PRIMITIVE NEUROECTODERMAL TUMOR OF THE UTERUS: A CASE REPORT

Tzu-Chen Yeh, Kian-Mei Chong, Yu-Hung Lin, Hun-Shan Pan, Kok-Min Seow, Jiann-Loung Hwang, Lee-Wen Huang*

Department of Obstetrics and Gynecology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan.

SUMMARY

Objective: Primitive neuroectodermal tumors (PNETs) are a group of unusual malignancies arising in the bone and soft tissue. Pure uterine neuroectodermal tumors are rare. We report the first case of PNET arising from the uterus in our hospital.

Case Report: A 52-year-old perimenopausal woman had multiple myoma and was regularly followed-up in our hospital. She suddenly developed lower abdominal pain without vaginal bleeding. Sonography revealed a pelvic mass measuring 10.7 x 6.8 cm with multiple myoma. The patient underwent tumor resection. There were multiple necrotic tumors on the uterus, bladder, broad ligaments, cardinal ligaments, and cul-de-sac. Final pathology revealed PNET because tumor cells were CD99 positive.

Conclusion: PNETs belong to the Ewing’s sarcoma family. They are closely related to malignant, small round-cell tumors of soft tissue and bones. They strongly express the glycoprotein p30/32 (CD99) on the cell membrane, which is encoded by the MIC2 gene. A translocation at t(11;22)(q24;q12) has been identified. PNETs are mostly recognized by the histologic characteristics of neural differentiation and immunohistochemical expression of at least two different neural markers. Uterine PNETs have a poor prognosis and, to date, there is no standard treatment. Total abdominal hysterectomy and bilateral salpingo-oophorectomy plus adjuvant chemotherapy or radiotherapy are recommended. [Taiwanese J Obstet Gynecol 2005;44(1):96-100]

Key Words: CD99, primitive neuroectodermal tumor, uterus

Introduction

Primitive neuroectodermal tumors (PNETs) are small round-cell tumors that often show neuroectodermal differentiation. They can be either central or peripheral. Central PNETs are derived from the neural tube predominantly involving the brain or spinal cord. Peripheral PNETs (pPNETs) are derived from the neural crest involving the sympathetic nervous system, bone, or soft tissue [1]. The most common site of pPNET in the female genital tract is the ovary, reported in 27 cases [2–4]. The uterus is the next most common site, with 14 cases reported to date [5]. Cervical, vaginal, and vulvar pPNET are rare, with seven, four, and three cases reported at each primary site, respectively [5–13]. To the best of our knowledge, we report the first case of uterine neuroectodermal tumor in Taiwan. We also review the literature on this topic.

Case Report

A 52-year-old perimenopausal woman, gravida 5, para 3 (all term vaginal deliveries), spontaneous abortus 2, had had a left ovarian tiny cyst and multiple small myoma uteri since 1997. She received regular follow-up examinations at our clinic without remarkable symptoms or signs. At one examination for Pap smear on August 29, 2003, two adnexal masses (6.6 x 3.2 cm and 5.5 x 4.2 cm) were found which suggested uterine myoma. The results of the Pap smear were normal. Blood carcinoembryonic antigen was elevated.
(6.25 ng/mL) but the CA125 level was normal (32.19 U/mL), as was the CA19-9 level (34.01 U/mL). Her last menstrual period began on April 16, 2003. Acute lower abdominal pain with intermittent dull sensation occurred on October 10, 2003, and she visited our clinic 3 days after the onset.

Pelvic examination revealed an enlarged uterus, approximately the size of a fist, with severe tenderness. Transvaginal ultrasound showed an ill-defined and heterocomplex pelvic mass measuring 10.7 x 6.8 cm on the anterior uterine wall and multiple uterine myomas (3.9 x 3.9 cm, 4.6 x 3.9 cm, 3.9 x 3.4 cm, 1.5 x 1.0 cm). Pelvic computed tomography (CT) with contrast medium disclosed a huge heterogeneous tumor with an irregular shape arising from the anterior wall of the uterus (Figure 1).

The impression of malignant pelvic tumor and multiple myoma led to exploratory laparotomy. After opening the peritoneum, 20 mL of yellowish ascites was found. A major friable and necrotic tumor measuring 11 x 13 x 6 cm arose from the anterior uterine wall and extended to the bladder (Figure 2). The vesicouterine fold was severely adhesive so that there would be bladder injury or even cystectomy if we performed a hysterectomy. Bilateral ovaries and tubes were atrophied and unremarkable. Multiple myoma uteri were also noted. Another two major polypoid tumors were located on the right posterior surface of the broad ligament and left uterosacral ligament (3 x 3 cm and 2 x 3 cm, respectively). There were many small tumors on the posterior wall of the uterus extending inferiorly to the vagina. Partial tumor resection with postoperative chemotherapy and radiation without hysterectomy and cystectomy was planned to give her a good postoperative quality of life. An intraoperative frozen section was interpreted as malignant neoplasm with a differential diagnosis of lymphoma, small cell carcinoma, and stromal sarcoma.

