—Case Reports—

Male Choriocarcinoma with Metastasis to the Jejunum: A Case Report and Review of the Literature

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Abstract

We report on a patient with male choriocarcinoma. The patient was a 31-year-old male patient with jejunal choriocarcinoma that metastasized from the mediastinum. He was admitted complaining of melena and severe anemia. Upper and lower gastrointestinal endosocopy was performed, but no source of bleeding was seen. Chest X-ray and CT revealed a mediastinal tumor 7 cm in size anterior to the arotic arch. Superior mesenteric arteriography showed irregularities and macular opacity in the jejunal artery. An emergency laparatomy was performed because of massive gastrointestinal bleeding. A jejunal tumor approximately 4 cm in size was resected and numerous metastases were observed in the liver and mesentery. Histopathological examination showed metastatic jejunal choriocarcinoma. Gynecomastia was not present and the testes were normal. Serum beta-human chorionic gonadotropin (HCG) was at an abnormally high level of 4,396 ng/mL. Because of metastases to the brain and invasion to the trachea, he died on postoperative day 20. We report this rare case of a male patient with metastases of choriocarcinoma to the gastrointestinal tract from the mediastinum, together with a review of the literature.
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Key words: choriocarcinoma, gastrointestinal tract, male, mediastinum, jejunum

Introduction

Choriocarcinoma is a cancer that typically occurs in females in the chorionic epithelium of the placenta[1] and is rarely seen in males. In the rare occurrences in males, it is most commonly seen in the testis. When the site of the primary tumor is extragonadal, choriocarcinoma occurs preferentially at the midline lesion[2] in the pineal body, the mediastinum and the retroperitoneum. However, some patients may present with unusual symptoms such as gastrointestinal hemorrhage[3]. We report a case of hemorrhagic metastatic jejunal choriocarcinoma from the mediastinum in an adult man.

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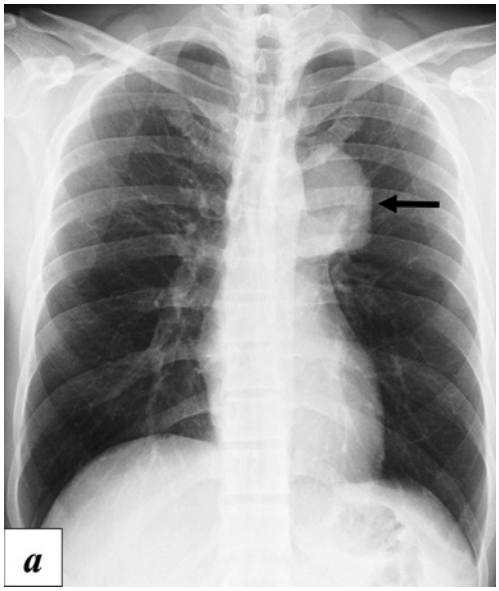

Fig. 1a Chest Radiograph
A nearly spherical shadow approximately 7 cm in size appears superimposed over the aortic arch in the upper left lung **(arrow)**.

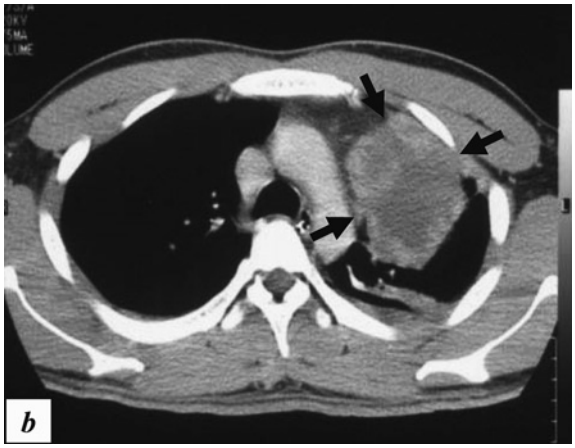

Fig. 1b Chest CT
A 7 cm mediastinal tumor with an irregular margin is seen adjacent to the anterior aortic arch **(arrows)**. No abnormal shadows are seen in the lung fields.

