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Conservative treatment for recurrent Ewing's sarcoma of the uterus in young women in Yemen

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Abstract

Ewing sarcoma-primitive neuro ectodermal tumors (ES/PNETs) constitute a family of neoplasms characterized by a continuum of neuro ectodermal differentiations. ES/PNET of the uterus is rare. A case of Ewing's sarcoma in a 19 years old woman presented with abdominal pain and mass without vaginal bleeding. There are 48 cases of ES/PNET of the uterus published in the literature as far as we know. The diagnosis was confirmed after surgical removal of the mass by histopathology and immuno histopathology. In spite of the rarity of ES/PNETs, they should be taken into account in the differential diagnosis of uterine neoplasms in young women.

Keywords: primitive neuroectodermal tumor, Ewing sarcoma, uterus

Introduction

Ewing sarcoma-primitive neuroectodermal tumor (ES-PNET) is group of tumors thought to be derived from fetal neuroectodermal cells that has morphologic features of small round cell tumors with variable degrees of neural, glial and ependymal differentiation [1]. Translocations involving EWS-FLI1 genes in approximately 85% of all cases. The term Ewing sarcoma has been used for undifferentiated tumors without evidence of neuroectodermal differentiation, as assessed by light microscopy and immunohisto chemistry. The term pPNET has been used for tumors with apparent neuroectodermal features. Almost all tumors of the Ewing sarcoma/PNET group have some form of EWSR1 (Ewing sarcoma breakpoint region 1) gene rearrangement, which is specific for this group of tumors [2]. Extra-skeletal Ewing's sarcoma though rare is found to arise from the chest wall, para-vertebral muscles, retroperitoneal space, extremities and buttocks [3]. PNET rarely involves the female genital tract; however a few cases have been reported to involve the ovary, uterine corpus, uterine cervix, and vulva [4]. Here, we report a case of PNET in the uterine body. In general, primary uterine Ewing's sarcoma is a rare and aggressive malignant disease that requires early diagnosis and treatment. In spite of that, differential diagnosis should be done for small cells malignancy [5]. The main problems are in cases occurring in very young women, when fertility sparing surgery is mandatory.

Case report

19-year old lady patient, single with non-significant menstrual history and family history. was admitted to our center with pelvic abdominal mass and pelvic pain without any vaginal bleeding. Ultrasound examination reported an enlarged uterus (12.5 × 11 × 8 cm) and solid mass 14x14 cm in the posterior wall of the uterus with cystic component Two 54 × 37 mm and 29 × 25 mm cysts with septa were reported in the left and right ovaries, respectively. Abdomen and pelvic CT scan showed a large soft tissue mass with cystic components is seen in the pelvic cavity in the posterior wall of the uterus and anterior to the rectum measuring about 15X15 cm in transactional diameters and 17 cm in craniocaudal diameter displacing the bowel loops upward. The Papanicolaou smear was negative for malignancy. Tumor markers including CA 125, AFP and CEA were in the normal range. Metastatic work up (chest CT scan) reported no evidence of any metastasis. Operation was done as excision of the mass and histopathological report was malignant cystic small round cell tumor, Microscopically, sections shows mitotic figures and large area of necrosis. The tumor cells infiltrating the fibrouspseudocapsule reaching margin 0.2 mm. Immunohistochemically, results CD99 strong positive. CD56, S100, Desmin and pancytokaratin all negative, keeping with Primitive neuroectodermal tumor (PNET)

The patient post-operative underwent chemotherapy with VACA protocol (Vincristine, Dactinomycin, Doxorubicin Cyclophosphamide) for 8 cycles. Follow-up untill the end of the fourth year revealed a normal clinical and radiological abdominal-pelvic, chest CT scan evaluation without evidence of any abnormality. After that patients, started to complained from abdominal pain and abdomen-pelvic CT scan revealed soft tissue mass with cystic components is seen in the right pelvic cavity showing heterogeneous enhancement. It measure about 90X50 mm in cross sectional diameters and 62mm in vertical diameter. So the patient was re-admitted due tumor recurrence. The patient then underwent chemotherapy with VACA/IE protocol (Vincristine, Dactinomycin, Doxorubicin Cyclophosphamide/ Ifosfamide, Etoposide) for 17 cycles. And re-evaluated every 3 cycle with good response. The pelvic mass markedly decreased in size until it measuring about 3.4 x 2.3 cm in the posterior side of the uterus (in pouch of Douglas) then the mass unchanged (stationary course) with chemotherapy. New metastatic work up to the chest revealed no metastasis. The patient subsequently underwent exploratory surgery and at the operation well defined mass was protruded from the posterior wall of the uterus, a clear cleavage plane allowed a dissection of the uterine mass from underlying uterine myometrium. excision

of the tumor with safety margin as conservative surgery was done. Gross picture, A tumor mass 42X30X25mm with gray white cross section. Microscopically, sections shows a malignant round cell tumor composed of sheets of malignant small blue round cells. The background shows neutrophil like material. Focal pseduorosstes are noted. Excision margin= 10 mm. Final histological examination and immunohistochemistry diagnosed as recurrent Primitive Neuroectodermal Tumor. The patient now underwent chemotherapy with Irinotecan and radiotherapy in the oncology center.

