

The Unusual Presentation of Gastric Adenocarcinoma as a Testicular Mass: A Favorable Response to Docetaxel and Cisplatin Plus Oral Tegafur/Uracil and Leucovorin

Kai-Chung Yang^{1,7}, Yee Chao^{2,6,7}, Jiing-Chyuan Luo^{1,7}, Junne-Yih Kuo^{3,7}, Rheun-Chuan Lee^{4,7},
Anna Fen-Yau Li,^{5,7} Chung-Pin Li^{1,7*}

¹Division of Gastroenterology, Department of Medicine, ²Cancer Center, ³Division of Genitouriology, Department of Surgery, ⁴Department of Radiology, and ⁵Department of Pathology, Taipei Veterans General Hospital; ⁶Central Clinic Hospital; ⁷National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Gastric cancer is one of the most common malignancies in the world. The routes of metastasis include direct extension, lymphatics, and peritoneal or hematogenous spread. Testicular metastasis is rare. We present here a 23-year-old gastric cancer patient who first presented with right-side testis swelling and pain. Diagnosis of metastatic adenocarcinoma was made after right-side orchiectomy. Gastric adenocarcinoma with ascites and peritoneal seeding was found after esophagogastroscope and abdominal computed tomography. The patient received chemotherapy consisting of docetaxel 36 mg/m² and cisplatin 30 mg/m² on day 1 and day 8, plus oral tegafur/uracil 300 mg/m²/day and leucovorin 90 mg/day on day 1 to day 14 in a 21-day cycle, and he had a partial response to the chemotherapy. Metastatic tumors, especially gastric adenocarcinoma, should be considered in the differential diagnosis of patients presenting with testicular mass and they may respond well to chemotherapy. [*J Chin Med Assoc* 2010;73(2):88–92]

Key Words: gastric cancer, metastasis, testis

Introduction

Gastric cancer is one of the most common forms of cancer worldwide, with approximately 870,000 new cases and 650,000 deaths per year.^{1,2} Of those, 85% are adenocarcinoma, with 15% due to lymphoma, gastrointestinal stromal tumor and leiomyosarcoma. Gastric cancer spreads by direct extension through the gastric wall and, therefore, surrounding tissues or organs such as the pancreas, colon or liver, could be involved. It also spreads via the lymphatics or by seeding peritoneal surfaces. Most frequently, gastric cancer spreads to intra-abdominal or supraclavicular lymph nodes (Virchow's nodes). Metastatic lymph nodes in the periumbilical area (Sister Mary Joseph's nodes) are not uncommon. Gastric cancer can also spread to the ovary and is called Krukenberg's tumor. In the hematogenous spread of

gastric cancer, the liver is the most common site. Compared with its counterpart of Krukenberg's tumor, which is most possibly spread via the lymphatics,^{3,4} the incidence of gastric cancer with metastasis to the testis is quite rare. We present a case of gastric cancer with unusual initial symptoms of testicular metastasis and a favorable response to chemotherapy with docetaxel and cisplatin.

Case Report

A 23-year-old male suffered from progressive right testis swelling and pain for 2 weeks. He denied other constitutional symptoms such as fever, epigastralgia, poor appetite, and body weight loss. Family history revealed that his father had died of thyroid cancer when



*Correspondence to: Dr Chung-Pin Li, Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: cpli@vghtpe.gov.tw • Received: June 8, 2009 • Accepted: November 25, 2009

he was a child. He was treated as having epididymitis and was given antibiotics by a general practitioner, but this was unsuccessful. The patient then came to our hospital. Physical examination showed right spermatic cord tenderness, and the swollen right testis had a hard texture and was the size of a golf ball.

Biochemistry and hemogram showed mild hyponatremia (Na, 134 mmol/L; normal range, 137–147 mmol/L) and mild normocytic normochromic anemia (hemoglobin, 11.2 g/dL; normal range, 14–18 g/dL). The tumor markers α -fetoprotein (3.87 ng/mL), carcinoembryonic antigen (1.82 ng/mL) and β -human chorionic gonadotropin (0.1 mIU/mL) were all within normal limits (normal ranges: α -fetoprotein, <20 ng/mL; carcinoembryonic antigen, <6 ng/mL; β -human chorionic gonadotropin, <10 mIU/mL). Sonography showed a heterogeneous nodule, with a size of 2.4 \times 3.2 cm, in the right testis (Figure 1). Malignancy was suspected.

