



Extra-gonadal germ cell tumor

A. ElRifai^{*}, S. Akel

Department of Surgery, American University of Beirut Medical Center (AUBMC), Beirut, Lebanon

ARTICLE INFO

Keywords:

Abdominal mass
Yolk sac
Extra-gonadal
Resection

ABSTRACT

This is a case report of a two years old girl that presented to us with an abdominal mass diagnosed on biopsy as Yolk sac tumor with elevated with Alpha fetoprotein. She received chemotherapy (3 cycles) then underwent definitive resection with en-bloc resection of the tumor, involved ileum and abdominal wall. Intraoperative findings confirmed that it was an extra-gonadal tumor. The patient did well postoperatively and received the fourth cycle of chemotherapy postoperatively and was committed for close observation.

1. Introduction

Germ cell tumors are rare tumors that arise from primordial cells and occurs commonly in the gonads and rarely in extra-gonadal locations [1, 2]. Few cases have reported on primary gastrointestinal locations for extra-gonadal germ cell tumors (EGGCTs). Here is a case report of primary ileal EGGCTs.

2. Case presentation

2 years old girl previously healthy presented to our institution for evaluation of an abdominal mass. History goes back to one and a half months prior to presentation when the patient started having change in bowel habits with alternating constipation and diarrhea. At the time the mother noticed an abdominal mass that became more visible upon straining. The patient was also complaining of abdominal pain. The pain became a daily occurrence; however, it wasn't awakening her from sleep nor requiring analgesics. There was no associated weight loss nor vomiting but there was decrease oral intake with more predilection for liquids. She was seen by her physician who ordered an ultrasound that showed an isoechoic mainly solid mass with cystic component and internal vascularity, the mass measured 9.2*5.7 cm.

She was referred to our children's cancer center for further evaluation and management.

On initial evaluation the patient had a normal metabolic profile with a B-HCG of 0.7 and LDH 405 however her Alpha fetoprotein was 65,817 U/mL. A CT scan was done that showed a large heterogeneously enhancing abdominal mass (Fig. 1a and b) measuring 9.1 x 6.1 x 9.7 cm with no calcifications. The mass displaces the bowel laterally and

posteriorly with no evidence of bowel obstruction. It is inseparable from the abdominal wall in the left lower quadrant with suggestion of invasion into the abdominal wall.

A CT guided biopsy was done that showed malignant solid tumor consistent with a Yolk Sac Tumor.

The patient underwent a right external jugular polysite insertion and was started on chemotherapy (Bleomycin, Etoposide and Cisplatin). After 3 cycles a repeat α FP decreased to 158.9 U/mL and a CT scan (Fig. 2a and b) was done to evaluate for response and it showed a significant interval decrease in the size of the previously seen heterogeneously enhancing cystic and solid abdominal mass, now measuring approximately 3.2 x 4.2 x 4.3cm with appearance of calcifications. The patient was admitted thereafter for surgical resection. She underwent an exploratory laparotomy with En-bloc resection of large left intra-abdominal tumor with resection of 10 cm of ileum and primary ileo-ileal anastomosis. She underwent excision of multiple jejunal and ileal mesenteric deposits with partial omentectomy.

At operation, there was a small amount of peritoneal fluid initially that was sampled and sent for cytology (Negative for malignancy). Then the mass that was identified in the left peri-umbilical region and was dissected carefully and part of the internal oblique and transversus abdominis on the left side had to be removed with a 1 cm margin to free the tumor from the abdominal wall and to ensure an R0 resection. After identification of the mass, it was evidently involving the proximal ileum (Fig. 3) and a 10 cm segment of the ileum had to be resected en-bloc with the mass along with part of the omentum. Sampling of the mesenteric lymph nodes was done. A 1.5 x 1 cm deposit was identified also in the base of the mesentery of the ileum that was removed en-bloc without insult to the ileal segment. An ileo-ileal primary end-to-end anastomosis (Fig. 4). Further examination of both ovaries and uterus showed no

^{*} Corresponding author. American University of Beirut Medical Center, Riad El-Solh, Beirut, 1107 2020, PO Box: 11-0236, Lebanon.