Case Report

A 31-year-old man was admitted to our hospital with a chief complaint of melena, which had persisted for 2 weeks. The past history was unremarkable. His initial vital signs were normal height was 166 cm, and weight was 68 kg. Complexion was poor, and severe palpebral conjunctival anemia was observed; no ocular jaundice was noted. The superficial lymph nodes were not palpable. There were no abnormal findings on physical examination of the thorax and abdomen. There was no gynecomastia. The testicles were equal in size and without nodules or mass. Rectal examination showed the presence of black stool. No tumors were palpable, and there was no prostate hypertrophy. Test findings at admission were as follows: WBC, 9,240 /μL; RBC, 201 × 10^4 /μL; Hb 5.9 g/dL, Ht, 19.0%; Pl, 27.0 × 10^4 /μL; CRP, 0.70 mg/dL; TP, 4.7 g/dL; T.Bil, 0.4 mg/dL; GOT, 20 U/L; GPT, 37 U/L; LDH, 269 U/L; CPK, 50 U/L; BUN, 9.6 mg/dL; and creatine, 0.87 mg/dL. The values obtained for tumor markers were: CEA, 0.5 ng/mL; CA 19-9, 8.6 U/mL; and AFP, 1.0 ng/mL. Serum beta-human chorionic gonadotropin (HCG) level was markedly elevated at 4,396.3 ng/mL (normal range, <0.1 ng/mL) post operation.

Upper and lower gastrointestinal endoscopy was performed, but no source of bleeding was present. Chest radiography **(Fig. 1a)** and CT **(Fig. 1b)** revealed a mediastinal tumor approximately 7 cm in size anterior to the aortic arch, and abdominal CT showed multiple metastases involving all lobes of the liver. Superior mesenteric arteriography showed irregularities and macular opacity in the jejunal artery. As melena was seen in large quantities, and blood pressure decreased to the 50s on day 6 after admission, an emergency laparotomy was performed. A dark red tumor approximately 4 cm in size was found in the jejunum 90 cm from the Treiz ligament, and the small intestine was partially resected **(Fig. 2a)**. In addition, numerous metastases were observed in the liver and mesentery. On postoperative day 4, hemiplegia and decreased consciousness level emerged suddenly due to the presence of numerous metastases in the brain. On postoperative day 9, severe hemoptysis occurred due to penetration of the mediastinal tumor into the trachea. The patient died on postoperative day 20. No autopsy was performed.

Pathological examination showed a metastatic tumor measuring 2.0 × 3.5 cm in size associated with marked bleeding in the small intestine. It was composed of small, round cytotrophoblasts, with relatively uniform nuclei and light cytoplasm, and large, irregular, multinucleated syncytiotrophoblasts

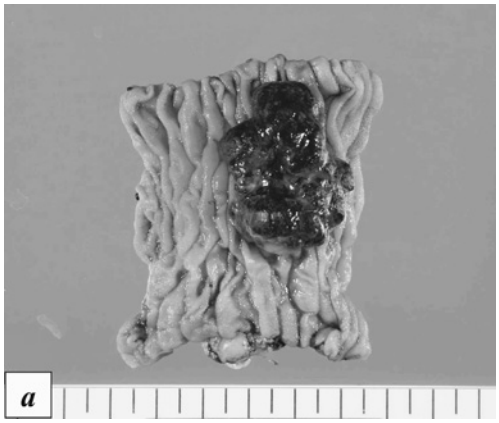

Fig. 2a Resected speciemen
A dark red jejunal tumor was located at 90 cm from Treiz ligament.

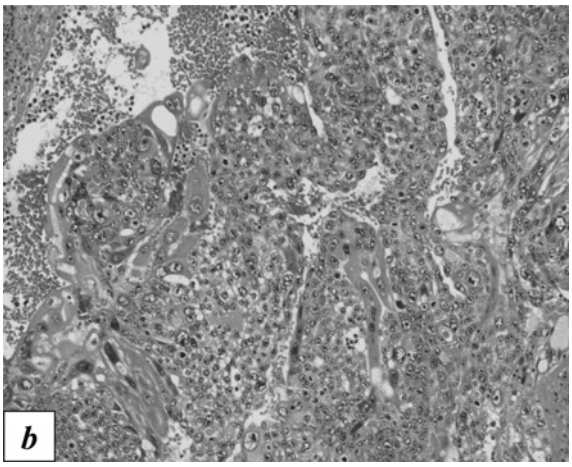

Fig. 2b Histopathological examination shows marked bleeding associated with the tumor, which consists of mixed cytotrophoblasts and syncytiotrophoblasts (HE, ×200).

(Fig. 2b). The tumor was mainly located on the serosal side. Immunohistochemical examination showed positive for HCG **(Fig. 2c)** and negative for AFP staining. The final diagnosis was mediastinal choriocarcinoma with metastasis to the jejunum, liver, brain and mesentery.

