A CASE OF PATHOLOGIC FRACTURE OF THE PROXIMAL FEMUR RESULTING FROM METASTATIC BONE TUMOR OF OVARIAN IMMATURE TERATOMA

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Ovarian immature teratoma affects mostly young women and constitutes approximately 1% of all ovarian malignancies [1]. The symptoms are often nonspecific, usually consisting of mass effect inflicting abdominal or pelvic discomfort and this tumor is rapidly progressive without treatment [1,2]. Although it was previously regarded as having a high mortality rate, the concurrent chemotherapeutic agents, combination of bleomycin, etoposide, and cisplatin (BEP), gives rise to better survival while minimizing toxicity profile [1,3].

Distant metastasis of immature teratoma of the ovary is uncommon [4]. In this report, we present the first case of bone metastasis from immature teratoma of the ovary followed by pathologic fracture.

Case Report

A 33-year-old female was diagnosed as ovarian immature teratoma with stage Ia, grade 3 following left ovarian cystectomy. She underwent staging laparotomy involving hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection and appendectomy. She did not receive adjuvant chemotherapy. Seven months following staging surgery, the patient revisited with complaints of right thigh pain and 4 × 3 cm sized palpable mass. The mass was diagnosed as metastatic immature teratoma of the ovary by imaging study and incisional biopsy (Figs. 1, 2). At this point, she was referred to Samsung Medical Center. She complaints of right thigh pain and initial workup was done at the Department of Orthopedics. It revealed about 20 cm sized...
Fig. 1. Initial imaging studies. (A) Plain radiography of the thigh. No pathologic fracture. (B) Magnetic resonance imaging finding. 20×5×4 cm sized solid mass in proximal to mid portion of right femur involving soft-tissue mass and vastus intermedius muscle.

Fig. 2. The pathologic finding of immature teratoma, incisonal biopsy at right thigh palpable mass. (A) Gandular, stromal and muscular differentiations was noted (H&E, ×40). (B) Multifocal malignant transforming area (H&E, ×100). (C, D) Mesenchymal and epithelial cell shows polymorphic and hyperchromatic change with prominent nucleoli. Malignant transformation was detected (H&E, ×200).
mass in the right femur with involvement of adjacent muscle without evidence of recurrence at pelvic cavity and another distant metastasis. The serum calcium was 9.5 mg/dL and phosphorus was 3.9 mg/dL. And all tumor markers including were not increased. Combination chemotherapy was considered as the first choice of the treatment, therefore she was referred to department of gynecologic oncology. Six cycles of combination chemotherapy with bleomycin (15 mg, day 1 to 3), etoposide (100 mg/m², day 1 to 3) and cisplatin (50 mg/m², day 1 to 5) every 3 weeks with concurrent radiotherapy (30 Gy/10 fx) were planned. However, 5 days after starting concurrent chemoradiation therapy, she got her right leg broken when sitting up. Plain radiography revealed a pathologic fracture of right femur mid-shaft (Fig. 3A). Treatment was stopped (after 1 cycle of BEP and 5 times radiation therapy, 15 Gy) and she was given a long leg splint.

After 4 weeks, the patient was transferred to the department of Orthopedics for preoperative evaluation. Right femoral vein thrombus was founded during right thigh Doppler doppler ultrasonography (USG) and inferior vena cava (IVC) filter was inserted before surgery. During surgery, tumor was present along the right femur mid-shaft fracture site with surrounding muscle infiltration. After wide excision of the tumor, approximately 14 cm sized bone defect was made and grafted by femur allo-bone followed by cementation. Then the patient was given closed reduction with internal fixation by femur intramuscular nail insertion (Fig. 3B). Pathology revealed metastatic immature teratoma with malignant transformation. Following surgery, thigh computer tomography (CT) revealed no remained mass.

Two weeks later she was referred back to the department of gynecologic oncology and completed additional 5 cycles of chemotherapy (total 6 cycles of BEP) followed by 5 times of radiotherapy (50 Gy/5 Fx). Follow-up images involving plain radiography, CT and positron emission tomography show no recurrence and distant metastasis. The patient is on regular follow-up outpatient clinic without evidence of recurrent disease for 14 months.

**Discussion**

As far as we know, only 11 cases of hematogenous metastasis of immature teratoma of the ovary have been documented in the English language literature (Table 1). This 33-year-old women presented with immature teratoma of the ovary which developed into systemic metastases to right femur within 1 year of initial diagnosis. Therefore, this case is the first documentation of the bone metastasis of immature teratoma of the ovary followed by pathologic fracture.

Fertility sparing surgery and adjuvant combination chemotherapy could be considered for the immature teratoma patients who are young and planning to have a child birth. Most patients with immature teratoma of ovary are in their reproductive years and wish to preserve fertility. Because of the excellent response to chemotherapy, unilateral salpingo-oophorectomy followed by combination chemotherapy has become the standard treatment for early stage of immature teratoma [5]. Nowadays, newly developed combination chemotherapeutic agents such as BEP gives us better survival than before [6].

