EJGO European Journal of Gynaecological Oncology

Case Reports

Primary adenocarcinoma with choriocarcinomatous differentiation of the sigmoid colon misdiagnosed choriocarcinoma of the uterus: case report and review of the literature

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Summary

Choriocarcinoma is a highly malignant tumor of trophoblastic cells that most often arises in the placenta, but may also develop in extragonadal tissues. Primary extragonadal choriocarcinoma, especially in the gastrointestinal tract, is extremely rare and is associated with poor prognosis. This report describes a 44-year-old Korean woman who was initially diagnosed incorrectly with choriocarcinoma of the uterus, but was ultimately diagnosed with primary adenocarcinoma accompanied by focal choriocarcinomatous differentiation in the sigmoid colon and secondary degeneration of submucosal myoma. Her progression was rapid and because of her poor general condition, she received only a single cycle of cisplatin chemotherapy. She died of multiorgan failure due to multiple metastases two months after the initial diagnosis.

Key words: Primary extragonadal choriocarcinoma; Adenocarcinoma; Submucosal myoma; Chemotherapy.

Introduction

Choriocarcinoma is a highly malignant tumor of trophoblastic cells that most often arises in the placenta, but may also arise in extragonadal tissues. Primary extragonadal choriocarcinoma, especially in the gastrointestinal tract, is extremely rare and is associated with poor prognosis. This report describes a 44-year-old Korean woman who was initially diagnosed incorrectly with choriocarcinoma of the uterus, but was ultimately diagnosed with primary adenocarcinoma accompanied by focal choriocarcinomatous differentiation in the sigmoid colon.

Case Report

A 44-year-old Korean woman was transferred from another clinic to undergo chemotherapy for choriocarcinoma. The patient presented with nausea, vomiting, and headache. She was nulliparous and had last had intercourse 13 months earlier. Her menstrual cycles were irregular; her last menstruation began six weeks earlier, and she had vaginal bleeding for more than one month. Physical examination revealed a tender mass, the size of a fist, in the left lower abdomen. Laboratory results showed mild inflammatory changes, with a white blood cell count of 10,300/μl, a C-reactive protein level of 8.75 mg/dl, and a ß-hCG level of 428,864 mIU/ml. Abdominal and chest CT showed a 9×8-cm sized mass in the uterus and multiple metastatic sites in the liver and both

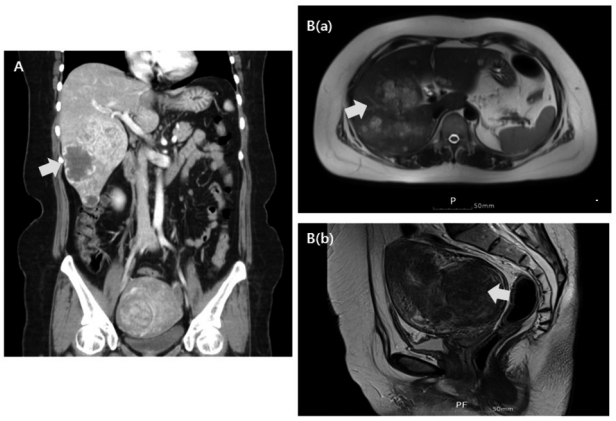

Figure 1. — (A) Abdominal CT of the patient, showing a well-defined, lobulated heterogeneous enhancing intrauterine mass, measuring 8.8×6.8 cm, and multiple (> 4), ill-defined, focal infiltrative hepatic masses, measuring < 12×8 cm, with a conglomerated multinodular and focal infiltrative mass at S5 and S6.
(B) T2 weighted pelvic MRI of this patient, showing (a) more than four, ill-defined and lobulated contoured high SI hepatic masses throughout the liver measuring less than 12×8 cm, along with conglomerated multinodular and focal infiltrative masses at S5 and S6 and (b) a well-defined, lobulated heterogeneous enhancing intramural mass, measuring 8.9×7.4×7.1 cm, in the right posterolateral wall of the uterine body.

