Mixt Germ Cell Tumor which Main Component is Immature Teratoma Derived from Uterine Myometrium: an Unusual Case

Uterin Miyometrium Kaynaklı İmmatür Teratom Alanları Baskın Bir Nadir Mikst Germ Hücreli Tümör Olgusu

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ABSTRACT Teratomas of uterus are rare, also immature and malign uterine teratomas are extremely rare. The tumor developed in the uterine myometrium has never been described before. We present the case of a 26-year old woman whose parity is 1 with lower abdominal pain and regular menstruation underwent laparotomy after a diagnosis of pelvic solid mass filling her pelvis. After frozen sections of tumor revealed malign teratoma, and then a total hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomy were performed. The pathologic examination revealed an immature uterine teratoma which originated from the myometrium. With adjuvant BEP (bleomycin, etoposide and cisplatin) therapy was applied to the patient and she was free from disease in six months follow-up. The immature teratoma arised in myometrium at the level of uterine isthmus. Since the endometrial cavity was free from tumor, the origin of the immature teratoma of uterus might be contraversial. Because of the limited cases in the literature, it is difficult to asses the prognosis of the disease.

Key Words: Uterine neoplasms; myometrium; teratoma

ÖZET Uterus kaynaklı teratomlar oldukça nadir görülürken, immatür ve malign uterin teratomlara daha da az rastlanmaktadır. Uterin miyometrium kaynaklı teratom olgusu daha önce bildirilmemiştir. Kliniğimize alt abdominal ağrı şikayeti ile başvurmuş, düzenli menstrüasyon öyküsüne sahip, 26 yaşında, paritesi bir olan hastaya pelvisi dolduran kitle tanısıyla laparotomi yapılmış, frozen sonucu malign uterin teratom olarak gelmiştir. Hastaya total abdominal histerektomi, bilateral salfingooferektomi, pelvik ve paraaortik lenf nodu disseksiyonu yapılmıştır. Patoloji sonucu uterin miyometrium kaynaklı immatur teratom olarak kesinleşmiştir. İmmatur teratom uterin istmus seviyesinde başlamakta ve uterin kavitede tümoral doku izlenmemektedir. Hastaya BEP (bleomycin, etoposide ve cisplatin) protokolü uygulanmakta olup, 6 aylık takipte hastalığa rastlanmamıştır. İmmature teratomun kaynağı tartışmaya açık olmakla birlikte, endometrial kavitede tümöre rastlanmamıştır. Literatürdeki olgu sayısının azlığı nedeniyle uzun dönem prognoz hakkında yorum yapmak oldukça zordur.

Anahtar Kelimeler: Uterus tümörleri; miyometrium; teratom

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The extragonadal germ cell tumors consist 1-2% of all the germ cell tumors. The retroperitoneum and the mediastineum are the most common sites. Teratomas of the uterus are very rare and a few cases reported in the literature.[1,2] Among these cases, immature teratomas are the fewest. Uterine teratomas are generally found in the endometrial or endocervical cavity. Here we present a case of immature teratoma, which originates from myometrium of uterus.

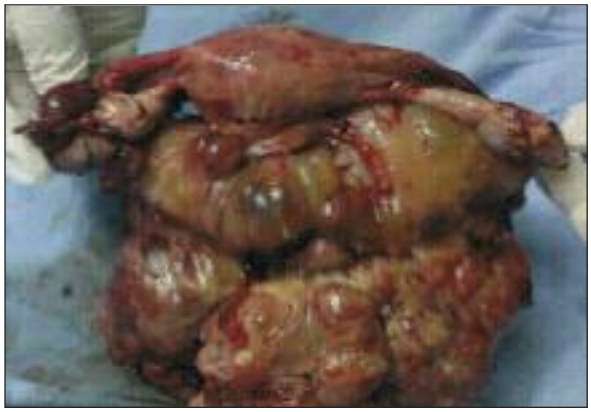

FIGURE 1: Macroscopic examination revealed a tumour with solid and cystic components originating from uterine corpus.

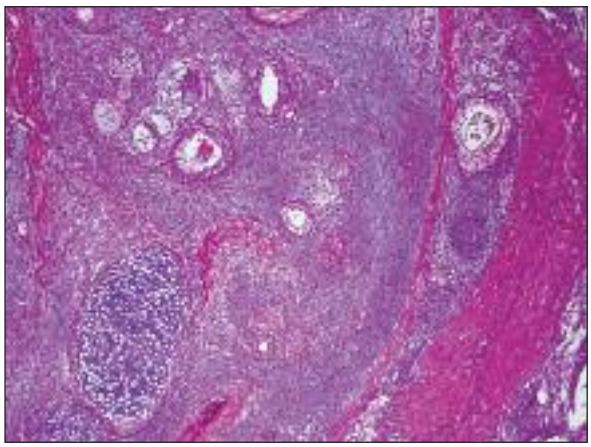

FIGURE 2: The various components include immature mesenchymal elements, such as immature cartilage and bone in the myometrium. (H&E, x100).

