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Case Report

Malignant mixed mesonephric tumor arising in mesonephric carcinoma: a case report with complete remission after concurrent chemoradiation therapy

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Summary

Purpose of Investigation: Malignant mixed mesonephric tumors very rarely arise in mesonephric carcinoma of the uterine cervix. These tumors tend to progress aggressively and belong to the histological group of mixed tumors with both epithelial and mesenchymal components. At diagnosis, most patients present with vaginal bleeding and a palpable mass in the cervix. Because this neoplasm is rare, there is no standard management for these patients, and they should be cared for on a case-by-case basis. *Materials and Methods:* The author treated a 74-year-old patient with a malignant mixed mesonephric tumor arising in the mesonephric carcinoma. The case report and a literature review are presented here. *Results:* Because the patient was elderly and had complicating medical problems, the authors could not perform surgical treatment and instead attempted concurrent chemoradiation (CCRT), which contrary to the authors' expectations, resulted in complete remission. *Conclusion:* For patients with advanced-stage tumors and medically complicating issues, CCRT may represent an alternative therapeutic strategy.

Key words: Malignant mixed mesonephric tumor arising in mesonephric carcinoma; Concurrent chemoradiation; Complete remission; Cervix; Uterus.

Introduction

Cancer of the uterine cervix is a common carcinoma of the female reproductive tract. Recently, vaccination against human papilloma virus (HPV) and cervical cancer screening programs have played an important role in decreasing the incidence of uterine cervical cancer. Malignant mixed mesonephric tumors are very rarely found in mesonephric carcinoma of the uterine cervix. However, a few case reports have been published. At diagnosis, most patients present with vaginal bleeding and a palpable mass in the cervix [1]. There is no standard management for this disease, and the prognosis is considered to be very poor. Concurrent chemoradiation (CCRT) has not been attempted as a first-line therapy without surgery. The authors recently encountered a case of malignant mixed mesonephric tumor arising in mesonephric carcinoma. Because the patient was elderly and had complicating medical problems, surgical treatment could not be performed, and the authors instead attempted CCRT. Contrary to their expectation, complete remission was achieved after CCRT. This case with a literature review are described below.

Case Report

A 74-year-old multiparous woman was referred to the Department of Obstetrics and Gynecology from the Internal Medicine Department for anemia and vaginal bleeding.

She had not undergone a cervical smear or gynecological examination; she did have type 2 diabetes mellitus and hypertension and was taking oral medication. Her height and weight were 150.4 cm and 75.7 kg, respectively. She had a body mass index of 33.5 kg/m^2. Because she had both knee osteoarthritis and compression fractures of the lumber spines, her daily activities and ambulation were limited.

Transvaginal sonography revealed hematometra with an 8.9 $\times$ 4.6-cm cervical mass. Colposcopy revealed no definite exocervical lesion with hemorrhage from the endocervical canal. A cervical smear revealed atypical glandular cells.

The pathological diagnosis obtained from an endocervical curettage biopsy was a malignant mixed mesonephric tumor arising in mesonephric carcinoma. Similar to mixed malignant tumors, the patient's tumor had both an adenocarcinoma component and a sarcoma component. The predominant component in one tumor and a minor component in another had a tubular pattern characterized by back-to-back, small, round, uniform tubules lined by cuboidal or flattened cells. A dense eosinophilic secretion was observed in some of the lumens that resembled that seen in normal and hyperplastic mesonephric tubules (Figure 1). Expression of CK PAN, CD 10, and inhibin was analyzed using paraffin immunohistochemistry. The area of the tumor was positive for CK PAN (AE1 and AE3) and negative for CD 10 and inhibin. The patient was diag-

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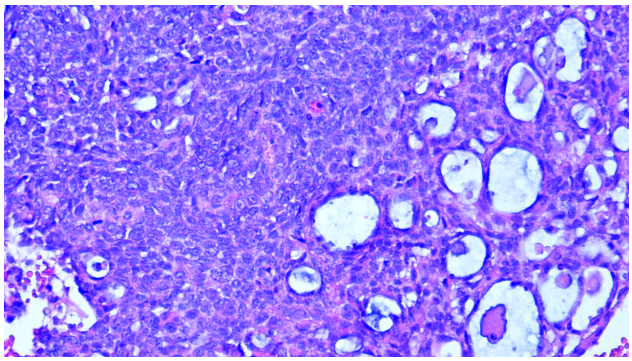

Figure 1. In the adenosarcoma component, the nonmucinous cuboidal epithelium and lumen containing eosinophilic hyaline secretions are diagnosed as a mesonephric adenocarcinoma with a tubular pattern (original magnification ×200).

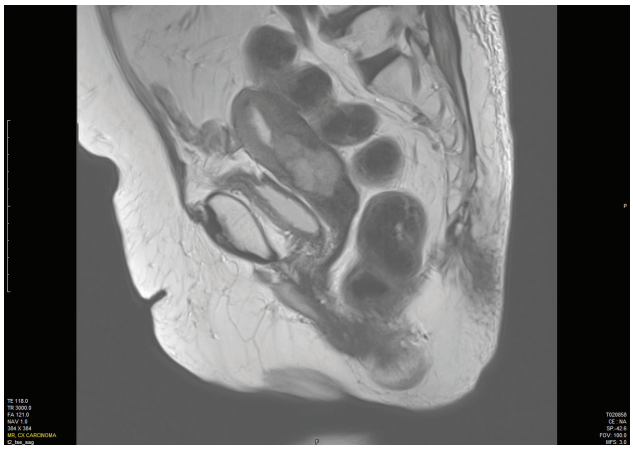

Figure 2. Sagittal T2-weighted magnetic resonance image showing a mass over 7 cm in size in the uterine cervix with hematometra.

nosed with a malignant mixed mesonephric tumor arising in mesonephric carcinoma of the uterine cervix.

