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CASE REPORT

Malignant Mixed Mullerian Tumor of Uterus Produced Alpha-fetoprotein

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ABSTRACT

A case of malignant mixed mullerian tumor of the uterus with alpha-fetoprotein (AFP) production in a postmenopausal woman is reported. This patient was initially diagnosed by rising of serum alpha-fetoprotein without any clinical symptoms. After primary surgery tumor rapidly relapsed. Adjuvant treatment by hormonal therapy was not responsive. Finally, tumor seemed to reach partial response (PR) by using platinum compounds with adriamycin. Serum alpha-fetoprotein level was correlated to tumor volume. This is one of the very rare case reports in the literatures.

Uterine sarcoma comprises of 2-5 % of all uterine malignancy.[1-5] Among this, Malignant Mixed Mullerian Tumors (MMMT) of the uterus is considered to be one of the most common. Its histopathology composed of neoplastic epithelial components and mesodermal elements, of which, either or both may show a spectrum of change varying from mild atypia to frank malignancy. Most MMMT patients present with vaginal bleeding. The poor prognosis of MMMT patients may reflect ineffective primary treatment or occult extrauterine spread early in its course. The histogenesis of MMMT remains unclear. To date, there have been only 9 reported cases of MMMT that could produce alpha-fetoprotein in the English literature. We report here a case of MMMT which produced alpha-fetoprotein and got a partial response after platinum and adriamycin treatment.

A 71-year-old Thai female, Para 8-0-0-8, visited Chulalongkorn Hospital in September 1998 for annual check up. She was asymptomatic except for medical history of hepatitis B carrier and ischemic heart disease. No familial history of cancer was noted. Physical examination including pelvic exam was within normal limit. But her serum alpha- fetoprotein was elevated (124.3 IU/ml, normal 0-5.3 IU/ml). Transvaginal ultrasonography disclosed thickening of the endometrium (27mm). Whole abdominal Ultrasonography and CT scan were normal. Endometrial tissue was obtained by fractional curettage. The histopathological specimen revealed malignant mixed mullerian tumor. Provisional diagnosis at that time was malignant mixed mullerian tumor of the uterus. She underwent expolatory laparotomy with surgical staging in September 1998. The operative finding showed a polypoid-like mass (diameter 2.5x1 cm) within the uterine cavity. The final

histopathology confirmed the diagnosis of carcinosarcoma of the endometrium. No myometrial invasion could be demonstrated. The same specimen was also sent for immunohistochemical stained of which was positive for alpha-fetoprotein (figure 1). On the seventh operative day her serum alpha-fetoprotein decreased to 57.1 IU/ml. After counselling with the patient about further treatment no adjuvant therapy was given.

In December 1998, she developed right upper abdominal pain. Abdominal ultrasonography revealed an echogenic mass, size 12x8x9 cm, in subhepatic area. Her alpha-fetoprotein was 32,971 IU/ml. She had second exploratory laparotomy. A solid tumor, diameter 15 cm, located at right hepatic flexure and a 3-cm vaginal cuff tumor were found. Omental seedings were also noted. Right half colectomy, omentectomy with tumor debulking was done. Pathological report was metastatic carcinoma (malignant mixed mullerian tumor). After operation she received adjuvant treatment consisting of carboplatin 300 mg/m^2 and Goserelin acetate (Zoladex) 3.6 mg every 4 weeks. Her alpha-fetoprotein one week and one month after treatment were 7,226 IU/ml and 5,611 IU/ml respectively. The patient continued on chemotherapy for 3 courses until the raised of alpha-fetoprotein was detected (35,826 IU/ml). CT scan of the whole abdomen demonstrated a mass at right lumbar region diameter 15 cm. She was given cisplatin (60 mg/m^2) and adriamycin (60 mg/m^2) every 4 weeks. The patient tolerated the treatment quite well. Her current condition, after 2 courses of this chemotherapeutic regimen, was asymptomatic. Her last serum alpha-fetoprotein, in May 1999, was 22,777 IU/ml. The tumor size was decreased to 10 cm in diameter. The corelation of serum alpha-fetoprotein and clinical course is demonstrated in Diagram 1.