The patient was admitted to our hospital and right radical orchiectomy was carried out. Pathology showed a metastatic adenocarcinoma (Figure 2). Hyperchromatic and pleomorphic neoplastic cells of signet ring cell type were noted. The tumor cells were immunoreactive for cytokeratin AE1/AE3, but were nonreactive for CD117 and placental alkaline phosphatase (Figures 2C–E). Abdominal computed tomography revealed a thickened gastric wall and a moderate amount of ascites with diffuse increased soft tissue density of the subhepatic peritoneal wall, mesentery, pelvic side wall and rectovesical pouch, indicating gastric cancer with tumor seeding (Figure 3A). Esophago-gastroscopy showed ulcerative lesions with bleeding in the stomach (Figure 4A). Pathology showed adenocarcinoma with the same morphology as that of the

previous specimen from orchiectomy (Figures 4B and 4C). The diagnosis of gastric adenocarcinoma with right testicular metastasis was confirmed.

The patient received 2 cycles of docetaxel and cisplatin (docetaxel 36 mg/m² and cisplatin 30 mg/m² on day 1 and day 8, plus oral tegafur/uracil 300 mg/m²/day and leucovorin 90 mg/day in 3 divided doses on day 1 to day 14 in a 21-day cycle). Abdominal fullness and appetite improved, and the patient's general condition was also good. Follow-up abdominal computed tomography showed a regressive change of the thickened gastric wall and peritoneal seeding (Figure 3B). However, relapse with a skin lesion over the patient's scalp was found after 6 cycles of chemotherapy. A biopsy was carried out, which showed metastatic adenocarcinoma. The response duration was 3 months. Chemotherapy was changed to cisplatin 30 mg/m², 5-fluorouracil 2,200 mg/m², and leucovorin 120 mg/m² intravenous infusion every week for 8 weeks with stable disease.

Discussion

Testicular mass lesions can result from neoplasms, infectious diseases or structural disorders. Among neoplastic diseases, the most common is primary germ cell tumor, constituting 95% of all testicular neoplasms, while metastatic testicular tumors make up approximately 2%.⁵ Infectious diseases, such as epididymo-orchitis, are not uncommon clinically. Structural disorders include hydrocele, inguinal hernia, torsion and cysts. Fever, pain, urinary symptoms or constituent symptoms often accompany infectious origin, while neoplastic disorders are usually painless. The diagnostic steps

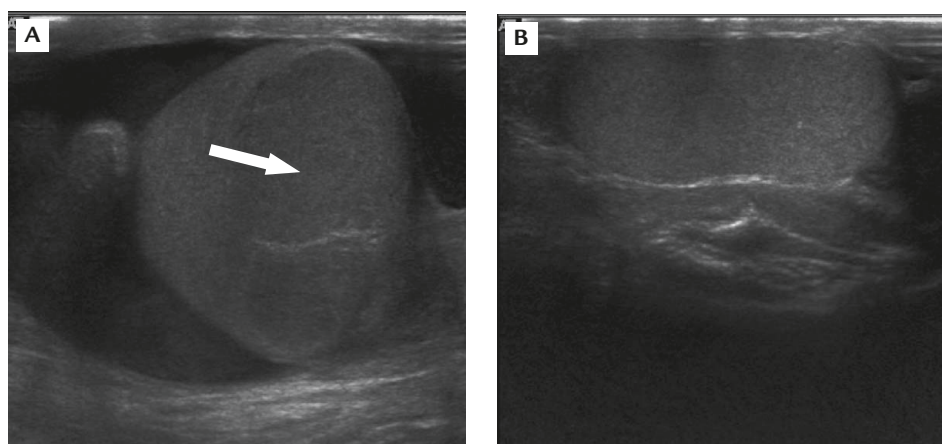


Figure 1. (A) Sagittal view of ultrasound shows a hypoechoic mass (arrow), measuring 2.2 \times 3.6 cm, in the right testis. A moderate amount of hydrocele can be observed around the testis. (B) Normal left-side testis.