Prognosis for immature teratoma of the ovary is related to stage and grade of the tumor. The 2-year disease-free survival for grade 1, grade 2, and grade 3 is 83%, 50%, and 33%, respectively [7]. Recurrence can be minimized by postoperative adjuvant chemotherapy. The combination chemotherapy was considered as the standard regimen for patients with stage I, grade 2 and 3 immature teratoma of the ovary [8]. However, Gadducci et al. [9] advised surgery alone as treatment for the tumor of stage I, grade 2 and 3. In addition, Cushing et al. [10] reported 31 cases of immature teratoma of grade 1-3 were found to have a 5-year survival of 97% after primary conservative therapy (surgical resec-

**Fig. 3.** Plain radiography findings. (A) Fracture of right femur mid-shaft. (B) Postoperation findings.
tion only), leading the authors to conclude that surgery alone is curative for most children and adolescent with resected ovarian immature teratoma of any grade.

In this case, final diagnosis was immature teratoma, stage Ia, grade 3. Although the exact onset of bone metastasis is not known, the patient’s disease-free interval was only 9 months without chemotherapy after primary debulking surgery. This case report suggests, even though it remains controversial, that aggressive postoperative adjuvant chemotherapy for immature teratoma Ia, grade 3 is necessary.

The patients with metastatic bone disease complain of painful palpable mass and swelling. Tumor markers can be used but the correlation with bone metastasis is not clear. Radiologic studies including plain X-ray, radionuclide bone scan and magnetic resonance imaging are helpful to diagnose the bone metastasis. Radiologic differential diagnosis include various disorder such as osteoporosis, osteomalacia, infections and plasma cell myeloma. Technetium bisphosphonate bone scans are extremely useful and can be positive up to 18 months before a lesion is detectable on a plain X-ray image [11]. However, a bone biopsy is needed to obtain a final diagnosis. Fine-needle aspiration biopsy is considered to have an accuracy rate, or sensitivity, of at least 90% of cases [12]. In the absence of definite tissue diagnosis, a surgical bone biopsy was required for further management. For the patients with low bone mineral density or rapid bone loss, systemic therapy with bisphosphonate administration are available to reduce skeletal-related events.

Surgical management of bone metastasis is contemplated in the case of fractures, or isolated and relatively localized disease, when the patient is in good general condition [13]. This is usually followed by palliative radiotherapy for control of pain and other local symptoms [14]. Combination chemotherapy may also be beneficial in cases with good performance status and synchronous involvement of other sites [15]. In this study, after debulking surgery,
chemotherapy then radiotherapy was done. Even in the presence of multiple bone metastasis or an inoperable bone lesion, patients may benefit from radiotherapy, chemotherapy or a combination of both, rather than palliative care alone [15]. In this study, after debulking surgery, chemotherapy then radiotherapy was done. Finally patients with chronic osseous pain and who demonstrated evidence of bone destruction, presenting a history of gynecology cancer, should be carefully evaluated because, although rare, metastasis can arise. This report also indicates that when impending fracture are suggestive, an aggressive approach to prophylactic fixation before a catastrophic fracture developed has distinct advantages [16]. Guidelines for the prediction of pathologic fracture would facilitate the management of patients with metastatic bone defects. Unfortunately, existing clinical guidelines have not been validated and do not accurately predict the risk of fracture for many patients. The load-bearing capacity of a long bone can be predicted using CT with simulated defects [17]. By combining new methods to predict the load-bearing capacity with estimated loads for activities of daily living, it is possible to calculate a factor of risk for pathologic fractures.

At the time of this report, our patient can walk to do the daily living and no evidence of recurrence has been observed for 14 months.

References

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대퇴골에 전이된 난소의 미성숙 기형종에서 발생한 병적 골절의 1예

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난소에서 발생하는 미성숙 기형종은 전체 난소암의 1% 미만을 차지하는 희귀종양으로, 평균 발생 연령은 10-20대로 젊은 여성에서 85%가 발생하고 있다. 예전에는 사망률이 매우 높은 질환으로 분류되었으나, 근래에는 항암제의 개발과 bleomycin, etoposide, cisplatin (BEP)의 복합투여요법으로 높은 생존율이 보고되고 있다. 또한 미성숙 기형종의 원격 전이는 매우 드물게 보고되고 있는데, 미성숙 기형종이 대퇴골에 전이되어 병적 골절이 발생한 1예를 경험하였다. 폐쇄정복/내부교정술과 BEP 화학요법 및 방사선 치료를 시행한 후, 환자는 혼자 보행이 가능한 상태로 14개월째 재발의 증거 없이 추적관찰 중에 있어 간단한 문헌과 함께 증례를 보고하는 바이다.

중심단어: 미성숙 기형종, 난소, 뼈전이, 병적 골절