Magnetic resonance imaging showed that the mass of the uterine cervix was over 7 cm; hematometra was associated with parametrial infiltration, especially of the right posterolateral portion of the cervix. Additionally, there was a smaller than 8-mm lymph node at the posterior right side of the external iliac chains (Figure 2). A PET-CT scan revealed a uterine cervical cancer lesion over 7 cm in size with no other metabolic lesions.

Her serum concentrations of CA-125 and SCC were 11.3 U/mL and 0.52 ng/mL, respectively. The clinical diagnosis of the patient was cervical cancer Stage II B with a cell type of malignant mixed mesonephric tumor arising in mesonephric carcinoma.

The treatment chosen in this patient was determined after discussions with her and her son and in consideration of her general condition. Despite limited clinical data available on the effect of CCRT for malignant mixed mesonephric tumors arising in mesonephric carcinoma, the patient and her son chose CCRT for the primary treatment. RT was performed 28 times with a WP of 50.4 Gy and was followed by six cycles of intracavitary brachytherapy (ICR) with concurrent six courses of weekly chemotherapy with cisplatin (40 mg/m^2).

At ten months post-CCRT, an abdominopelvic CT revealed no visible cervical mass, but a small amount of fluid had collected in the uterine cavity without visible intraabdominal metastasis. Cervical smears performed at 9 and 12 months post-CCRT were negative. At the present time, she has been clinically free of the disease for 12 months since undergoing CCRT.

Discussion

Cancer of the uterine cervix is a common carcinoma of the female reproductive tract. Recently, vaccination against HPV and cervical cancer screening programs have played an important role in decreasing the incidence of uterine cervical cancer. The most common pathological type of carcinoma of the uterine cervix is squamous cell carcinoma, and its incidence has also been decreased by cervical cancer screening programs and HPV vaccination. Nonetheless, rare types of carcinomas of the uterine cervix are constantly arising.

Malignant mixed mesonephric tumors developing in mesonephric carcinoma of the uterine cervix are extremely rare neoplasms of the female reproductive tract and are derived from remnants of the mesonephric ducts. The mesonephric or Wolffian ducts run parallel to the Müllerian ducts and, in males, the excretory duct system, which includes the epididymis, vas deference, common ejaculatory duct, and possibly the rete testis. The rete testis connects the mesonephric ducts and sex cord derivatives [2]. Ferry and Scully described four cervical mesonephric carcinomas and emphasized the importance of distinguishing them from mesonephric hyperplasia and other cervical carcinomas of a Müllerian nature, such as clear cell carcinoma and adenoma malignum [3].

All eight such tumors reported by Clement *et al.* [4] were confirmed to be in the cervix, and none of the patients died of the disease (one died of other causes). The authors suggested that malignant mesonephric tumors exhibit indolent behavior and have a prognosis that is better than that of malignant Müllerian tumors. Furthermore, Silver *et al.* [5] proposed that some mesonephric adenocarcinomas are associated with aggressive behavior. In that study, none of the patients with mesonephric adenocarcinomas and follow-up information died of the disease; half of the tumors were Stage I, and the patients had favorable outcomes after long-term follow-up [6]. Regardless, two of the four patients with mixed malignant mesonephric tumors and follow-up information had an adverse outcome. The other two patients were alive and clinically free of disease, though one of them had a short follow-up.

Histologically, distinguishing between mesonephric hyperplasia, mesonephric adenocarcinoma, and malignant

mixed mesonephric tumors is challenging. Moreover, the histological findings of mesonephric adenocarcinoma vary from case to case [7]. Clemet *et al*. [4] classified morphologies into five patterns: ductal, tubular, solid, retiform, and sex-cord-like. Additionally, the immunoprofile of mesonephric neoplasms is usually but not always positive for vimentin, retinin, CD10, and CK7 and negative for ER and PR [5]. In the present case, expression of CK PAN, CD 10, and inhibin was analyzed by paraffin immunohistochemistry. The tumor area was positive for CK PAN and negative for CD 10 and inhibin. In general, histology combined with tumor immunoprofiling is the best way to diagnose malignant mixed mesonephric tumors. The immunoprofiles of mesonephric hyperplasia and mesonephric adenocarcinoma though similar, and the former can sometimes mimic the latter. Cytological atypia, an infiltrative border, and staining for Ki-67 can assist in differential diagnosis [4]. The presence of sarcomatous components, including either spindle cells or heterologous elements, is key to diagnosing malignant mixed mesonephric tumors (or mesonephric carcinomas).

Unlike other common types of uterine cervical adenocarcinoma, HPV is not part of the etiology of mesonephric adenocarcinoma [8]. Therefore, preventing HPV may have less value for preventing mesonephric adenocarcinoma and malignant mixed mesonephric tumors [9].

Only a few case reports have been described to date; there is no standard management for affected patients, and the prognosis is thought to be very poor. Tseng *et al*. [7] described 13 cases of malignant mesonephric mixed tumors; 12 of the patients underwent (radical) hysterectomy with/without adjuvant radiation and/or chemotherapy, but information was unavailable for the other case. Therefore, CCRT has not been applied as a first-line therapy without surgery.

The present authors recently encountered a case of malignant mixed mesonephric tumor arising in mesonephric carcinoma. Because the patient was elderly and had complicating medical problems, surgical treatment could not be performed, and CCRT was attempted instead. Contrary to expectations, complete remission was achieved after CCRT. Hence, CCRT may be an alternative therapeutic strategy for cases of advanced-stage tumors with medically complicating problems.

Conflict of Interest

The authors declare no competing interests.

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