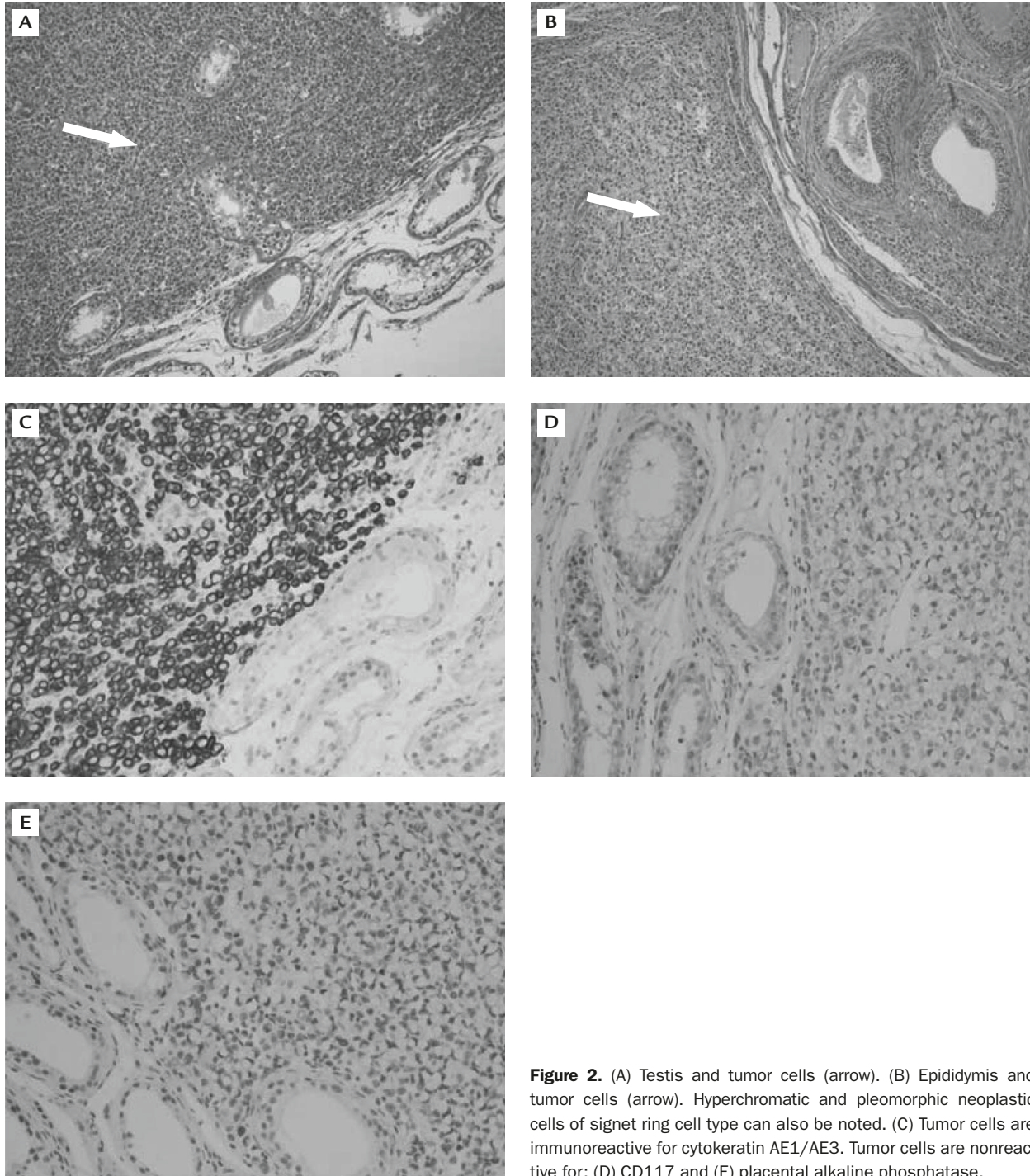


Figure 2. (A) Testis and tumor cells (arrow). (B) Epididymis and tumor cells (arrow). Hyperchromatic and pleomorphic neoplastic cells of signet ring cell type can also be noted. (C) Tumor cells are immunoreactive for cytokeratin AE1/AE3. Tumor cells are nonreactive for: (D) CD117 and (E) placental alkaline phosphatase.

include determination of clinical history, tumor marker measurement, and most importantly, ultrasound examination. Clinical history is important, as conditions such as tumors or hydrocele often develop gradually and are chronic, but infection or torsion often appears suddenly.

