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An Unusual Incidental Finding: Epithelioid Trophoblastic Tumor (ETT) on the Site of Surgical Repair of a Ventral Incisional Hernia after a Caesarean Section

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Abstract

Epithelioid Trophoblastic Tumor is a rare form of gestational trophoblastic neoplasia only reported in approximately 110 cases in literature. We present the case of a 50 years old woman incidentally diagnosed with a ETT on the site of surgical repair of a ventral incisional hernia after a Caesarean section.

Keywords: Epithelioid trophoblastic tumor; ETT; Ventral incisional hernia; Gestational trophoblastic neoplasia; GTN

Introduction

Epithelioid Trophoblastic Tumor (ETT) is a rare form of gestational trophoblastic neoplasia (GTN), it arises from chorionic leave-type extravillous trophoblasts and it usually occurs in women of reproductive age as a sequela of any gestational event. The most common presenting symptom of ETT is abnormal vaginal bleeding, despite it can also manifest with amenorrhea or extra uterine disease due to metastasis. This neoplasia is commonly associated with mild elevation of serum β hCG (beta human chorionic gonadotropin) [1].

We present the case of a 50 years old woman incidentally diagnosed with a ETT on the site of surgical repair of a ventral incisional hernia after a Caesarean section and we discuss the diagnostic path and the medical treatment performed.

Case Presentation

In 2016 a 50-year-old woman presented to general surgery routine visit after a first surgical correction of a ventral incisional hernia with the placement of preperitoneal mesh and reconstructive plastic of the rectus muscles of the abdomen for a suprapubic laparocele on a previous cesarean section scar. Her physical exam was notable for a wound dehiscence with secretion of foul-smelling purulent material in the site of the previous laparoplasty surgery.

Her past medical history was significant for heterozygosity of the prothrombin gene with factor II overexpression and increased risk of thrombosis. Her obstetric history was suggestive for two full term pregnancies (1998, 2006) one of which was twin and a voluntary abortion; both pregnancies ended with a cesarean section. She denied intermenstrual bleeding, post-coital bleeding and any kind of vaginal secretion.

Because of the findings at the physical exam, she underwent abdomen ultrasound and CT scan, revealing a modest thickening of the subcutaneous tissue in the median pelvic area and at the anchorage of the surgical mesh. It was subsequently posed the indication to a second surgery in which were performed an excision of the fistulous tract and a toileting and repackaging of the wound. After a few months the patient developed a recurrence of fistulization of the surgical scar shown off with secretion of purulent material from the wound; due to this the patient underwent a MR of the abdomen and pelvis which was conclusive for a flogistic process in the site of the mesh and of the anterior part of the rectus muscles of the abdomen.

Consequently, in December 2017, the patient sustained a new surgery in which the part of the abdominal wall with a triple fistulous orifice and the infected mesh were removed and a direct surgical correction of the incisional hernia was performed. The microbiological culture of the mesh was positive for the growth of Staphylococcus Aureus and Prevotella Bivia. The pathology specimen was consistent with epithelioid trophoblastic tumor and at immunohistochemistry its cells were positive for cytokeratin MMFF116, P63, PLAP, β-catenina, alpha inhibin staining, Ki67 was reported to be 25-30% and the surgical resection margins were positive for tumor.

Due to the rarity of this neoplasia, the specimen had also been reviewed by a referent pathologist who confirmed the diagnosis. Based on this finding an evaluation of the oncological hematic markers CEA, CA 125 and CA 15.3 was required, all of them resulted negative. β -HCG value was in a normal range. The genetic analysis of the neoplasia di not confirm the gestational origin deriving from the last pregnancy even though it was considered the most probable.

Upon completion of the diagnosis and with the aim of staging the disease the patient underwent hysteroscopy with biopsy samples that did not reveal localization of the disease, and a CTA (Computed Tomography Angiography) of the abdominal and thoracic vessels which demonstrated the presence of some nodules in the anterior mesenteric area, posteriorly to the right rectus muscle, compatible with localization of the disease.