Discussion

In 1918, South discovered this tumor but the term PNET was coined by Hart and Earle in 1973 to show a number of small round cell tumors which may be derived from neuroectodermal cell showing different signs of neural, ependymal and glial differentiation [6]. PNET has a mesodermal origin and is associated with tumors of known Mullerian origin [7]. Ewing's sarcoma family tumor, characterized by the specific translocation t (11; 22) (q24; q12) and the specific transcript FLI1/EWS (and by the less common subvariants that involve chromosome 22 and EWS gene, with chromosome 21, 17, or 7). Classic Ewing's sarcoma and the peripheral primitive neuroectodermal tumor (pPNET) are the most two common structures: most of the cases arise from the skeleton (and are often characterized by large soft part involvement); however in some cases (less than 20%) these tumors do not involve bone structures, arising from soft tissues. Extraskeletal tumors are most commonly found along the central axis in the paravertebral site, particularly in the chest wall. However, these tumors can arise in any soft tissues and rarely in some organs like lungs and kidneys [8]. In the female genital tract Primitive neuroectodermal tumors (PNETs) are extremely rare. and these tumors can be found in vagina, cervix and vulva, and most commonly in the ovary, while the uterine localization is very rare [8] Uterine PNET mostly shows various types cells rosette like cells, astrocye like cells, rossets, ependymal and medulloepithelial differentiation [1]. Until now, only 48 cases have been recorded in the literatures of Ewing's sarcoma occurs in the female genital tract [9]. The differential diagnosis of PNET in the uterus usually includes other uterine tumors including small cell carcinoma, sarcoma and lymphoma [9]. Risk factors for uterine PNET have a bimodal age distribution occurring in postmenopausal age, where most cases (over 75%) of Ewing sarcoma occur or in adolescence, where fertility sparing surgery could be extremely important [8]. A very limited experience is available on diagnosis and treatment of cases occurring in young women [2, 9]. The clinical presentation of PNET in the uterus are mostly abnormal vaginal bleeding (95%), uterine enlargement, pelvic mass (53%) as in our patient and rarely abdominal pain (11%) [8]. In contrast to early detectable endometrial cancer due to vaginal bleeding occurred most often in patients with endometrial cancer, Unfortunately about 42% of PNET cases have been described at the advanced stages (above stage III), explaining the aggressive behavior of the Uterine PNET [5]. Ca125 may play a role as marker in the prognosis and follow-up of PNET of the female genital tract [3]. Immunohistochemical staining can help in the diagnosis and prognosis of PNET (1). CD99 is the most practical immunohistochemical marker for diagnosis of PNET.14 [1]. CD99 is a monoclonal antibody of the surface protein MIC2 whose gene is located on pseudoautosomal region of X and Y chromosomes.8, 9 CD99 prognostic properties vary in different tumors. For example, CD99 presentation predicts good prognosis in diffuse large Bcell lymphoma (DLBCL) with the germinal center B-cell subtype and non-small cell lung cancer (NSCLC), while in DLBCL with non-GCB, CD99 is a marker of poor prognosis.15,16 [1] Our patient's tumor was strongly positive for CD99. Membranous expression of CD99 is sensitive but not specific for Ewing sarcoma [2]. Unfortunately, no study has evaluated CD99 in uterine PNET; however, it has been shown that atypical Ewing Sarcoma (including CD99, FLI1, HNK1, and CAV1 negative tumors) is associated with less favorable clinical outcome [11]. In the case of PNET, surgery with or without chemotherapy and/or radiotherapy is the usual course of treatment [5]. Without adequate treatment, more than 90% of patients with Ewing sarcoma die due to secondary blood metastases. 5 year survival rate can increase up to 60% in localized disease with satisfactory cytotoxic treatment [10]. PNET has high malignant feature which progresses and metastasizes rapidly [6]. Only few data are available in Primitive neuroectodermal tumors of uterus (PNETs) regarding diagnostic procedures, treatment, prognosis and follow-up modalities. In conclusion Identification and management of more cases of ES/PNETs in uterus is important to clarify the biological behavior of the disease [11].

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