Primitive Neuroectodermal Tumor of the Cervix Uteri: A Case Report

Wahda Mohammed Taib Al-Nueimy,1* Sahba Mazin Mahmood2

Abstract

Objective: Peripheral Primitive neuroectodermal tumor of the cervix uteri is extremely rare, and to the best of our knowledge between 1987 and 2011 only ten cases were described in the English literatures.

Case presentation: A 27-year-old Iraqi woman who presented to AL-Butool Maternity Teaching Hospital in Eastern Mosul with history of obstructed labour due to presence of mass in the cervix. A caesarean section was performed; a big mass was noticed in the cervix, incisional biopsy was taken. It is characterized histologically by small round blue cell tumor which was confirmed by immunohistochemistry as primitive neuroectodermal tumor of the cervix uteri.

Conclusion: According to current knowledge, primitive neuroectodermal tumors belong to the Ewing’s sarcoma family. An immunohistochemistry plays an important role in confirming the diagnosis of Ewing’s sarcoma by excluding other common types of sarcoma which occur in the cervix uteri.

Keywords: primitive neuroectodermal tumor of the cervix uteri, immunohistochemistry, CD99, NSE.

Introduction

Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET), is a primitive round cell sarcoma showing varying degrees of neuroectodermal differentiation, has rarely been reported in the uterine cervix. Between 1987 and 2011 only ten reported cases of primary PNET of the cervix were described in the current literature survey(1-10). Our aim of this study is to present this rare case which expands the number of primitive neuroectodermal tumors in the cervix.

Case Report:

A 27-year-old Iraqi woman admitted to AL-Butool Maternity Teaching Hospital in Eastern Mosul with history of obstructed labour due to presence of mass in the cervix. A caesarean section was performed; a big mass was noticed in the cervix, an incisional biopsy was taken from bulging cervical tumor, and a diagnosis of a small round blue cell malignant tumor was made based on analysis of the

1. Department of Pathology, College of Medicine, University of Mosul, Mosul, Iraq.
2. Al-Butool Teaching Hospital, Mosul, Iraq.
* Correspondence should be addressed to: Professor Wahda Mohammed Taib Al-Nueimy. Dept. of Pathology, College of Medicine, University of Mosul, Mosul, Iraq. E-Mail: drwahda62@yahoo.com

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sample. This patient was then referred to our center. Bimanual pelvic examination under general anesthesia revealed a 6 x 4.5 cm. mass apparently arising from the anterior lip of the cervix, producing blood stained vaginal discharge. There was no extension of the lesion into the vagina, parametria, or adjacent organs including the bladder and rectum. A second cervical biopsy was taken for confirmation of the tumor type, which was prepared and analyzed carefully by using immunohistochemistry (IHC). The slides of the biopsy which were taken in the Al-Jumhori Teaching Hospital were reviewed. Both biopsies showed the same histological appearances: small round blue-staining tumor cells with little cytoplasm lying closely packed arranged in sheets with rosette and pseudo rosette formation (Figure 1). The cytoplasm of the tumor cells was clearly shown to contain glycogen on staining with periodic acid-Schiff (PAS). Immunohistochemical stains for a number of epithelial markers such as cytokeratin and CEA were negative. In addition stains for CD3, terminal deoxynucleotidyl transferase (TdT), leukocyte common antigen (LCA), neurofilament, CD10, CD20, and desmin, were negative (Fig 2,3 and 4). However immunostain for CD99 showed strong membranous positivity and immunostain for neuron-specific enolase (NSE) showed focal cytoplasmic positive staining. (Figures 5 and 6). On the basis of these findings, a diagnosis of PNET of the cervix was made.

Laboratory examination results for hematology, liver and renal function tests and spiral computerized tomography (CT) scanning of the chest and abdomen were normal. The results of recto-sigmoidoscopy, as well as a whole body scan, were normal. There were no signs of lung or liver metastasis. After discussion in our weekly meeting, we concurred that the surgical treatment is necessary. The patient underwent radical hysterectomy with bilateral salpingo-oophorectomy and lymphadenectomy with excision of the proximal third of the vagina, and the bilateral parametrium. At the time of surgery there were no enlarged pelvic or para-aortic lymph nodes. Unfortunately, the patient’s general condition prohibited a complete para-aortic and pelvic lymphadenectomy; therefore only sampling of the pelvic nodes was performed.

A macroscopic examination showed a tumor of 6 x 4.5 x 4 cm & weighing 55g. in the anterior lip of the cervix. Cut sections showed variegated surface of predominant solid areas with foci of necrosis and hemorrhage.

Microscopic examination of the removed tumor tissue showed a small round blue-tumor cells with little cytoplasm lying closely packed in sheets with rosette and pseudo rosette formation (Figure 1). The cytoplasm of the tumor cells was clearly shown to contain glycogen on staining with periodic acid-Schiff (PAS). The tumor showed an 8 mm invasion. Histological examination of uterus, vagina and parametrium showed no malignant cells. No lympho-vascular invasion was reported. Only three pelvic nodes from the left pelvic side and right pelvic nodes were retrieved from the specimen, which were all negative for malignancy.

Finally, after completion of the treatment, chest and abdomen CT scans consistently showed no enlargement of lymph nodes and no sign of tumor spread.