E-mail addresses: ae80@aub.edu.lb, arwarifai00@gmail.com (A. ElRifai).

<https://doi.org/10.1016/j.epsc.2020.101505>

Received 9 May 2020; Received in revised form 19 May 2020; Accepted 21 May 2020

Available online 26 May 2020

2213-5766/© 2020 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

List of abbreviations:

B-HCG	Beta human chorionic gonadotropin
α FP	Alpha fetoprotein
LDH	Lactate dehydrogenase
CT	Computerized tomography
EggCTs	Extra-gonadal germ cell tumors

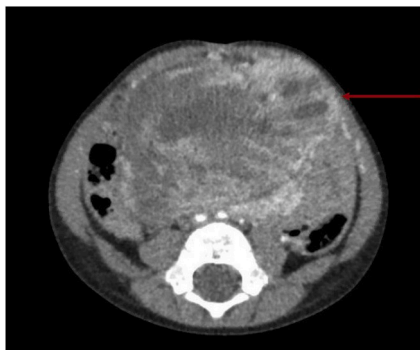


Fig. 1a. CT scan, Axial cut, showing the tumor prior to initiating treatment. Red arrow: Showing the tumor invading the abdominal wall musculature. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



Fig. 1b. CT scan, Coronal cut, showing the tumor prior to initiating treatment. Red arrow showing mass effect of the tumor on the small and large intestines. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

obvious microscopic disease. The laparotomy wound was closed without any drains placed there. The specimen was sent for pathology (Fig. 5).

The final pathology showed residual germ cell tumor in a background of extensive (>95%) therapy related changes and negative surgical margins. The mesenteric nodule excision showed therapy related changes. Omentum and Lymph nodes were negative for malignancy.

The patient did well postoperatively and was tolerating diet by day 4. On day 6 she received the fourth and last cycle of chemotherapy and was discharged home by day 10 and planned for close monitoring. On follow up a repeat α FP was taken and was normal (2.0 U/mL).

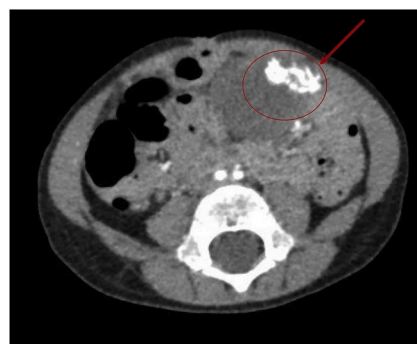


Fig. 2a. CT scan, Axial cut, showing the decreased size of the tumor after three cycles of treatment.

Red arrow: Showing the new calcifications that appeared within the tumor after starting treatment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

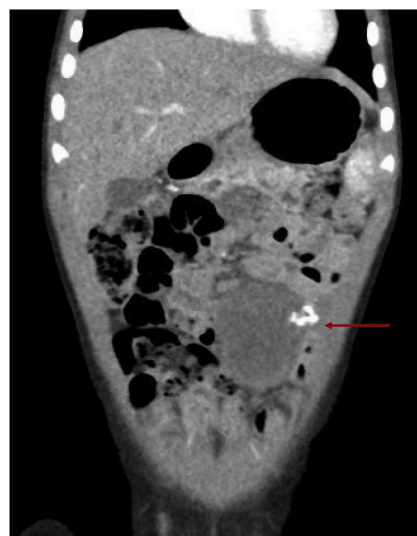


Fig. 2b. CT scan, Coronal cut, showing the tumor after three cycles of treatment.

