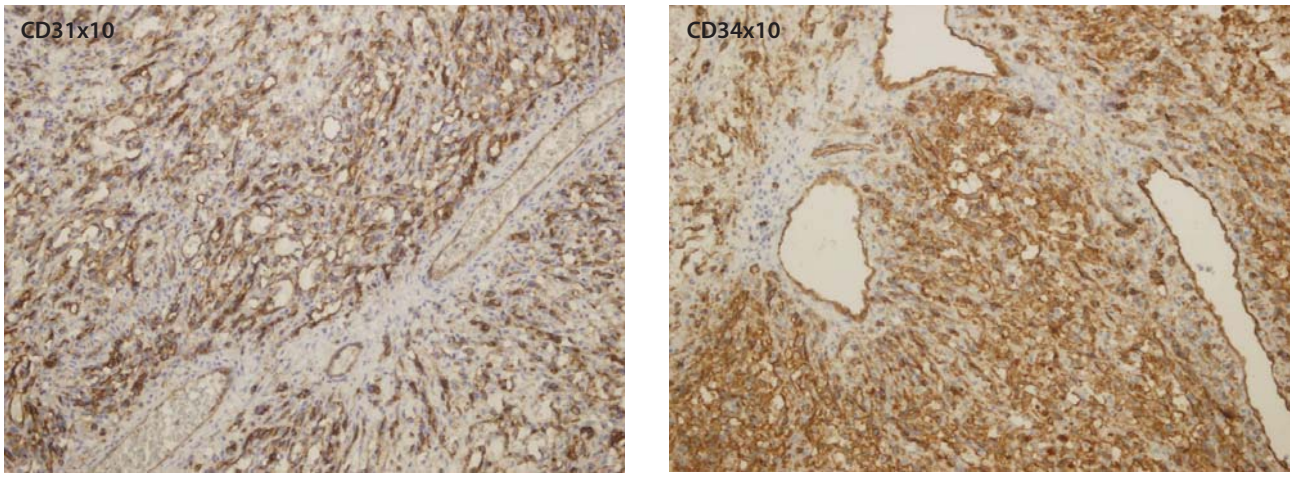

FIGURE 1. Rich, dense vascular weft and numerous very small and larger vascular lumens with CD31 and CD34 positive endothelial cells

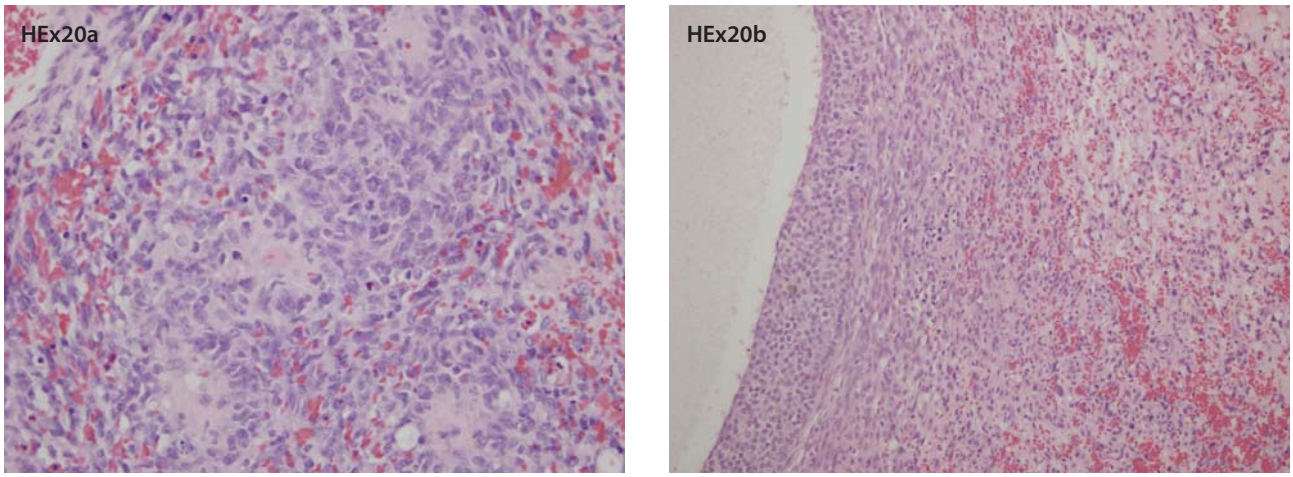

FIGURE 1. (a) Tumor cells form a pseudorosette-like formation, and have pleomorphic bland nuclei; (b) Folicular epithelia on left and tumor tissue on right

Pathological findings:

