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Seminoma presenting as a solitary metastasis in gastric mucosa with regressed testicular mass

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A B S T R A C T

Gastric involvement by seminoma is extremely rare and all the reported cases were associated with bulky retroperitoneal disease or occurred late as part of advanced disease. We report a unique case of seminoma presenting as gastric mucosal metastasis. The diagnosis of this case was complicated by no residual testicular tumor or pelvic/retroperitoneal lymph nodes metastasis and no available specific serum markers. The histological morphology and immunostains allowed the correct diagnosis to be made in this case. This case highlights the rare manifestation of seminoma, which appears to be a primary tumor of an unusual site of germ cell tumor metastasis.

Introduction

Pure seminoma accounts for about 50–55% of all testicular germ cell tumors (GCTs). When GCTs metastasize, the primary landing sites are the retroperitoneal lymph nodes, while organ metastases occur in more advanced stage. Gastric metastasis as the initial presentation of a seminoma has been only very rarely reported.[1–3] The "burned-out phenomenon" in germ cell tumors is a very rare but well documented event.[4] We present here a unique case of metastatic seminoma to gastric mucosa as the initial presentation with a regressed testicular mass and no other metastasis.

Case presentation

A 60-year-old man presented with gastrointestinal bleeding. The abdominal CT with iv-contrast demonstrated thickened gastric fundus and gastroesophageal junction (Fig. 1A). Upper GI endoscopy found nodular thickening of the fundal mucosa and biopsies were taken from this area.

Microscopic examination showed fragments of gastric mucosa focally being infiltrated by a neoplastic process (Fig. 1B). The malignant cells showed nesting and single cell patterns surrounded by a mixture of chronic inflammatory cells. The tumor cells had large nuclei, prominent nucleoli and a small amount of basophilic-to-clear cytoplasm (Fig. 1C). The immunostains showed that the tumor cells were negative for markers of lymphoid, melanocytic and neuroendocrine cells, including CD45, CD3, CD20, CD30, CD15, PAX-5, TIA-1, EBER-ISH, S100, Melan-A, chromogranin, synaptophysin and CD56. The tumor cells were also negative for pancytokeratin, CD30, ERG, CD34, and DOG1 but positive for CD117 (Fig. 1D), OCT3/4 (Fig. 1E), PLAP, and D2-40. Ki-67 stained about 90% of the tumor cell nuclei. The overall morphology and immunostaining pattern were consistent with a seminoma.

A diagnostic workup for metastatic seminoma was next undertaken. Serum tumor markers α-FP and beta-human chorionic gonadotrophin (β-HCG) were within reference ranges. High resolution CT scans of the head, thorax, abdomen, and pelvis were negative for primary tumor or other sites of metastasis. However, positron emission tomography (PET) scan showed focal FDG activity present in left testicle, in addition to the lesion in the stomach (Fig. 2A). A testicular ultrasound was performed. The left testis measured 1.7 × 2.8 × 3.9 cm, with heterogeneous echogenicity and contained a 1.3 × 1.0 × 1.0 cm lobulated hypoechoic hypervascular solid mass, corresponding to the FDG-avid lesion on the PET scan (Fig. 2B). The right testis measured 1.4 × 2.3 × 3.8 cm and contained microlithiasis. There was a 1.7 × 1.3 × 1.5 cm ill-defined

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mainly hypoechoic and hypovascular area, in the mid pole of the testis, with no definite mass or abnormal FDG uptake on PET scan. A left radical orchiectomy was performed and demonstrated a slightly atrophic testis with a 1.5-cm hyalinized scar, fibrosis and granulomatous inflammation (Fig. 2C). No viable residual tumor or intratubular germ cell neoplasia was identified.

After an uncomplicated postoperative course, he received four cycles of chemotherapy with etoposide and cisplatin chemotherapy (EP). This regimen was chosen instead of a BEP (bleomycin, etoposide, and cisplatin) or VIP (etoposide, ifosfamide, and cisplatin) regimen because of the patient's age and comorbidities. The patient remained disease-free radiographically after 4 years of follow up, but died from HCV related hepatocellular carcinoma.

Discussion

Gastric involvement by seminoma is extremely rare; with only a few reported cases in the English literature.[1–3] Most of the cases were associated with bulky retroperitoneal disease or occurred late as part of advanced disease. In the case reported by Mesa at el., gastric metastasis was the initial manifestation of the disease. Although the patient showed no size significant adenopathy in the pelvis, retroperitoneum, or mediastinum, a PET scan did show intense uptake in pelvic and retroperitoneal lymph nodes.[3] Here we report a unique case of classic seminoma presenting as a solitary metastasis in the gastric mucosa with neither residual testicular tumor nor lymph nodes metastasis.

Normal serum lactic dehydrogenase (LDH), lack of detectable extragastric disease at the time of the biopsy, and the predominantly mucosal location of the tumor caused the diagnostic challenge in this unusual case. Therefore, the combination of germ cell marker immunostains has been extensively validated for the recognition of seminomas in unusual locations. In this case, the immunoreactivity of the tumor cells to CD117, OCT3/4, PLAP, and D2-40 confirmed the diagnosis of metastatic seminoma.

The clinical management of GCT traditionally relies on the serum biomarkers (α-fetoprotein, HCG and LDH), but these markers are only expressed in 50–60% of cases. So far, serologic tumor markers for germ cell tumors' diagnosis and monitoring have limited value in the diagnosis of pure seminomas. Recent studies have focused on miRNA clusters, identifying miR371 as a potential new serum biomarker, and the plasma miR371 expression predicts GCT with high specificity and positive predictive value.[5]

The "burned-out" phenomenon is defined as the presence of metastatic germ cell tumor with evidence of a regressed testicular primary.[4] Sonographically, the features suggestive of a regressed primary include microlithiasis and ill-defined hypo- or hyperechoic areas, as noted in our patient. Histologically, the regressed testicular primary shows a fibrous scar, with or without intratubular germ cell neoplasia.