Gross examination showed tumorous tissues, yellow-white and elastic with a gelatinous cut surface, measuring 13 x 11 x 6 cm and 4 x 3 x 1.5 cm. There were focal myxoid changes. Microscopically, the tissue was composed of monotonous hyperchromatic oval cells with a high nucleus/cytoplasm ratio. No particular Homer-Wright pseudorosettes or neuroectodermal differentiation was identified (Figure 3).
3). Immunohistochemically, the tumor cells revealed positive membranous staining for CD99 (O13 antibody) (Figure 4) and some showed weakly positive reactivity for smooth muscle actin. Other immunohistochemical results including leukocyte common antigen, CD20, CD45R0, vimentin, desmin and S100 were all negative. Final pathologic diagnosis was uterine PNET. No malignant cells were found on washing cytology. According to the International Federation of Gynecology and Obstetrics staging system for cancers of the uterine corpus, this patient was diagnosed with at least stage III disease. We could not rule out the tumors invading the bladder mucosa because of microscopic hematuria with 5–7 red blood cells/high-power field, although cystoscopy was not performed preoperatively. Postoperative recovery was uneventful but her family refused any further treatment. At the next outpatient department visit, there was a palpable abdominal mass that grew rapidly and aggressively. The patient was lost to follow-up 1 month after the last examination.

Discussion

The Ewing’s family of tumors is composed of Ewing’s sarcoma (ES) and pPNETs. The latter term includes different tumors, depending on their location and neural differentiation, such as peripheral neuroepithelioma, Askin tumor, adult neuroblastoma, peripheral neuroblastoma, and PNET. Approximately 83% of cases with ES/pPNETs present with the translocation t(11;22)(q24;q12), which can be detected by reverse transcription–polymerase chain reaction [14]. This translocation results in the formation of a chimeric gene, EWS/FLI1 [15], which may act as an alternative transcriptional factor, potentially promoting oncogenesis or malignant behavior in PNET and ES [16]. However, immunohistochemistry provides a more convenient method to diagnose ES/pPNETs.

Most cases of uterine pPNET present with postmenopausal bleeding, intermenstrual bleeding, an enlarged uterus, or a pelvic mass [17], but our case presented with acute lower abdominal pain without abnormal vaginal bleeding. Spontaneous tumor rupture is usually the cause of lower abdominal pain. Perimenopausal status may mask abnormal vaginal bleeding. However, there was no vaginal bleeding so we could only suppose that the tumor might not have involved the endometrium.

Mature glial tissue and neuroectoderm in the uterus have been recorded secondary to incomplete therapeutic abortion, or within a uterine teratoma. Benign neoplasms of neuroectodermal origin in the uterus include neurofibroma, ganglioneuroma, and glioma, and these usually arise in the uterine endocervix or endometrium in women who typically present with intermenstrual bleeding [18]. The histogenesis of PNETs of the uterus remains unclear. They may evolve from ectopic neural tissue or may represent differentiation of Mullerian histogenesis [19]. One of three teenagers with uterine pPNET had a history of pregnancy losses that made some believe the tumors arose from implanted neuroectodermal fetal tissue or neuroectodermal migrating cells [1,20–22]. However, an implanted neuroectodermal fetal tissue origin seems unlikely because most women with uterine PNETs are postmenopausal. Our patient had had several uterine myomas for years that may have masked the co-existence of uterine PNET. No other mesodermal components or epithelial elements were identified in our patient, precluding the diagnosis of malignant mixed Mullerian tumors (MMMTs). Mullerian derivations (mesodermal), such as endometrial adenocarcinoma and sarcoma, were also suggested by the admixture of PNETs. However, we did not obtain endometrium or uterine myoma using fraction dilatation and curettage or hysterec-
omy. The question of whether this malignancy arose from uterine myoma and shifted to a neural differentiated tumor remains unknown.

ES and pPNETs are related to malignant small, round-blue cells. The diagnosis is sometimes difficult using routine microscopy because of the nonspecific histologic characteristics. However, membrane reactivity to antibody O13 and identification of translocations facilitate the diagnosis. In 2000, Sinkre et al examined O13 immunoreactivity retrospectively in 40 cases of MMMTs [23]. No O13 immunoreactivity

Figure 4. Immunohistochemistry: tumor cells reveal diffuse positive membranous staining of CD99 (O13).
peripheral primitive neuroectodermal tumor of the uterus.

References