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CASE REPORT

Case Report: Germ cell tumor presenting as cecal mass

[version 1; peer review: 2 approved with reservations]Venkata Satish Pendela ¹, Anisleidys Munoz¹, JulieAnn Warner²,
Roopa Yarlagadda¹¹Internal Medicine, Rochester General Hospital, Rochester, NY, 14621, USA²Pathology, Rochester General Hospital, Rochester, NY, 14621, USA

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Abstract

Extra gonadal germ cell tumors most frequently occur in the anterior mediastinum, retro-peritoneum, and pineal and suprasellar regions. The infrequency of its occurrence inside gastrointestinal tract makes it an arduous diagnostic challenge.

A 23 year old male with no significant past medical history presented to the emergency department with increasing abdominal pain, diarrhea, episodic vomiting for 3 weeks. Review of systems was positive for melena and shortness of breath on exertion. Fullness and irregularity along with tenderness was noted around the right iliac region.

CT scan (computed tomography) of the abdomen revealed a cecal mass with multiple metastases to liver, lungs and abdominal lymph nodes. Colonic endoscope was performed but it could not be advanced beyond the cecal mass. Biopsies from the mass were reported as poorly differentiated metastatic carcinoma. During the course of hospitalization, he developed symptomatic small bowel obstruction with perforation. Colonic resection was performed and histology showed Germ-Cell Tumor. Beta HCG level was 118789 IU/L suggestive of a non-seminomatous germ cell tumor. Ultrasound of the scrotum, MRI brain (magnetic resonance imaging) and CT scan of the chest did not reveal a primary tumor. Chemotherapy was started with Bleomycin, Etoposide and Cisplatin after which beta human chorionic gonadotropin (HCG) levels dropped dramatically. His hospital course got complicated with neutropenic sepsis with shock which progressed to multi-organ dysfunction and unfortunately, he succumbed to the disease burden.

This case demonstrates one of the rare presentations of extragonadal germ cell tumors and the diagnostic challenges associated with it. Very few cases have been reported in the literature, and none of them presented as a cecal mass. Early recognition of this presentation will help in reducing the tumor burden and the mortality associated with it, as germ cell tumors are highly susceptible to chemotherapy.

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1. **Joost Blok** , University Medical Center
 Utrecht, Utrecht, The Netherlands
 Netherlands Cancer Institute, Amsterdam,
 The Netherlands

2. **Shi-Ming Tu**, The University of Texas MD
 Anderson Cancer Center, Houston, USA

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

germ cell tumor, cecal mass, chemotherapy

Corresponding author: Venkata Satish Pendela (satish.pendela@rochesterregional.org)

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Introduction

Extra gonadal germ cell tumors (EGCTs) are rare and account for 1–3% of all the gonadal tumors^{1–3}. Several mechanism have been described, including possible migration of pluripotent stem cells, which convert to germ cells during embryonic development. The usual sites of EGCTs are mediastinum, retro-peritoneal organs, and pineal gland^{1–4}. Involvement of gastrointestinal tract is rare and is very unlikely in the absence of a primary elsewhere. Shogbesan *et al.* reported an EGCT presenting as duodenal mass with primary tumor identified in the testis. There are a few cases reported in literature without an identifiable primary in the gonads; none of which presented as a cecal mass^{1,2}.

Case presentation

A 23 year old Caucasian male who worked part-time as a waiter at a restaurant, with no significant past medical history presented during the fall of 2018 to the emergency department with increasing abdominal pain, diarrhea, and episodic vomiting for 3 weeks. Review of systems was positive for melena and shortness of breath on exertion. Family history was only relevant for an aunt who died from lung cancer. He had a five pack year smoking history and smokes marijuana socially. On admission, he was tachycardic and febrile, and exam revealed cachexia with bitemporal wasting. Fullness and irregularity in the right ileac fossa with associated tenderness was noted on palpation of the abdomen. See [Figure 1](#) for full timeline.