CASE REPORT

A 26 year-old gravida 1, para 1 woman was admitted to the our hospital with lower abdominal pain and abdominal fullness. Her menstrual cycle was regular. Physical examination revealed a tender fixed palpable solid mass filling her pelvis. The uterus was not palpated separately from the mass. The vulva, vagen and cervix were normal in routine gynecologic examination. Transabdominal and transvaginal ultrasound examination showed a 130 X 140 mm solid and heterogeneous mass enclosing cystic and ecojenic foci in lower abdomen. The bilateral adnexes were normal (Figure 1). Endometrial thickness was 6 mm and was regular in structure. The patient had no history of antecedent laparotomy. At admission her serum tumor markers were measured as CA-125 345 IU/ml, CA19-9 5.5 IU/ml, CEA 17.2 ng/ml, CA 15-3 35.5 IU/ml, Alpha-fetoprotein (AFP) 972 ng/ml, and beta-hCG 7.56 iu/ml respectively.

At laparotomy, a lobulated cystic tumor with irregular hemorrhagic irregularly encapsulated surface with whitish color was filling all mid-pelvis. When explored carefully, it was discovered that the mass originated from the isthmus of the uterus. The bilateral ovaries and the tubes were normal. The pelvic viscera were infiltrated by the tumor. A biopsy was taken from the mass. Frozen sections of tumor were suspicious of malign teratoma, so a total hysterectomy, bilateral salpingo-oopherectomy, pelvic and paraaortic lynphadenectomy were performed. The tumoral infiltrations on sigmoid colon

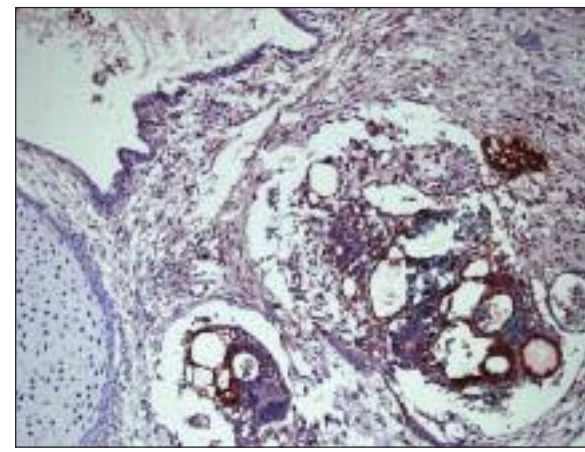

FIGURE 3: Yolk sac tumor is the source of cytoplasmic immunoreactivity for AFP is presented in focal areas AFP, (H&E, x100).

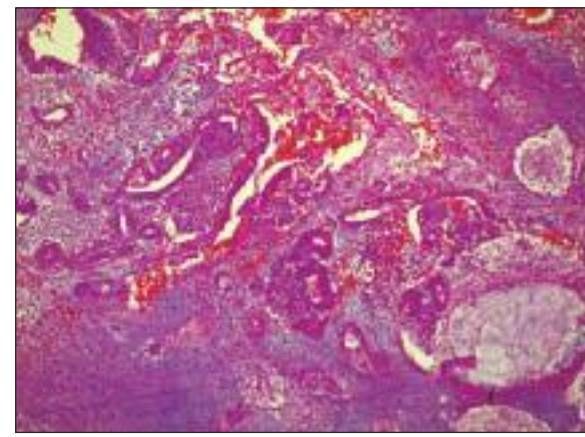

FIGURE 4: Immature mesenchimal and immature neuroectodermal tissues (H&E, x100).

and bladder were excised. An appendectomy was performed because of tumoral infiltration of terminal appendix. There was no macroscopic residual disease at the end of the procedure.

Macroscopic examination revealed 17 x 16 x 11 cm mass with solid and cystic components in the uterine corpus (Figure 1). Fifteen samples were taken from the tumor and many sections were done from the samples. The diagnosis of immature teratoma, grade II was confirmed by histological examination. Microscopically, the tumor was composed of variable amounts of immature embryonic type tissue, immature mesenchimal tissue and mature tissue, derived from all three germ layers. Yolk-sac tumor component was present in focal areas but these fields were not extensive. These findings could be seen in mixt germ cell tumors.

The various immature components included immature cartilage and bone (Figure 2) immature mesenchimal tissue and immature neuroectodermal tissue (Figure 3). The tumor had fewer mature tissues and was not exceed three low-magnification fields in any one slide, grade was 2.