Discussion

The term choriocarcinoma is generally used to refer to gestational choriocarcinoma, which most commonly occurs with hidatidiform mole [1], spontaneous abortion, ectopic pregnancy or normal delivery. It is a malignancy specific to females and rarely occurs in males. There are many reports on choriocarcinoma in the testis[4–7], but there has been

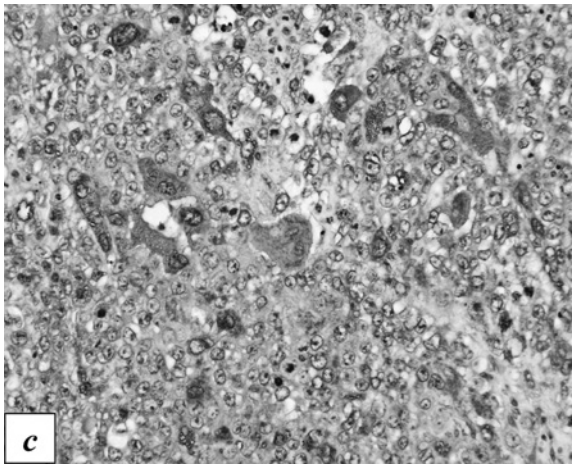

Fig. 2c Diffuse positive HCG staining is seen (HCG, ×400).

only 1 original article [8] on choriocarcinoma investigated from the viewpoint of males. Therefore, we examined the characteristics based on 106 cases of male choriocarcinoma reported during the previous 12 years (1995 to 2006).

The testis is the most common primary site, at 33.0% (35/106), followed by the mediastinum[9], pineal body [10], gastrointestinal tract [11,12], lung and retroperitoneum[13] **(Fig. 3)**. According to the "burned out tumor" theory[14–16], however, there are no primary sites other than the test is in male choriocarcinoma, as the other sites are metastatic sites. In other words, this is a problem related to the mechanism of onset of extragonadal germ cell tumor (GCT). The mechanism has long been debated, and no conclusions have yet been reached. There are three hypotheses: 1) the tumor is a metastasis from a testicular choriocarcinoma that regressed spontaneously[14–16]; 2) the tumors arise from retained primordial germ cells that migrate abnormally during embryogenesis[8]; and 3) the tumor is a cancer that develops originally as a nontrophoblastic neoplasm and is transformed into a choriocarcinoma[17]. The first hypothesis is the "burned out tumor" theory. However, because autopsies have shown no tumor or scarring in the testis with extragonadal GCT[18–20], many authors[21,22] including us, disagree with this hypothesis. Moreover, Luna et al.[23] autopsied 20 patients with mediastinal GCT and found a tumor in the testis of 1 patient and scarring in the testis of another, while

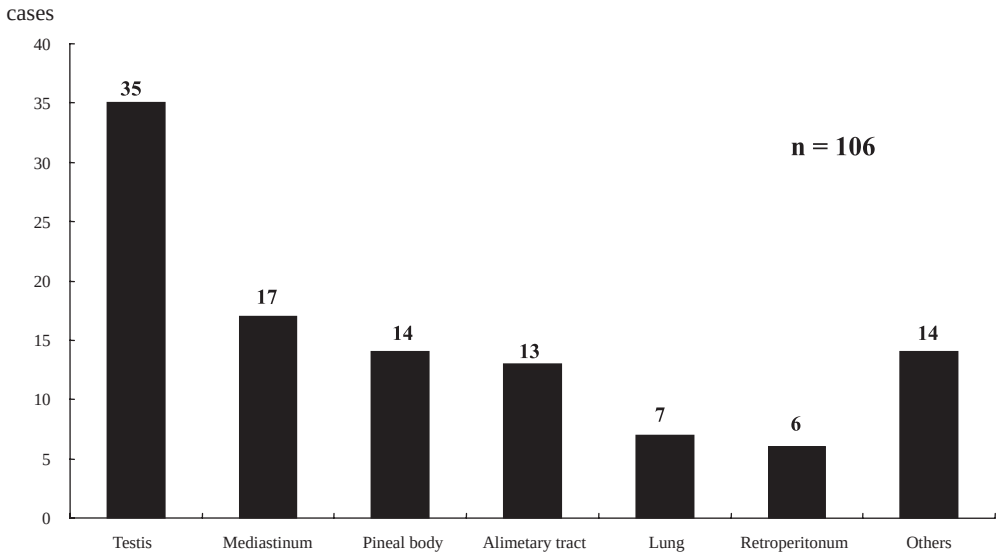

Fig. 3 Frequency of male choriocarcinoma by primary site (1995 to 2006)