Investigations

Computed tomography (CT) of the abdomen revealed a cecal mass with multiple metastases to liver, lungs and abdominal lymph nodes ([Figure 2](#), [Figure 3](#)). Colonoscopy was performed, but the endoscope was unable to be advanced beyond the cecal mass. The tumor was poorly differentiated, and urothelial carcinoma was in the differential due to the positive GATA3 immunohistochemical staining. Liver biopsy reported an undifferentiated metastatic carcinoma. Beta HCG (human chorionic gonadotropin) level was 118,789 IU/L. After the

elevated beta HCG level was detected, the colonic specimen was stained with the markers for germ cell tumors (beta HCG and PLAP) which was positive. Ultrasound of the scrotum was done to look for a primary tumor, which was negative. Magnetic resonance imaging (MRI) of the brain and a CT scan of the chest did not reveal any growth in the pineal gland or mediastinum, respectively.

Treatment

Chemotherapy was started with Bleomycin (30 units/wk IV on days 1, 8 and 15 regimen), Etoposide (100 mg/m²/day IV) and Cisplatin (20 mg/m²/day IV on days 1–5); given the high Beta HCG levels and deteriorating clinical status. Within 7 days of starting this regimen, beta HCG levels dropped dramatically to 31,163 IU/L. During the course of hospitalization the patient developed symptomatic small bowel obstruction with perforation, which was confirmed with a CT scan. Colonic resection was performed. The resected mass was identified to be germ cell tumor as it picked up beta HCG, SALL4, GATA3, OCT 4 as well as PLAP stains on histo-path exam ([Figure 4](#), [Figure 5](#)).

Outcome and follow-up

The patient responded to chemotherapy initially with a drop in HCG levels; however, hospital course was complicated with tumor lysis syndrome and neutropenic sepsis, which progressed to multi-organ dysfunction. He required mechanical ventilatory support along with vasopressors for blood pressure support. As a result of deterioration, the family opted for comfort care measures. The patient expired 36 hours later. Even though his cancer burden was responding to chemotherapy, he unfortunately succumbed from complications of the treatment.

Discussion

EGCTs are considered metastatic from an occult or “burned out” gonadal cancer if a primary testicular tumor is not apparent. An ultrasound of the scrotum should always be performed to rule out a testicular tumor. A gonadal biopsy to rule out such tumor is not recommended⁵. The patient in the present study

Figure 1. Patient timeline. CT – computed tomography, HCG - human chorionic gonadotropin, MRI – magnetic resonance imaging.

Figure 2. Cecal mass with multiple metastases (Computer tomography of the abdomen).

Figure 3. Liver metastases (Computer tomography of the abdomen).

Figure 4. Hematoxylin and eosin stain of the cecal mass.

Figure 5. Beta HCG (human chorionic gonadotropin) stain of the cecal mass.

was found to have an EGCT in the cecum and colon. Similar to GCTs, EGCTs are sensitive to radiotherapy and chemotherapy.

Currently, common drugs used for chemotherapy include cisplatin, etoposide and bleomycin⁶⁻⁹. Our patient received these medications along with surgery which helped in reducing his tumor burden. The International Germ Cell Cancer Collaboration Group (IGCCCG) places the patients into poor prognosis category if they are found to have a primary tumor or visceral metastases elsewhere apart from the lungs and retro peritoneum. The 5-year survival rate in such patients is 48%^{4,10-12}.

This case demonstrates one of the rare presentations of extra-gonadal germ cell tumors and the diagnostic challenges associated with it. Early diagnosis entails high index of suspicion, especially in young males presenting with tumor of unknown origin. Early recognition of this presentation will help in reducing the tumor burden and the mortality associated with it. It also allow for early treatment, which usually entails surgery (for accessible tumors) along with chemotherapy. However, our knowledge about these tumors and their presentations is still limited, and as seen in this patient, treatment can result in complications well. This limitation warrants the need for studies on EGCTs and their management.

Conclusion/learning points/take home messages

- Gonadal tumors should be among the differentials in patients presenting with abdominal mass, especially in younger adults.
- The importance of this case is to identify a constellation of symptoms, obscurities, diagnostic difficulties, adverse effects of treatment of an extra gonadal germ cell tumor.
- The authors would encourage testing with Beta HCG in young males presenting with a tumor of unknown origin.