The left adnexa were sized 17x14x6 cm, with an irregular, glistening, grayish surface. On cut section tissue was wet, heterogeneous, and partly cystic with dark red and brown areas, imbued with blood; no normal ovarian tissue was identified. Tuba was irregular, with dark red surface on gross examination. Right adnexa was sized 14x7x5 cm, with almost the same macroscopic characteristics on gross examination as on left ovary, except for one irregular, well circumscripted area on cut section, sized 15x10 mm, bright brown color; no normal ovarian tissue was identified. Tuba as previously described. All samples were fixed in 10% formalin, and processed using routine methods. Histological evaluation revealed malignant neoplasm present diffusely in both ovaries with focally recognizable normal ovarian tissue (slight cystic follicles, white bodies). The tumor showed an aggressive, infiltrative growth pattern into tubal wall, peritubal fat and ovaries, with extended hemorrhagic areas, scattered necrosis, with rich, dense vascular weft and numerous very small and larger vascular lumens with Factor VIII, CD31 and CD34 positive endothelial cells (Figure 1). Endothelial cells were mild, pleomorphic, and hyperchromatic. Most of the tumor consisted of highly cellular, nodular, areas with moderate pleomorphic cells in storiform pattern, with oval and slightly elongated bland nuclei, and eosinofilic nucleoli. Sporadically, tumor cells form a pseudorosette-like formation, (Figure 2) where microcystic areas filled with bright pink materials. There were frequent mitoses with 27 mitoses per HPF and no bizarre forms. Proliferative index was 30% stained for Ki67. Tumor cells showed diffuse positivity for vimentin, WT1, with Factor VIII focally, and CD34 and CD 31 diffuse positivity of tumor cells. Tumor cells were negative for SMA, desmin, melan A, S-100 protein, calretitnin, inhibin, HMB45, ER, PR, LCA, AE1/AE3, MNF116, CK7, CEA, EMA, chromogranin A, synaptofizin, CD 68, PLAP, alfa feto protein, CD99, GFAP and NF.

Pathohistologic diagnosis

Angiosarcoma, grade 2 (FNCLCC)

Through examination, clinical data and presentation, laparatomy and imaging studies, the ovaries appeared

to be the only acceptable site of origin for this tumor. She received 3 cycles of chemotherapy according to the CWS-2002P protocol, cycle 1: I2 V Ad (ifosfamid, actinomycin, VCRx3), and patients was in good condition after therapy. Four months after the initial diagnosis, a control CT scan and MRI showed a mass sized 35x55x30 mm, (possible residual tumor mass) reaching the posterior wall of the bladder, without sign of infiltration, encircled the perirectal fat tissue and reaching anterior left part of the rectum with less visible intestinal wall. Ureters were also without the clear signs of infiltration. Uterus was not clearly visible, but checked by an Echo focused on the uterus (endometrial and endocervical). No visible significant lymph nodes. Liver, spleen, pancreas, kidneys and adrenal glands were negative. No ascites detected. The patient was operated on again five month after the first surgery. Relaparatomia mediana were performed with omentectomio, and lypmhadenectomio (2 lymph nodes). There was no residual tumor mass in pelvis. Peritoneal aspirate was taken for cytological analysis.

Pathological findings:
Two lymph nodes sized 1.5 x 1.0 x 0.3 cm and 1.0 x 1.0 x 0.6 cm with glistening, whitish capsule and homogenous, whitish tissue on cut surface. Excised omentum sized 18x6 cm, with yellow fat tissue imbued with delicate fibrous bands.

Patho-histologic diagnosis:
Chronic reactive changes in lymph nodes (Sinus histiocytosis lymphonodorum II) and omentum with granulomatous reaction (Granuloma corporis alieni). No tumor cells were found. The patient received 3 more cycles of chemotherapy, again according to the same CWS-2002P protocol. All laboratory data were in reference values. Alpha feto protein and beta HCG were normal. At last control, 8 months after the initial diagnosis was established, there were no signs of tumors, according to the ultrasound, CT scan, and MRI. The girl was in good psychological and physical condition.