Revised manuscript accepted for publication September 14, 2017

Figure 2. — Gross appearance of the sigmoid colon, showing a 4.5×3.5-cm sized ulcerofungating mass.

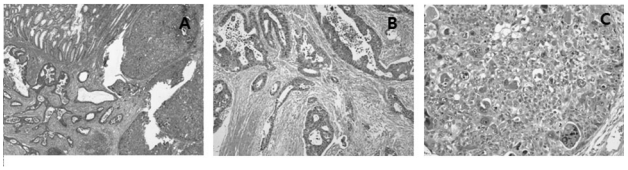

Figure 3. — Histologic assessment of the tumor.
(A) Abrupt transition from a conventional adenocarcinoma on the left to a choriocarcinoma on the right (H&E ×40).
(B) The adenocarcinoma component is composed of well-formed glandular structures (H&E ×200).
(C): The choriocarcinoma cells, similar to syncytiotrophoblasts, have abundant eosinophils in the abundant cytoplasm with pleomorphic and hyperchromatic nuclei, resulting in multinucleation (H&E ×400).

lungs. She was initially diagnosed with choriocarcinoma of the uterus (Figure 1A). Pelvic MRI suggested that the mass in the uterine cavity was an intramural uterine myoma with degeneration or a leiomyosarcoma, and that the multiple ill-defined, focal infiltrative hepatic masses were likely unusual multinodular and focal infiltrative hepatocellular carcinoma (HCC) or hypervascular hepatic metastases from an unknown malignancy (Figure 1B). Colonofiberscopy revealed a circular mass in the sigmoid colon. Biopsy of this mass resulted in a diagnosis of moderately differentiated adenocarcinoma. To determine whether the liver masses were metastases from colon cancer, a CT guided liver biopsy was performed, which showed that these lesions were not hepatomas. To rule out other types of malignancy, tissue samples were analyzed immunohistochemically. Because the patient experienced continuous vaginal bleeding during this time, a total abdominal hysterectomy was performed to evaluate the uterine mass, along with anterior resection of the colon. Surgery revealed a 9×8-cm sized degenerated myoma in the anterior wall of the uterus, a 4.5 ×3.5 cm-sized ulcerofungating mass in the sigmoid colon (Figure 2), and a hemangioma in the liver. Pathologic analysis showed that the lesion in the sigmoid colon was a well-differentiated adenocarcinoma, containing areas of choriocarcinomatous differentiation, penetrating to the surface of the visceral peritoneum (Figure 3). The patient was positive for lymphatic (+), venous

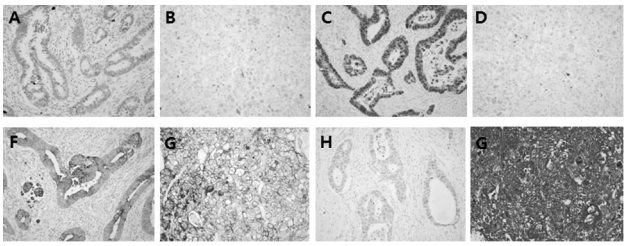

Figure 4. — Immunohistochemical staining of tumor. The adenocarcinoma cells were negative for (A) CK7 and (G) hCG and positive for (C) CK20 and (E) CDX-2. In contrast, the choriocarcinoma cells were negative for (D) CK20 and (F) CDX-2 and positive for (B) CK and (H) hCG (×200).

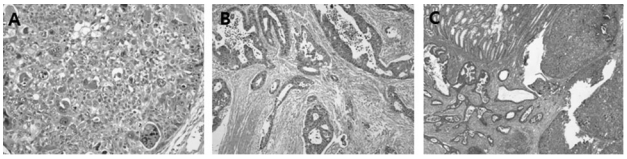

Figure 5. — Histologic findings, showing the presence of (A) metastatic colonic choriocarcinoma components in the liver biopsy sample and (B) usual leiomyoma in the uterine mass (both, H&E ×100).