Red arrow: Showing the new calcifications that appeared within the tumor after starting treatment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Discussion

Germ cell tumors arise from primordial cells and occur primarily in the gonads however rarely so do they occur in extra-gonadal locations [1]. They are considered uncommon and account for around 3% of all pediatric tumors [2]. Extra-gonadal germ cell tumors also referred to as EggCTs are considered to be a different entity with a distinctive biological course even though histologically they are similar to gonadal germ cell tumors [3]. Several other tumors fall under the umbrella of EggCTs such as teratomas, choriocarcinoma, yolk sac tumors and dysgerminomas and seminomas [3]. They can arise in anatomically variable locations and most often occur in any midline structure in the body [1] with no evidence of a concomitantly associated primary gonadal tumor [3].

The incidence is estimated to be 1.8–3.4/1million with a higher incidence amongst males than females [1]. The most frequent extra-gonadal sites were mediastinum among males and placenta among females [1]. EggCTs have been reported to occur in the mediastinum and can infiltrate vital structures such as the heart [4] they can also occur in the pelvis and vulva [5]. They have been reported in the

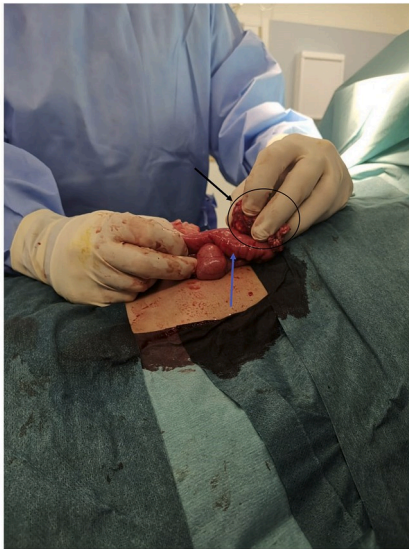


Fig. 3. Tumor involving the ileum.
Black arrow and circle: Showing the tumor. Blue arrow: Showing the segment of ileum involved with tumor. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

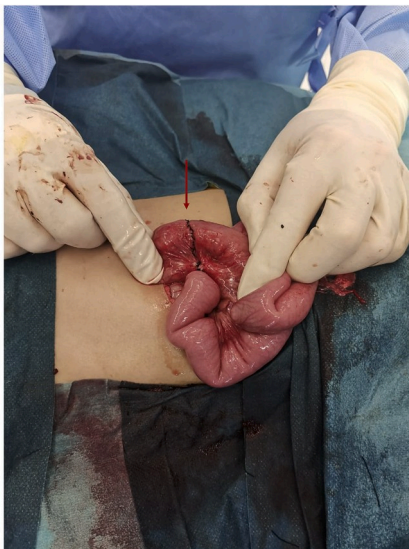


Fig. 4. Connell manner ileo-ileal primary end-to-end anastomosis.
Red arrow: Showing the suture line after completing the anastomosis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

gastrointestinal tract namely retroperitoneal organs such as duodenum and colon and thus can present with obstruction or gastrointestinal bleeding [6,7].

For establishing diagnosis, it is important to have tissue sampling either via a tru-cut biopsy which is preferable to a Fine needle aspiration to allow for histopathologic and immunohistochemical examination [3]. Moreover, tumor markers have an essential role in diagnosis and follow up. The most commonly used markers are α FP, β -HCG and lactate dehydrogenase (LDH). Klinefelter syndrome is a known predisposing factor [8]. Lastly, prognosis is dependent on age, the subtype of the tumor and the anatomical location and its effect on adjacent organs [3]. Yolk sac tumors as in our case are a subcategory of EGGCTs and they are grossly described as large tumors with mixoid and necrotic areas [3]. It is estimated that 10%–15% of yolk sac tumors will be of extra-gonadal



Fig. 5. En-bloc resection of germ cell tumor with involved ileal segment and abdominal wall.
Black arrow: Showing the tumor as part of the en-bloc resection specimen. Red arrow: Showing the segment of abdominal wall that was resected. Blue arrow: Showing the segment of ileum that was resected. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

origin [5]. Adult extra gonadal germ cell tumors have been reported in a similar variety of anatomic locations [9,10].