- The authors would also encourage a multidisciplinary approach with surgery and early initiation of chemotherapy in such patients to control the disease burden.
- This report also increases awareness that one should be watchful for complications after implementing treatment with chemotherapy, as early detection of complication may help prevent negative outcomes.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the parent of the patient.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

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Version 1

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Shi-Ming Tu

Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

This is an unfortunate 23 yo diagnosed with an extragonadal GCT (EGGCT) arising from the cecum and metastatic to the liver, lungs, and abdominal LN. His HCG was 118,789. He received and responded to standard BEP x1, but developed and succumbed to complications as a result of treatment. Specifically, he developed neutropenic sepsis, bowel perforation, and multiorgan failure. This case has important educational value.

1. The first sentence in Discussion is incorrect: "EGGCTs are considered metastatic from an occult or "burned out" gonadal cancer."
One of the acceptable criteria for a diagnosis of primary EGGCT (according to Abell MR *et al.*, Cancer, 1965)¹ are:
 - Absence of any detectable tumor or subsequent appearance of a tumor in either testis;
 - An encapsulated lesion without nodal involvement;
 - The lesion is located high in the retroperitoneum with adjacent lymph node involvement but without involvement of the lower aortic, iliac, or pelvic lymph nodes.
2. Pathology is incomplete. Please clarify if the report stated that the tumor was choriocarcinoma or adenocarcinoma with choriocarcinomatous differentiation. Of note, a patient with EGGCT arising from the GU tract (kidney) with choriocarcinomatous differentiation was curable with a modified chemotherapy regimen (Msaouel P *et al.*, Clin Genitourin Cancer 2017).²
3. Most extragonadal GCT arising from the GI tract are yolk sac tumors, which produces AFP. To be complete, what were his AFP and LDH levels before chemotherapy?
4. Often enough when patients are very debilitated and especially when they have a tumor that is likely to respond quickly to chemotherapy and when the tumor regresses before the bowel heals, they may develop bowel perforation. When they also become neutropenic at the same time, this is when catastrophic sepsis occurs.
To ensure response but avoid neutropenia and other complications, it is prudent to give

gentle upfront chemotherapy (such as BOP, published by Shamash J *et al.*, BJUI, Nov 2019)³ in such cases.

5. Needs to better define and confirm tumor lysis syndrome in the setting of a patient with a solid tumor rather than hematological malignancy, who has received nephrotoxic chemotherapy and is septic with multiorgan dysfunction.

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Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 23 July 2020

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Joost Blok ¹ Department of Oncological Urology, University Medical Center Utrecht, Utrecht, The Netherlands² Netherlands Cancer Institute, Amsterdam, The Netherlands

This is a case of a young man presenting with a metastasized extragonadal germ cell tumor. The case is impressive and has educational value. The report is well-written but I have the following questions/suggestions:

1. What was the timeline (days since presentation) for the various diagnostic procedures? E.g. at how many days after presentation was beta HCG checked?
2. What was the level of other markers for germ cell tumor (AFP, LD)?
3. Was the histology of the GCT nonseminoma or seminoma? Histology of liver biopsy showed undifferentiated carcinoma, which suggest nonseminoma (this would also be in line with the high levels of HCG). Was the histology of liver biopsy/colonic resection revised? Any presence of subtypes of nonseminoma (e.g. embryonal carcinoma, choriocarcinoma).
4. I would suggest to revise the first and third learning point. The first learning point can be stated more firmly. My suggestion: Testicular or extragonadal germ cell tumor should always be considered in young males presenting with an abdominal mass. The third learning point can be moved up to the second spot. I would suggest to rewrite it as follows: The diagnostic workup of young males presenting with an abdominal tumor or tumor of unknown origin should always include workup for germ cell tumor (beta-HCG, AFP, LD, scrotal palpation and testicular ultrasound).
5. I believe the first sentence of the Discussion is not correct. An EGCT originates outside the gonads and therefore does not originate from a (burned out or occult) testicular tumor. Please include a statement that although it is a cancer of the germ cells, it can also originate in the retroperitoneum or mediastinum.
6. The Discussion would benefit from a more extensive description of (E)GCT. What is the survival rate for EGCT? Is it better or worse compared to testicular GCT? I think it is also important to note that GCT is the most common cancer type in young men, but that the extragonadal subtype is rare (of course the testicular subtype being much more common). Is the incidence of GCT and EGCT known for this age category?
7. I would also suggest a more extensive discussion of tumor lysis syndrome and neutropenic sepsis. How common is this? How should this be treated according to the guidelines? How often succumb patients to this condition?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Testicular germ cell tumor

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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