Peripheral primitive neuroectodermal tumor (PNET) of the vulva: a case report

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Summary

Introduction: Ewing's sarcoma/peripheral primitive neuroectodermal tumor (ES-PNET) is a high-grade malignant neoplasm that often develops in the skeletal system. Primary extraskeletal ES-PNET is an uncommon condition that rarely affects the female genital tract. Tumors in the ovary, cervix, and uterine corpus and vulva are occasionally reported. Reports on the Ewing family of tumors involving the vulva are extremely rare in the relevant literature. Only a few cases of vulvar ES–PNET have so far been reported. *Case presentation:* A 14-year-old adolescent girl presented to the clinic with a 4-month history of a left vulvar mass. The mass was excised under general anesthesia, and re-resection was performed three weeks later to obtain negative microscopic margins. The patient received chemotherapy and radiotherapy; however, she died of pulmonary metastasis within nine months of the initial surgery. *Conclusion:* In summary, we describe a rare case of vulvar ES-PNET with distinct rosette-like structures in a 14-year-old adolescent girl with a very poor prognosis.

Key words: PNET, Vulva.

Introduction

Ewing's sarcoma/peripheral primitive neuroectodermal tumor (ES/PNETs) is a high-grade malignant neoplasm that often develops in the skeletal system. It is considered to be a neurally derived neoplasm in the central nervous system, autonomic parasympathetic ganglia, and peripheral nerve tracts [1]. The scope of the term has expanded and encompasses peripherally located tumors that are histologically similar and called peripheral PNETs (pPNETs). In general, these tumors affect the gastrointestinal tract (the stomach, intestines, and pancreas) and the lungs. PNETs that occur elsewhere in the female genital tract – including the vagina, endometrium and vulva are rare [2].

Only a few cases of vulvar ES/PNET have so far been reported. Here, we describe another case of vaginal ES/PNET with distinct rosette-like structures in a 14-year-old adolescent girl.

Case Report

A 14-year-old adolescent girl presented to the clinic with a nine-month history of a left vulvar mass. Her physical examination revealed a painless and mobile lesion. Clinically, it was thought to represent a Bartholin's gland cyst or lipoma. The patient did not have any medical or surgical illness and there was no malignancy in her family history.

The mass was excised under general anesthesia. Pathological results showed an ES/PNET. Three weeks after the first operation, re-resection was performed to obtain negative microscopic margins. The patient was treated by 12 courses of chemotherapy (etoposide, vincristine, adriamycin, ifosfamide, mesna) and radiotherapy, and was hospitalized two times on account of fever and neutropenia. Within nine months of initial surgery, she died of pulmonary metastasis.

Pathology

The excisional material that was sent to pathology was a nodular mass measuring 4.5 x 3.5 x 2 cm. The cut section of the specimen was yellow-white in color and soft-friable in consistency. There were focal areas of hemorrhage and necrosis. The whole specimen was submitted for microscopic examination. Histologic examination demonstrated a malignant lesion composed of a monomorphic population of small round blue cells. Within the cellular aggregates, a diffuse growth pattern was observed without any evidence of keratinization or glandular differentiation. Periodic acid-Schiff stain was negative for tumor cells. Three to five mitoses were counted per single high-power field. Rosette-like structures were observed. The tumor cells were immunohistochemically focally positive for CD99 in a membranous staining pattern.

Immunoperoxidase stains for vimentin and synaptophysin were diffuse and focally positive respectively, and stains for chromogranin, desmin, SMA, S100, CD 34, HMB 45 and pancytokeratin were all negative. The diagnosis of ES/PNET was made based on the microscopic and immunohistochemical data.

Discussion

ES/PNET is a high-grade malignant neoplasm that is often found in the skeletal system. Although Ewing's sarcoma typically develops in bones, extraosseous tumors resembling Ewing's sarcoma were first described in 1969 by Teft *et al*. [1]. Those who first used the term "primitive neuroectodermal tumor" (PNET) in 1973 were Hart and Earle and they used it to describe a group of small round cell tumors appearing to have developed from neuroectodermal cells [2]. The first series was reported by Angervall and Enzinger in 1975 [3].

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Primary extraskeletal ES/PNETs are rarely observed and the most frequent extraskeletal sites include the chest wall, lower extremities, and the paravertebral region, while the less frequent sites are the pelvis and hip region, the retroperitoneum, and the upper extremities. Mostly observed among young patients, ES/PNETs had a peak incidence in the 1920s showing a slightly male predominance [4].

Extraosseous ES/PNETs of the female genital tract are also uncommon and tumors are occasionally reported in the ovary [5] cervix [6], uterine corpus [7] and vulva. Reports on the Ewing family of tumors (EFTs) involving the vulva are extremely rare in the relevant literature. The reports on vulvar ES/PNET in the literature have been limited to a few cases so far [8, 9].

Immunohistochemical, karyotypic, and reverse transcription-polymerase chain reaction analyses can be used to diagnose the tumors belonging to the ES/PNET family. CD99, a monoclonal antibody to the cell surface protein MIC2, whose gene is located on the pseudoautosomal region of the X and Y chromosomes is the most useful immunohistochemical marker to diagnose PNET [10]. Cytogenetic and molecular genetic identification of the ES/PNET-associated translocation is the ''gold standard'' since nearly 90% of ES/PNETs are characterized by the translocation t(11, 22)(q24, q12) that leads to the fusion of the EWS gene on chromosome 22 to the FlI-1 gene on chromosome 11 [11]. Due to its high cost, and very limited availability two years ago, we could not use this method in the present case. In cases where molecular genetic evaluation could not be applied, immunohistochemical detection of CD99 antigen expression was shown to be valuable in diagnosis. The tumor in our case showed strong positivity for CD99 antigen, which has been proven to be a very useful and sensitive diagnostic marker to identify extraosseous ES/PNET.