(+++), and perineural (+) invasion. Hard nodular, enlarged, and densely fixed lymph nodes, positive for metastases, were observed. Immunohistochemical staining showed that the lesion was positive for ß-hCG, cytokeratin 7, cytokeratin 19, and cytokeratin AE1/AE3, and negative for TTF-1, hepatocytes, carcinoembryonic antigen (CEA), and PLAP (Figure 4). Metastases were observed in the liver. The patient was diagnosed with a metastatic high grade carcinoma, best classified as a choriocarcinoma component of the sigmoid colon, along with uterine leiomyomata and adenomyosis (Figure 5). As the patient was diagnosed with primary colon choriocarcinoma, she was started on systemic chemotherapy with cisplatin. However, her general condition worsened rapidly, with decreased liver function and severe jaundice. Her ß-hCG level remained high, over 200,000 mIU/ml, after the first course of cisplatin chemotherapy, and she complained of continuous right upper quadrant (RUQ) pain. Follow-up CT showed tumor progression, with the hepatic mass having increased in size and a tumor thrombus appearing in the right portal vein, along with several enlarged lymph nodes in the aortocaval and left para-aortic spaces. The patient refused further chemotherapy and died two months after the initial diagnosis of multiorgan failure due to multiple metastases.

Discussion

Choriocarcinoma usually arises in trophoblastic tissue following gestational events, such as pregnancy, ectopic pregnancy, and abortion. Non-gestational, extragonadal choriocarcinoma is rare, but may occur in the digestive tract, most frequently in the stomach [1]. Primary choriocarcinoma of the colon is extremely rare, with only 20 cases

previously reported; of these, only eight involved the sigmoid colon [1-7]. Rectosigmoid lesions near the uterus or gonads accounted for two-thirds of choriocarcinomas of the large intestine, but physical and/or histological examinations of these patients showed no abnormal findings in the uterus or genitalia [1]. Serum ß-hCG levels were markedly elevated in all assessed patients with choriocarcinoma of the large intestine, but there was no relationship between initial serum ß-hCG concentration and patient prognosis. Because these tumors tend to progress rapidly, they are associated with very poor prognosis, with almost all patients described to date dying within one year of diagnosis. Although intestinal resection with lymph node dissection is regarded as the standard treatment for colorectal choriocarcinoma, systemic chemotherapy may be effective, with a significantly higher survival rate in patients who did than did not receive chemotherapy [6]. To date, however, no standard chemo-therapy regimen has been established for the treatment of colorectal choriocarcinoma.

The pathogenesis of primary extragonadal choriocarcinoma is unclear. These tumors may migrate abnormally during embryonic development [8] or may be metastases from latent primary lesions in the genitalia [1]. Alternatively, based on the hypothesis that an adenocarcinoma may retrodifferentiate into a choriocarcinoma, both functionally and morphologically [7], a primary extragonadal choriocarcinoma may represent the retrodifferentiation or dedifferentiation of a pre-existing colonic carcinoma [4]. In addition, a genetic evolution model has reported that genes located on the X chromosome may be involved in the phenotypic switch from adenocarcinoma to choriocarcinomatous differentiation [9]. As 70% of primary choriocarcinomas of the colon are associated with adenocarcinoma, dedifferentiation is considered most likely. However, the absence of concurrent adenocarcinoma from 30% of primary choriocarcinomas of the colon suggested that these tumors likely arose directly from malignant changes in the ectopic chorion or totipotent cells [10] or from a more aggressive choriocarcinomatous component that dedifferentiated from adenocarcinoma [11].

The prognosis of patients with colonic choriocarcinoma is extremely poor, with a mean patient survival period of only 108 days [1]. Choriocarcinomas progress rapidly, with generalized metastasis being common [12]. These features are thought to be due to tumor derivation from chorionic tissue, which normally invades and destroys adjacent tissue, a behavior that persists after malignant transformation. Thus, hematogenous and lymphatic metastases are common at the time of the initial diagnosis [13]. Almost all reported patients with primary colonic choriocarcinoma died within one year. This overall poor prognosis may reflect the late diagnosis of these tumors, as well as the presence of liver and/or lung metastases.

Acknowledgement

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean Government (MEST) (No. 20120009380).

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