Discussion

In contrast to osseous EW/PNET, in which the affected patients are generally less than 20 years old(9), It seems that PNET of the cervix
can happen at any age. In a literature review performed by Snijders-Keilholz et al.\(^9\), the range of age at the time of diagnosis of the disease was between 21 and 60 years (mean 38 years)\(^9\). Most of these patients present with abnormal vaginal bleeding. Preoperative radiographic analysis will generally show a well-circumscribed mass of approximately 37 cm, which caused its misinterpretation as a cervical leiomyoma in at least 2 cases\(^8\). Farah et al.\(^10\) have previously summarized the outcomes in these 10 patients: Six of the seven patients who presented with localized disease were alive without evidence of recurrence or metastatic disease at an average follow-up of 19 months (range 5-42 months). The seventh patient died 4.2 years after initial assessment with pulmonary metastases\(^10\). Initial management modalities for this group of 7 patients included various combinations of surgical resection, adjuvant or neo-adjuvant chemotherapy (with radiotherapy in 2 cases). In two patients, the tumors were considered non-resectable. For both patients, hysterectomies were preceded by neo-adjuvant chemotherapy\(^10\). One patient reportedly "achieved full remission". Follow-up information was not given in the other. Snijders-Keilholz et al.\(^9\) have recently advocated that the management approach to cervical EW/ PNET be similar to their osseous counterparts: induction chemotherapy, surgery, and consolidation chemotherapy.

PNET of the uterine cervix belongs to the Ewing’s sarcoma family\(^11\). Cytogenetic studies now indicate that Ewing’s sarcoma and PNET have similar histological features and should be considered as one entity\(^12\). In our patient’s case, we did not have the facilities to test for the t\(^{(11,22)}\) translocation found in Ewing/PNET. However, strong membranous staining with CD99 was very characteristic and sensitive. Furthermore, negative staining for a wide variety of other markers including CD3, TdT, LCA, neurofilament, CD10, CD20, cytokeratin, desmin, and CEA excluded other types of small, blue, round cell tumor that entered in the differential diagnosis as rhabdomyosarcomas which represent the most commonly reported sarcoma at this location. Other uncommon sarcomas of the uterine cervix including leiomyosarcoma, liposarcoma, alveolar soft part sarcoma, undifferentiated endocervical sarcoma and malignant peripheral nerve sheath tumor (MPNST). Ewing’s sarcoma is considered a systemic disease without adequate treatment in which more than 90% of patients die from secondary hematogenous metastases, occurring mainly in the lung. Therefore, the five-year survival rate can increase to 55% to 60% with dose-intensive cytotoxic treatment regimens in localized disease; the three-year disease-free survival rate was reported to be 15% to 22% among patients with detectable metastases at time of diagnosis\(^11,13\).

**Conclusions**

Peripheral Primitive neuroectodermal tumor of the cervix uteri is extremely rare aggressive tumor which is in general has unfavorable outcome. Immunohistochemical markers play an important role in confirming the diagnosis of Ewing’s sarcoma and excluding of other common types of sarcoma which occur in the cervix uteri.

A complete tumor resection followed by neo-adjuvant chemotherapy is the suitable type of treatment for this type of tumor.
Figure 1: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET), small round blue-staining tumor cells with little cytoplasm lying closely packed in sheets with rosette and pseudo rosette formation (H&E 100X).

Figure 2: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET) LCA negative immune staining (400X).
Figure 3: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET) CD10 negative immune staining (400X)

Figure 4: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET) desmin negative immune staining (400X)
Figure 5: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET) membranous CD99 positive immune staining (400X)

Figure 6: Ewing sarcoma (primitive neuroectodermal tumor, EW/PNET) cytoplasmic NSE positive immune staining (400X)

References

1- فرع الأمراض، كلية الطب، جامعة الموصل، الموصل، العراق
2- مستشفى البتول التعليمي للنسائية والولادة، دائرة صحة نبوي، الموصل، العراق

المتخلص

المقدمة: ورم عنق الرحم المحيطي البدائي الأدمي الظاهر العصبي نادر جداً، والمعلومات التي لدينا تفيد بتسجيل 10 حالات ما بين عامي 1987 و2011 في المصارد الإنجليزية.

تسجيل حالة: تم إدخال مريضة عراقة عمرها 27 سنة إلى مستشفى البتول التعليمي في شرق الموصل لأعراض تعب ووجع وصداع، ونجعلها مريضة عراقة، وكانت ذكرت وحيدها تصلح في عقاقين، وأخذت علاجًا نسيجيًا بوجود خلايا ورمية كروية زرقاء صغيرة، ولقد أثبتت بالتشخيص النسيجي - الكيميائي - بوجود ورم الأدمي الظاهر العصبي البدائي.

الاستنتاج: حسب المعلومات المتاحة، فإن ورم الأدمي الظاهر العصبي البدائي يوجد في عائلة ورم (غردن بونك)، والطريقة النسيجية - الكيميائية تلعب دورًا مهمًا في تشخيص ورم بونك، وبعد استبعاد الأعراض الأخرى الأكثر شيوعاً التي تظهر في ععق الرحم.