DISCUSSION

An angiosarcoma is an uncommon malignant neoplasm characterized by rapidly proliferating, extensively infiltrating, anaplastic cells derived from blood vessels and lining irregular blood-filled spaces. This term is applied to a wide range of malignant endothelial vascular neoplasm that may arise at different sites and different organs and may have some distinct features. Approximately 50% of angiosarcoma occurs in the head and/or neck [10]. Sarcomas of the female genital tract are rare, accounting for approximately 4% of uterine and 1% of ovarian malignancies [11]. A small subset of these, primary ovarian angiosarcoma, is even rarer, with only 26 cases reported in the literature, according to the Bradford et al. [12], in the English language literature, with age range at presentation of 19 through 77, and a mean age of 29.7. The reported cases were in different stages, mostly in stage I and III. Our patient is the youngest one (11 years) with diagnosis of primary ovarian angiosarcoma diagnosed at stage IIA and no presented cases in currently available literature. Most of the previously described ovarian angiosarcomas were presented with nonspecific, gastrointestinal symptoms, the most common of which was abdominal pain. Our patient was presented with left hip pain. Abdominal and retroperitoneal angiosarcomas usually present as asymptomatic masses and generally grow to large sizes because the abdomen can accommodate tumors. Patients may present with neurologic symptoms from compression of lumbar or pelvic nerves [13,14]. A review of the English language literature revealed 6 patients with histological verified malignant vascular tumor angiosarcomas-who had a median age at diagnosis of 11.8 years (range, 8 months-21 years). There were five females and one male. The primary tumor sites were skin (one patient), soft tissue (one patient), bone (two patients), and internal organs (two patients: liver/spleen and liver) [15]. Our patient has pure bilateral ovarian angiosarcoma, with no sign of the involvement of any other internal organs or the retroperitoneum. In a large series of vascular tumors, Coffin and Dehner reported that of 228 vascular tumors in children, only 3% were hemangiopericytomas, 2% were malignant hemangioendotheliomas, and 1% was angiosarcomas [16]. The main problem in the diagnosis of angiosarcoma is histopathologic recognition. The histopathologic differential diagnosis of angiosarcoma should include certain sex-cord stromal and germ cell tumors, malignant melanoma, poorly differentiated carcinoma, as well as metastatic angiosarcoma. In general, angiosarcoma is composed of a solid histological pattern and network of vascular lumina. On microscopic findings there are vascular spaces more or less obvious and lined by tumor cells showing atypia. Low-grade lesions have vascular spaces lined by large plump endothelial cells that penetrate the stroma and papillary fronds of cells that project into the lumen. In its more aggressive form, irregular sheets of anaplastic cells may have only poorly defined vascular channels and may be difficult to differentiate from anaplastic melanomas and carcinomas. Staining for epithelial markers and HMB 45, melan A, S-100 protein may help in differentiation in order to rule out or confirm the sex cord stromal or germ cell origin of the tumor cell markers. The sensitivity for sex cord-stromal lineage may vary between markers, and some markers may not be as sensitive in some types of sex cord-stromal tumors compared with other tumors in this spectrum of neoplasms.

We performed a wide panel of markers (WT1, calretinin, inhibin, CD99, melan A), and tumor cell were positive only for WT1, which rule out the sex cord stromal origin as well as germ cell origin, WT1 is positive in 74% of the ovarian tumor overall [17], while inhibin and calretinin (which is more sensitive than inhibin) are more specific for sex cord stromal tumor (SCST) [18]. Also, calretinin has only slightly greater sensitivity (76% versus 65%) and equal specificity to inhibin (92%) in the differential staining of granulosa or Sertoli-Leydig cell tumors, that is, nonstromal SCST [19]. Panel of epithelial markers and neurendocrine markers assisted to rule out primary or metastatic carcinoma and malignant carcinoid. Angiosarcoma may be confused with vascular tumors of intermediate malignancy (e.g., epithelioid and spindle cell hemangioendotheliomas, histioid hemangioma, and malignant endovascular papillary angioendothelioma). Hemangio-endothelioma is a designation for vascular tumors that are a histological intermediate in appearance between a hemangioma and a conventional angiosarcoma. Anaplasia is prominent in these tumors comprised of groups of irregular vascular elements lined by immature endothelial cells. The diagnosis of angiosarcoma can be confirmed by immunohistochemical staining. Use of antibodies specific for endothelium cells, such as factor VIII- related antigens, CD31 and CD34, with vimentin positivity, as in our case, lead to a definite diagnosis of angiosarcoma [20]. Factor VIII related antigen is a marker of endothelial cell differentiation, and as such, its sensitivity drops significantly from 84 to 29% as vasoformative areas become more poorly differentiated. CD31, a glycoprotein present in endothelial cells, and CD34, a hematopoietic progenitor cell antigen tend to be more sensitive and specific. CD31, however, appears to be the most sensitive and specific for endothelial cells, with reported sensitivity rates of 80% versus 62% in vasoformative and poorly vasoformative angiosarcomas, respectively [12]. An optimal adjuvant therapy is unknown, but patients receive both single agent therapy as well as multiple-drug regimens. Because local or distant recurrence is possible despite adequate excision, adjuvant therapy may be of benefit. Two of the larger reported adult series suggested that radiation therapy may be of value in the treatment of angiosarcoma [3]. At the time of this writing, the girl had completed 6 cycles of chemotherapy and is in good condition, without evidence of the disease 10 month after the initial surgery.

CONCLUSION

Malignant vascular tumors are rare and aggressive in children and adolescents. Angiosarcomas are rare tumors that predominantly affect adults and elderly patients and have an aggressive clinical course with high mortality. Although angiosarcomas are well described in a variety of clinical settings, they have been incompletely characterized [7]. Although, extremely rare, these tumors can, and do, affect children. This diagnosis should be considered carefully in tumors with a rich vascular network, necrosis and brisk mitotic activity. Because of the poorly reported survivals, and the success of systemic chemotherapy in some case reports in children, cytotoxic therapy should be considered in pediatric and adolescent patients.

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DECLARATION OF INTEREST

No competing financial interests exist. The work has been done in University Clinical Center Tuzla and in collaboration with Clinical Center Split. None of the funding agencies had a role in the design, conduct, analysis, or reporting of the results.

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