In our case, swelling and pain of the right testis was noted initially and, therefore, infectious disease could not be excluded and a trial of antibiotics was the logical

choice. However, follow-up was necessary for fear of etiologies other than infectious disease. An interval of 1 week for follow-up is recommended according to expert opinion.⁶

Metastasis to the testis is reported to be as low as 0.02–0.25% of all autopsies.⁵ Other than leukemia and lymphoma, the most common origins of secondary testicular tumor are prostate (35%), lung (18%),

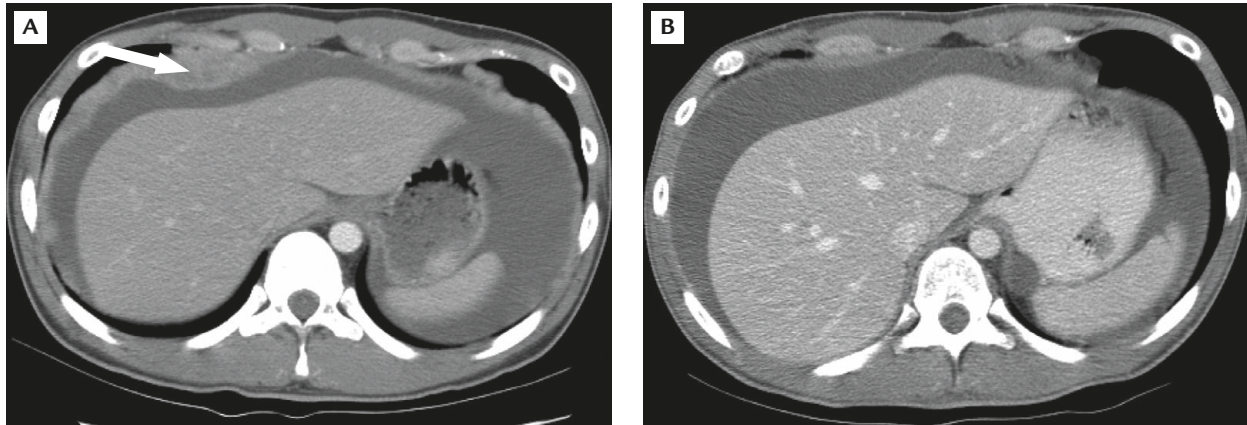


Figure 3. (A) Abdominal computed tomography shows ascites and peritoneal seeding (arrow). (B) Improved peritoneal seeding after treatment.