Immunohistochemical study showed that neuroepithelial structures were positive for Neuron specific enolase (NSE) . Positivity for S100 protein in immature cartilage and neural tissue was marked. Neoplastic cells were immunreactive to AFP (Figure 4).

The tumor showed full thickness myometrial invasion with involvement of uterine serosa. There was a tumor implant in 0.4 cm in diameter on the serosa of right ovary. The fallopian tubes and the left ovary were intact. İmmature tumoral implants were displayed on serosal surfaces of appendix, sigmoid, rectum and bladder. Pelvic and para-aortic lenf nodes were free of tumoral deposits. Endometrium and endocervix were free of tumor.

The final pathology revealed a mixt germ cell tumor which includes yolk sac and immature teratoma component but mainly includes immature teratoma. which originates from the myometrium, with direct spread to pelvic viscera. Postoperatively the patient was commenced on chemotherapy including bleomicyn, etoposide, cisplatin. The patient is alive with no evidence of disease 6 months after the resection of the tumor.

DISCUSSION

In women, germ cell tumors are seen %97 of time in the ovary. The extragonadal germ cell tumors are histologically identical to those of gonadal origin. Extragonadal germ cell tumors mostly occur in the mediastinum, retroperitoneal region, pineal gland, and presacral area. Extragonadal germ cell tumors usually exist in the midline of the body. Teratomas of the uterus are extremely rare. A few cases were reported in the literature. It is not clear whether uterine teratomas are true neoplasm or not. They may arise in misplaced totipotential embryonic cells or a prolireration of fetal tissue, retained or implainted into uterus during delivery or proliferation.[3,4] Most reported cases have history of previous pregnancy but at least one case of uterine terotoma of a nulliparous woman has been reported.[5]

The diagnostic criteria for a teratoma include ectodermal, mesodermal, and endodermal derivatives. In this case, in addition to all 3 germ layers, there were significant amounts of neuroepidermal tissue with brisk mitosis, significantly immature mesenchimal tissue and immature cartilage. It was grade II immature teratoma. Ansah-Boateng et al in1985 reported the first case of primary immature uterine teratoma.[6] Iwanaga et al in 1993 reported primary immature uterine teratoma, which developed into pelvic cavity.[7] Severe menorrhagia and severe dysmenorrhea were the major complaints of the patients with uterine teratomas that were reported.[5,7] The reason for these symptoms was the nature of uterine teratoma's location in the uterine cavity or cervical canal. Our patient had no complaint other than pelvic pain, since the origin of the immature teratoma was myometrium. This appears to be the first case reported as primary immature teratoma of uterine myometrium.

It is still debated whether teratomas of the uterus and uterine cervix are true neoplasm. According to the literature review, some cases have been

reported as implants of fetal tissue. Residual fetal tissue suggested as the origin of the tumor because the genital canal is natural pathway of a fertilized ovum.[4,8] Reports of glial tissue heterotopia were strongly associated with a fetal remnants implantation, so that the lesion might be suspected as being a fetal remnants implantation if we found glial tissue instead of bone or cartilage[9] In our case, the arragement of tissues resembles to a gonadal immature teratoma with immature neuroectodermal tissue, immature mesenchimal tissue and rest of fetal type cartilage. Moreover, the tumor had wide variety of components derived from all three germ layers, so it is most unlikely to be a fetal remnants implantation. The origin of immature teratoma of uterine myometrium may be explained to develop from the germ cells that get trapped along their migration during embryonic development.

The prognosis of immature teratomas can be correlated to the grade determined by the quantity of the neuroepithelial elements; with a higher grade there is poorer prognosis.[10] The basic demonstration of malignancy is the inability of tissue to mature rather than the presence of individual cell anaplasia (i.e., the mitotic activity may be low. In our case the tumor had the pathologic grade 2.

Since the patient had grade 2 immature tumor, the BEP regimen (bleomycin, etoposide and cisplatin) was started. After the three courses of BEP regiment, the patient was clinically free of disease at six months follow up. AFP was used for monitoring chemotherapy regimen, since it was elevated before the surgery. Serum AFP was declined to normal levels in the end of three courses of chemotherapy.

The method of treatment in uterine immature teratoma with pelvic metastasis is total hysterectomy, bilateral salpingo-oopherectomy, pelvic and paraaortic lymphadenectomy with the resection of the extended tumoral implants as in invasive malign ovarian tumor. With adjuvant BEP therapy the patient is free from disease in six months follow-up. The further prognosis is difficult to assess because of the limited cases reported and the absence of advanced follow-up of patients in case presentations.

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