She has subsequently been evaluated by two different oncologic centers which proposed a surgical treatment consisting of the demolition and the reconstruction of the abdominal wall versus a conservative chemotherapy treatment. The patient wished to pursue the chemotherapy treatment. From May to September 2018, she had four chemotherapy cycles with cisplatin, paclitaxel and etoposide, with an imaging evidence of regression of all the nodules previously described (Table 1).

Table 1: Chemotherapy regimen.

	Regimen	**Schedule**
Day 1	Dexamethasone	20 mg oral (12 h and 6 h before paclitaxel)
	Dexamethasone	20 mg oral (6 h before paclitaxel)
	Cimetidine	30 mg in 100 ml NS over 30 min i.v.
	Chlorphenamine	10 mg bolus i.v.
	Paclitaxel	135 mg/m^2 in 250 ml NS over 3 h i.v.
	Mannitol	10% in 500 ml over 1 h i.v.
	Cisplatin	60 mg/m^2 in 1 l NS over 3 h i.v.
	Posthydration	1 l NS + KCl 20 mmol + 1 g $MgSO_4$ over 2 h i.v.
Day 15	Dexamethasone	20 mg oral (12 h and 6 h before paclitaxel)
	Cimetidine	30 mg in 100 ml NS over 30 min i.v.
	Chlorphenamine	10 mg bolus i.v.
	Paclitaxel	135 mg/m^2 in 250 ml NS over 3 h i.v.
	Etoposide	150 mg/m^2 in 1 l NS over 1 h i.v.

Patient's oncologic follow up consisted of CT scans every six months.

After two years of PFS (Progression Free Survival), in 2020 she was diagnosed at the CT-PET scan with liver lesions suspected for secondary localizations. For a better characterization of these findings the patient underwent a liver MRI and a liver biopsy with evidence of metastasis of epithelioid trophoblastic tumor positive for cytokeratin CAM 5.2, P63, PLAP, alpha-inhibin and negative for SOX-10 staining. At this point serum β -HCG value started to increase up to 14.4 mUI/ml (Figure 1).

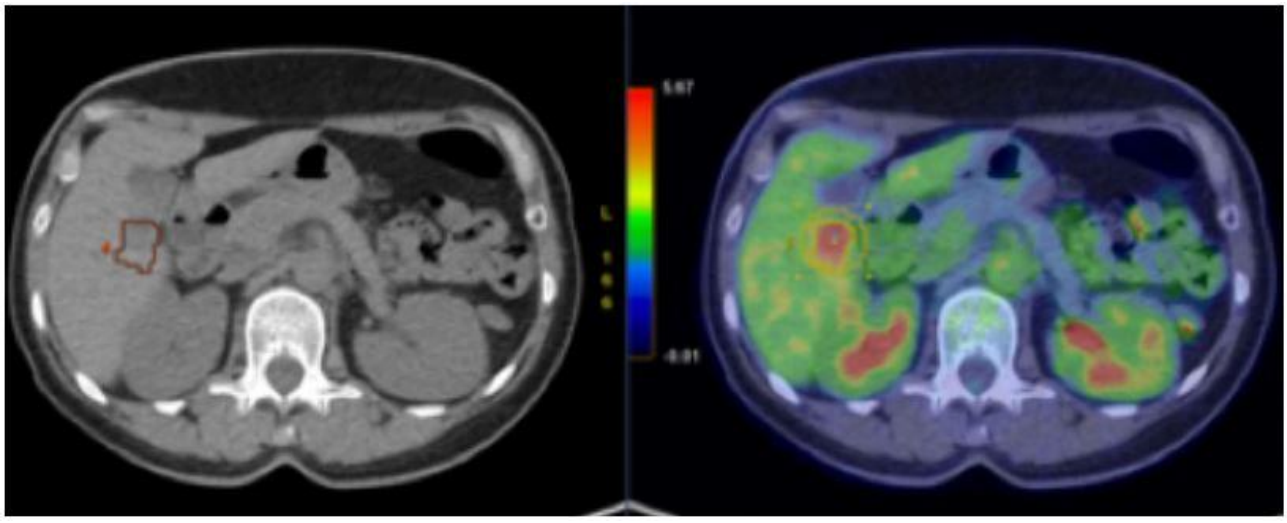

Figure 1: Liver lesion found at the CT.