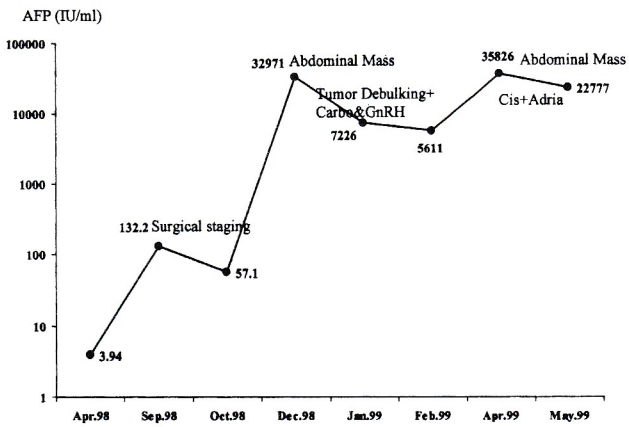

Diagram 1 Corelation of serum alpha-fetoprotein and clinical course.

Discussion

This article aimed to report the case of malignant mixed mullerian tumor produced alpha-fetoprotein. There were less than 10 cases reported in the literatures.[1-4]

Uterine sarcoma accounts for less than 10% of all uterine neoplasm.[5] The malignant mixed mullerian tumor is a mixture of carcinoma and sarcoma. Although any combination is possible, serous carcinoma admixed with endometrial stromal sarcoma is the most common histologic type.[5] The behavior of this type of tumor is aggressive.[5-7] Patients with tumor confined to the uterus at the time of surgery had a 5-year disease-free survival of 52%. When there was extension outside of the uterus, the 5-year disease-free survival dropped to 28%.[6] Treatment of early stage should begin with

surgical resection of primary tumor.[5] Adjuvant treatment after surgery still has no definite benefit to overall survival in early stage.[7-9] Hannigan et al[8] reported no benefit of VAC chemotherapy. The gynecologic oncology group prospectively studied stage I or II uterine sarcoma treated with adriamycin.[10] But no survival improvement was noted. Rose PG[9] reported a decreased recurrence of both pelvic and distant tumor for endometrial sarcoma but not for leiomyosarcoma treated with adjuvant radiation. However, the role of radiotherapy in malignant mixed mullerian tumor seemed to be controversial. In recurrent or advance cases, multiagents chemotherapy were given with overall response rate 18-30% .[11-15] Most of chemotherapeutic agents were cisplatin, adriamycin, ifosfamide and etoposide. Among these, cisplatin showed significant overall response.[16;17] There was a study which reported positive steroid receptor in 50% of the specimens.[18;19] But there were only anecdotal cases which reported hormonal therapy in MMMT.[19-21]

Although abdominal recurrence was the most common pattern[22], as in our case report, lymphatic and hematogenous spread were also common. According to the patient's underlying heart disease, platinum compounds plus GnRH were used for adjuvant treatment without any improvement. Finally, combination chemotherapy consisting of cisplatin and adriamycin showed clinical partial response under close cardiac monitoring.

Alpha-fetoprotein is produced only very little in normal adult tissue.[23] It can be used as a convenient tumor marker, regardless of the type of tumor. It's easily measured in the serum and has a known half-life of 4-6 days. It's an effective marker in germ cell tumor. When present at raised concentrations, provides an accurate means of tumor activity and response to treatment. Occasionally, upper GI tract cancers and ovarian mucinous cystadenocarcinomas of intestinal type express alpha-fetoprotein.[24] Alpha-fetoprotein may express by tumors which seem to be histologically unrelated including lung, renal carcinoma and rhabdomyosarcoma.[23] From what we' ve known, there have been only 9 reported MMMT cases in the English literature that express alpha–fetoprotein.[1-4] The clinical importance of alpha-fetoprotein production in MMMT remains unclear. Some authors suggested that MMMT producing alpha-fetoprotein might exhibit different clinical behavior. On the other hand, elevated alpha- fetoprotein may provide a useful marker for monitoring the treatment of this tumor. Further studies are needed to understand histogenesis and behavior of this special type of MMMT.

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