Several theories as to the origin of the extra-gonadal germ cell tumors exist. One of the accepted theories refer to the misplacement of germ cells during their embryologic migration and thus result in germs cell tumors in various locations. Another accepted theory is that EGGCTs are the result of an anomalous differentiation of pluri-potent mucosal cell [7].

The treatment is multimodal depending on the stage at diagnosis. If the tumor is at stage I upfront surgical excision is the mainstay of treatment. If risk for incomplete resection is present, then Platinum based chemotherapy is given prior to resection. Similarly, chemotherapy is given after resection for residual disease [11].

It is imperative to identify correctly foci of yolk sac tumors within other germ cell tumors on final pathology as it portends an aggressive course [12]. This is usually done via immunohistochemical examination for specific yolk sac tumor markers. These are typically AFP and glypican-3. Other markers exist that can help for recognition of uncommon variants such as CDX2 and TTF-1 [13].

4. Conclusion

We conclude that Extra-gonadal germ cell tumors should remain on the differential diagnosis of intra-abdominal, pelvic and retroperitoneal tumors in the pediatric age group. The surgeon should be aware of the challenges of accurate diagnosis and its implications on therapy.

Patient consent

Consent to publish the case report was obtained from the patient's mother in view of being below 18 years of age. This report contains radiology images as well as intraoperative images without identifiers for which consent was obtained as well.

Funding

No funding or grant support

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The following authors have no financial disclosures: A.E, S.A.

References

- [1] Stang B, et al. Gonadal and extragonadal germ cell tumors in the United States, 1973–2007. *Int J Androl* 2012 August;35(4):616–25. <https://doi.org/10.1111/j.1365-2605.2011.01245.x>.
- [2] Vineeth G, et al. Pure primary extragonadal retroperitoneal yolk sac tumour in a young child: a case report. *J Clin Diagn Res* 2017 May;–11(5):ED09–11. <https://doi.org/10.7860/JCDR/2017/24892.9781>.
- [3] Ronchi A, et al. Extragonadal germ cell tumors: not just a matter of location. A review about clinical. *Mol.Pathol.Featur.Cancer Med.* 2019;8:6832–40. <https://doi.org/10.1002/cam4.2195>.
- [4] Imaniar R, et al. Mediastinal yolk sac tumor infiltrating the heart. *Exp Oncol* 2018; 40:82–4 (March).
- [5] Euscher E, et al. Unusual presentations of gynecologic tumors extragonadal yolk sac tumor of the vulva. *Arch Pathol Lab Med* 2017;141:293–7. <https://doi.org/10.5858/arpa.2016-0151-SA>.
- [6] Kucukonera M, et al. Germ cell tumor located in gastrointestinal system: a report of two cases. *World J Oncol* 2012;3(3):134–7.
- [7] Bansal A, et al. extra-gonadal yolk sac tumor of the sigmoid colon: a rare entity. *Clin Cancer Investig J* 2016;5:259–61.
- [8] Shinagare A, et al. Adult extragonadal germ cell tumors. *AJR* October 2010;195.
- [9] Zeremski V, et al. Diagnostic and therapeutic challenges in extragonadal yolk sac tumor with hepatoid differentiation: a case report. *Mol.Clin. Oncol.* 2017;6:79–82.
- [10] Dede M, et al. Extragonadal yolk sac tumor in pelvic localization. A case report and literature review. *Gynecol Oncol* 2004;92:989–91.
- [11] Horton Z, et al. Pediatric germ cell tumors. *Surgical Oncology* 2007;16:205–13.
- [12] Shojaei H, et al. High-level expression of divergent endodermal lineage markers in gonadal and extra-gonadal yolk sac tumors. *Mod Pathol* 2016;29:1278–88.
- [13] Nogales F, et al. Yolk sac tumours revisited. A review of their many faces and names. *Histopathology* 2012;60:1023–33. <https://doi.org/10.1111/j.1365-2559.2011.03889.x>.