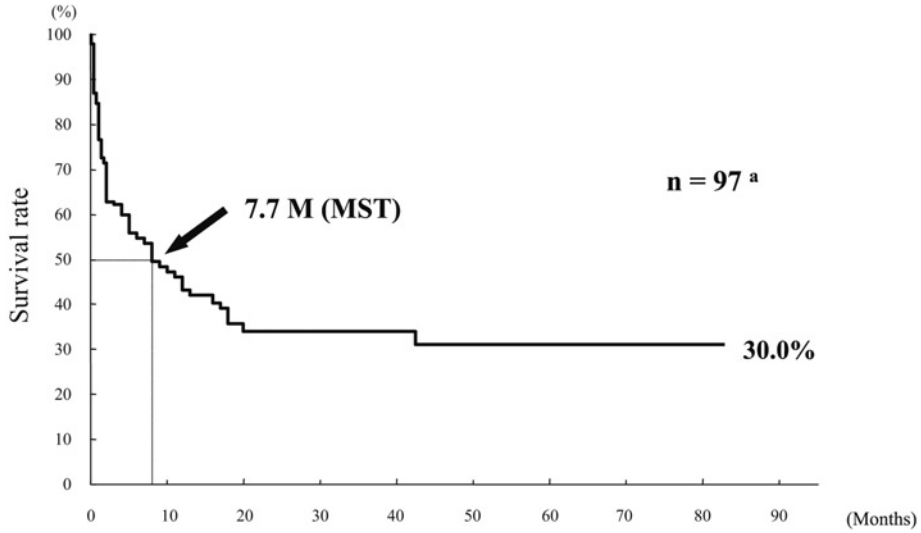

Fig. 4 Survival curve for male choriocarcinoma (1995 to 2006)
[a]9 patients excluded from the group of 106 due to missing data.
MST: median survival time

the mediastinum was the primary site in the remaining patients. In any case, palpation of the testis is essential in patients with extragonadal GCT, and ultrasound examination should be performed when possible.

The mean age of male choriocarcinoma was 36.0 years, and the frequency peaked at 20–29, followed by 30–39 and 10–19 years of age. It is a disease that tends to occur in children and adolescents, with patients in their 30s or younger accounting for 2/3 of all cases (69/106). Metastasis was seen in 83% (81/98; due to missing data for 8 patients) of patients, with multiple metastases seen in most. The cases were characterized by hematogenous metastasis to the lung, liver, or brain. The frequency of metastasis to the gastrointestinal tract was low at 11% (9/81), with metastasis to other organs having already occurred. None of the patients had metastasis only to the gastrointestinal tract.

Diagnosis is possible if the site is near the body surface and partial or total biopsy can be performed relatively safely. However, biopsy cannot be performed at many sites, such as the mediastinum, pineal body, lung, and retroperitoneum, making preoperative diagnosis very difficult[24,25]. In the gastrointestinal tract, biopsy can be performed to

the extent that an endoscope can reach the site, but this does not mean that choriocarcinoma can easily be diagnosed preoperatively. This is because choriocarcinoma of the pure type is rare, while mixed types consisting of choriocarcinoma and adenocarcinoma are common[26–28]. Moreover, due to the small size of the biopsy specimen, choriocarcinoma is often misdiagnosed as adenocarcinoma in pathological examinations. Kobayashi et al.[12] reported that only 8% of the gastric choriocarcinoma cases were diagnosed correctly by biopsy. We think serum HCG test has a diagnostic value equal to that of histopathologic examination because the proportion of patients with abnormal serum HCG values is high, at 96.4% (81/84, due to missing data for 22 patients), which means the test is highly precise. Moreover, because it is easy to perform and noninvasive, it can be repeated and performed quickly, and it places little burden on the patient. However, serum HCG is almost never tested in males. Consequently, an important consideration is the level of awareness that this blood test is available.

In many cases, hematogenous metastasis to multiple organs, such as the lung, liver, or brain, has already occurred by the time of diagnosis, and sustained bleeding is present. Chemotherapy is therefore often administered after palliative surgery is performed. Methotrexate and actinomycin D are often selected for chemotherapy in the gynecological setting. With male choriocarcinoma, however, a BEP regimen consisting of bleomycin, etoposid and cisplatin in combination is administered in many cases[29].

This investigation based on 97 cases excluding 9 cases which were not recorded, showed that the prognosis for male choriocarcinoma was very poor, the cumulative survival rate being 30%, and that the course of the disease was rapid: mean survival time was 7.7 months, 1-month mortality was 23.8%, 2-month mortality was 37.2%, and 6-month mortality was 45.4% **(Fig. 4)**.

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