Based on these latest findings, the patient was prospected of a combined general and gynecological surgery in order to perform an exeresis of the hepatic lesions and bilateral prophylactic salpingooophorectomy and hysterectomy. However, peritoneal carcinosis was found during the procedure, therefore in absence of an informed consent and lack of knowledge of the natural history of this histological form, it has been decided in agreement with the referent oncologist, to postpone the hysteroannexectomy and peritonectomy, with the reservation of reconsidering it after a chemotherapy treatment and the opinion of a centre with experience in this neoplasia. Consequently, the surgery was limited to the removal of the gallbladder, the known lesion in the hepatic segment 4b and omentectomy.

The pathology specimen confirmed that the excised lesions in the hepatic and omental areas were consistent with metastases of epithelioid trophoblastic tumor. An analysis of the immunophenotypic profile of the protein of mismatch repair (MLH1, PMS2, MSH2, MSH6) was also carried out and it revealed a tumor with stability of microsatellites. In addition to that an evaluation of the expression of PD-L1 on tumor cells was carried out, revealing an overexpression of this protein on tumor cells.

A month after the last surgery the patient came to the ER complaining with foul-smelling greenish secretion from the surgical wound, consequently she underwent a CT scan which showed the presence of collections in the right flank, in the pelvic area and in the subhepatic region. The interventional radiologists then positioned a percutaneous drainage to evacuate the collection in the right flank. The patient was also given antibiotic therapy.
Nowadays the patient has started a new chemotherapy regimen with 6-8 cycles of cisplatin, etoposide, methotrexate and actinomycin-D [8]. Considered the overexpression of protein PD-L1 on the tumoral cells, oncologists also recommended the use off-label of Pembrolizumab in order to obtain a major regression of the disease.

Discussion

To our knowledge, this represents one on the few reported case of an ETT on the site of a surgical Caesarian scar. Due to the increase in Caesarian sections performed in recent years, there has been an increase in the number of similar cases reported, especially in some countries, such as China. Because of the rarity of this tumor and due to the non-specific symptoms, there is a high rate of misdiagnosis at the initial presentation as showed in a 2018 study [2].

In the case of our patient, the neoplasia presented with totally nonspecific symptoms and without suspected lesions in the uterus and ovaries. The initial presentation of the disease brought to think that it could be an infection or a dehiscence of the wound. Even though there aren't any specific guidelines for the treatment of ETT, some authors suggested that surgery seems adequate for early-stage disease with a shorter interval from the latest pregnancy. Advanced-stage disease requires a combination of treatment modalities [2]. Adjuvant chemotherapy should be considered for patients with advanced stage or with incomplete surgical resection, however the optimal chemotherapy regimen or treatment duration remains unknown [3].

Although our patient had poor prognostic factors (advanced-stage disease and an interval of >48 months since the antecedent pregnancy) and she was a right candidate for a demolitive surgery of the abdominal wall and possible chemotherapy, she decided to adopt the conservative treatment based on only chemotherapy. This choice could have led to a non-optimal control of the disease and its consequent recurrence and metastasis.

Conclusion

The presence of GNT, including ETT, should be taken into consideration in any fertile age woman with abnormal vaginal bleeding and raised serum β -HCG, especially after an antecedent pregnancy event [4]. Owing to its rarity and nonspecific symptoms, GNT located in the cesarean scar is prone to misdiagnosis. In patients without typical manifestations, the definitive diagnosis often relies on pathology [2].

In consideration of the peculiarity of the tumor described, ETT should be treated in a center with experience on this kind of disease.

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