Though translocation t(11, 22)(q24, q12) was not feasible in the present case, we were assisted in diagnosing ES/PNET by immunohistochemical studies including CD99 positivity, along with the evidence of neuroectodermal differentiation (numerous Homer-Wright rosettes).

EFTs are usually aggressive, showing a poor prognosis [12], which quickly lead to metastatic disease and death. In fact it is difficult to ascertain whether vulvar and vaginal tumors behave similarly to those neoplasms developing at more usual sites because there are too few cases reported, many of which have limited or no follow-up. Due to their rarity of these tumors, optimal methods to treat these tumors have not yet been established and it is also impossible to provide any survival rates based on limited data. Even admittedly limited data suggest that EFTs in the vulva or vagina could have more favorable outcomes [8, 9] opposed to those involving more usual sites as in the current case they may present with poor prognosis and may be aggressive even the patient has undergone surgery and received chemotherapy and radiotherapy, and may be lethal within months.

Due to the rarity of vulvar ES/PNET cases, information about the diagnosis, treatment, follow-up and prognosis are insufficient. Also the low number of the cases precludes accurate standardization of therapies.

In conclusion, vulvar PNETs are extremely rare tumors. Due to their rarity, optimal methods to treat these tumors have not yet been established and it is also impossible to provide any survival rates based on limited data. Even admittedly limited data suggest that EFTs in the vulva or vagina could have more favorable outcomes opposed to those involving more usual sites as in the current case they may present with poor prognosis and may be aggressive even if the patient has undergone surgery and received chemotherapy and radiotherapy, and may be lethal within months. Each and every vulvar PNET case should be reported to ensure data accumulation.

References

[1] Teft M., Vawter G.F., Mitus A.: "Paravertebral "round cell" tumors in children". *Radiology,* 1969, *92*, 1501.
[2] Hart N.H., Earle K.M.: "Primitive neuroectodermal tumors of the brain in children". *Cancer,* 1973, *32,* 890.
[3] Angervall L., Enzinger F.M.: "Extraskeletal neoplasm resembling Ewing's sarcoma". *Cancer,* 1975, *36,* 240.
[4] Primitive neuroectodermal tumors and related lesions. Chapter 32. In: Weiss S.W., Goldblum J.R. (eds.). Enzinger and Weiss's Soft Tissue Tumors. 4th edition, Mosby, 2001, 89.
[5] Kawauchi S., Fukuda T., Miyamoto S., Yoshioka J.-I., Shirahama S., Saito T., Tsukamoto N.: "Peripheral primitive neuroectodermal tumor of the ovary confirmed by CD99 immunostaining, karyotypic analysis, and RT-PCR for EWS/FLI-1 chimeric mRNA". *Am. J. Surg. Patho*l., 1998, *22*, 1417.
[6] Sato S., Yajima A., Kimura N., Namiki T., Furuhashi N., Sakuma H.: "Peripheral neuroepithelioma (peripheral primitive neuroectodermal tumor) of the uterine cervix". *Tohoku J. Exp. Med.,* 1996, *180,* 187.
[7] Hendrickson M.R., Scheithauer B.W.: "Primitive neuroectodermal tumor of the endometrium: report of two cases, one with electron microscopic observations". *Int. J. Gynecol. Pathol*., 1986, *5*, 249.
[8] Vang R., Taubenberger J.K., Mannion C.M., Bijwaard K., Malpica A., Ordonez N.G. *et al*.: "Primary vulvar and vaginal extraosseous Ewing's sarcoma/peripheral neuroectodermal tumor: diagnostic confirmation with CD99 immunostaining and reverse transcriptase-polymerase chain reaction". *Int. J. Gynecol. Pathol.,* 2000, *19,* 103.
[9] Takeshima N., Tabata T., Nishida H., Furuta N., Tsuzuku M., Hirai Y., Hasumi K.: "Peripheral primitive neuroectodermal tumor of the vulva: report of a case with imprint cytology". *Acta Cytol.,* 2001, *45,* 1049.
[10] Isotalo P.A., Agbi C., Davidson B., Girard A., Verma S., Robertson S.J.: "Primary primitive neuroectodermal tumour of the cauda equine". *Hum. Pathol*., 2000, *31*, 999.
[11] Folpe A.L., Hill C.E., Parham D.M., O'Shea P.A., Weiss S.W.: "Immunohistochemical detection of FlI-1 protein expression: a study of 132 round cell tumors with emphasis on CD99-positive mimics of Ewing's sarcoma/primitive neuroectodermal tumor". *Am. J. Surg. Pathol*., 2000, *24*, 1657.
[12] Shankar A.G., Ashley S., Craft A.W., Pinkerton C.R.: "Outcome after relapse in an unselected cohort of children and adolescents with Ewing sarcoma". *Med. Pediatr. Oncol*., 2003, *40*, 141.

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