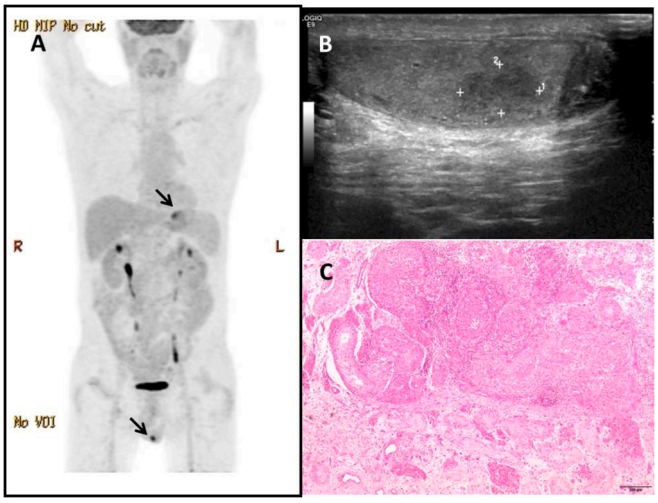

Fig. 2. A, positron emission tomography (PET) scan showing a FDG avid (SUVmax 7.4) focus at gastric fundus, corresponding to the nodular thickening on the CT, and a FDG avid (SUVmax 8.7) focus in the left testicle (arrows). B, scrotal ultrasound showing a 1.3cm ill-defined lobulated hypoechoic solid mass, corresponding to the aforementioned FDG-avid lesion. There is also microlithiasis in the left testis. C, microscopic examination of the left testis demonstrating granulomatous inflammation, fibrosis and hyalinized scar.

Retroperitoneal lymph nodes are thought to be the primary landing sites for testicular germ cell tumors including classic seminoma. Consistent with this statement, the previously reported gastrointestinal involvement of GCT were all concurred with or directly involved by retroperitoneal lymph nodes metastasis. However, the current case presented as a solitary metastasis in the gastric mucosa with no evidence of residual testicular tumor or pelvic/retroperitoneal lymph nodes metastasis. The metastatic route of the seminoma in this case is unknown, although the mucosal location implies a hematogenous route, contrary to serosal nodules, secondary to peritoneal carcinomatosis.

In summary, we report a unique case of classic seminoma presenting as gastric mucosal metastasis. The diagnosis of this case was complicated by no residual testicular tumor or pelvic/retroperitoneal lymph nodes metastasis and no available specific serum markers. Oncologists and pathologists should be aware of these rare manifestations of GCT when encountering a poorly differentiated malignancy which appears to be a primary tumor of an unusual site of GCT metastasis.

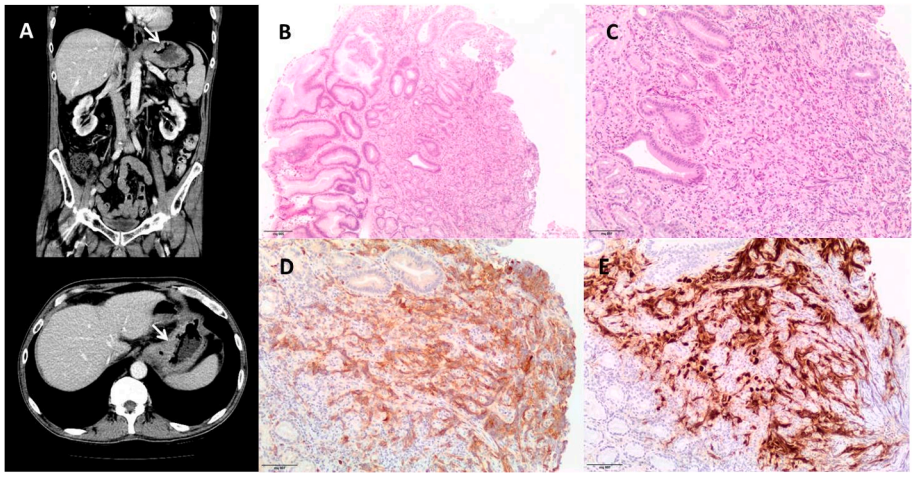

Fig. 1. A, the coronal (upper) and axial (lower) abdominal CT with iv-contrast demonstrated nodular thickening of the gastric fundus and gastroesophageal junction B, microscopic examination at low magnification showing fragments of gastric mucosa focally being infiltrated by a neoplastic process. C, microscopic examination at high magnification showing the malignant cells with large nuclei, prominent nucleoli and a small amount of basophilic-to-clear cytoplasm. D, the immunostain showing the tumor cells positive for CD117. E, the immunostain showing the tumor cells positive for OCT3/4.

Compliance with ethical standards

This case study was approved by the institutional review boards of University of British Columbia. The patient passed away, so consent could not be obtained. For the purpose of protection of the patient, any identifiable attributes were anonymized in the manuscript and its supplementary files.

Funding disclosure

None.

Contributions

Ren Yuan, Chen Zhou and Gang Wang conceived and designed the study, wrote, edited and reviewed the manuscript. All authors collected data, edited and reviewed the manuscript. All authors gave final approval for publication. Gang Wang takes full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript.

Declaration of competing interest

The authors report no conflict of interest.

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