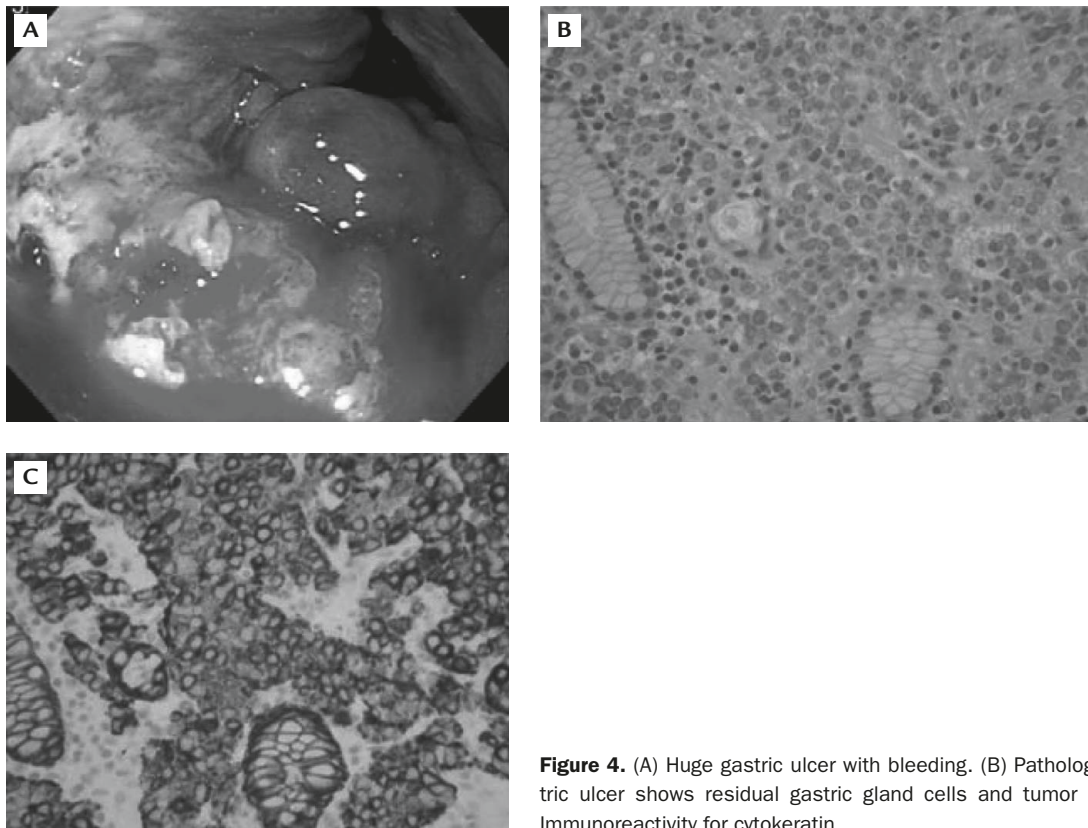


Figure 4. (A) Huge gastric ulcer with bleeding. (B) Pathology of gastric ulcer shows residual gastric gland cells and tumor cells. (C) Immunoreactivity for cyokeratin.

melanoma (11%) and kidney (9%).⁷ Gastric cancer with testicular metastasis is reported to be rare.^{8,9} Several routes of spread of gastric cancer are postulated, including lymphatic, hematogenous, and retrograde extension through the vas deferens. In our patient, we performed designated stains for cyokeratin AE1/AE3, placental alkaline phosphatase and CD117. Cyokeratin AE1/AE3 is well suited to distinguish epithelial carcinoma from non-epithelial malignancies, while placental

alkaline phosphatase and CD117 are sensitive markers of germ cells, and their negativity is useful for excluding seminomas/dysgerminomas.^{10,11}

Gastric cancer with metastasis to the testis can be presumed to be Krukenberg's tumor in males. In our case, peritoneal carcinomatosis, ascites and regional lymphadenopathy were found. There was no previous history of surgery. Although a "true" Krukenberg's tumor spreading through the lymphatics was highly

suspected based on previous studies,^{3,4} the possible route of spread in this case could not be confirmed. Transperitoneal seeding is probable since peritoneal carcinomatosis was present.

Chemotherapy regimens for advanced gastric cancer include 5-fluorouracil, cisplatin, etoposide and mitomycin, but the response is poor if singly used.^{12,13} Several new agents used in combination with the above, including paclitaxel, docetaxel, irinotecan and epirubicin, have shown better activity against gastric cancer.¹⁴⁻¹⁸ The clinical course and treatment results of our patient are similar to those of a recent report in which gastric cancer did not have testicular metastasis and was treated with docetaxel plus cisplatin and fluorouracil.¹⁸ Although there are many agents for combination therapy of gastric cancer, there is no standard first-line chemotherapy with a superior effect compared with other therapies. The time to tumor progression, toxicity and side effects must be taken into consideration and they are largely dependent on the patient's age, performance status and comorbidity. Many clinical trials are underway with results pending. In our case, 2 cycles of docetaxel and cisplatin were used and follow-up abdominal computed tomography showed effective results with this regimen. Gastric adenocarcinoma may present as a testicular mass and has a response to docetaxel-and-cisplatin-based chemotherapy that is similar to that of other gastric adenocarcinomas.

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