Treatment of Metastatic Placental Site Trophoblastic Tumor in the setting of Pulmonary Arteriovenous Malformations

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INTRODUCTION

- Placental Site Trophoblastic Tumor (PSTT) is an extremely rare form of Gestational Trophoblastic Disease
- PSST can occur after any gestational event, caused by abnormal proliferation of the intermediate trophoblast at the placental implantation site
- Slower growing than choriocarcinoma, but can metastasize through lymphatic system
- Treatment traditionally involves surgery for local disease and chemotherapy for metastatic disease

CASE PRESENTATION

- 34-year-old G2P1 woman presented to her Ob/Gyn with vaginal mass
- 7 months prior, underwent c-section at 27 weeks for preeclampsia with severe features and HELLP syndrome
- Abdominal ultrasound at presentation showed enlarged uterus with dilated varicose vessels concerning for vascular malformation (Figure 1)
- MRI and CT additionally revealed left and right adrenal lesions and multiple lung nodules (Figure 2). Brain imaging was negative.
- Initial beta-HCG found to be 1114mIU/mL
- Biopsy of the tumor was consistent with PSTT

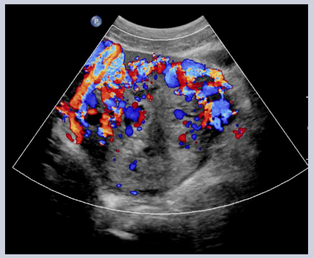

Figure 1. Ultrasound at presentation shows enlarged uterus with dilated varicose vessels throughout the myometrium and surrounding the endometrium with exuberant color Doppler flow

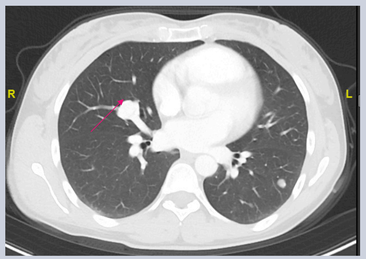

Figure 2. CT Chest at time of presentation demonstrating lung nodules (arrow)

TREATMENT COURSE

- Chemotherapy with low dose cisplatin and etoposide (3 cycles)
- Underwent preoperative bilateral uterine artery embolization followed by cytoreductive surgery with hysterectomy
- Gross surgical pathology showed extensive tumor involvement with positive parametrial and anterior vaginal wall margin and lymphovascular space involvement
- Immunohistochemical analysis revealed diffuse GATA3 positive, scattered expression of HCG and human placental lactogen. Found to have high PD-L1 staining (90-100%) (Figure 3)

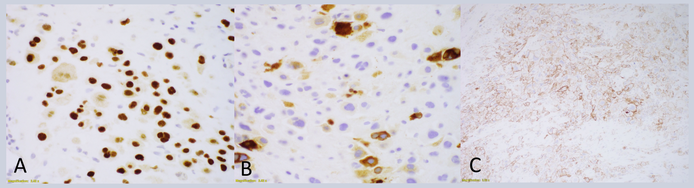

Figure 3. Immunohistochemical staining of A) GATA3 positivity B) focal HCG and C) PD-L1 staining

- Postoperatively, started on chemo regimen of Etoposide, cisplatin/etoposide, methotrexate, Dactinomycin (EP/EMA)
- Given PD-L1 expression, also initiated on pembrolizumab (anti-PD-1 antibody)

ADVERSE EVENTS

- After of 5 cycles of EP/EMA, the patient developed abdominal pain and was found to have splenic vein thrombosis, started on anticoagulation therapy
- Developed fevers and chills with sepsis secondary to port placement. Found to have a PFO and possible atrial mass as well as pulmonary pseudo-aneurysms with arteriovenous shunting. Brain MRI showed multiple embolic infarcts
- Underwent IR embolization of pulmonary shunts in right lung (Figure 4). One month later, MRI revealed resolution of atrial thrombus and cystic lung disease but with new pseudoaneurysms in left lobe, again underwent IR embolization
- Patient experienced thrombocytopenia and ototoxicity secondary to chemotherapy and inflammatory thyroiditis secondary to immunotherapy

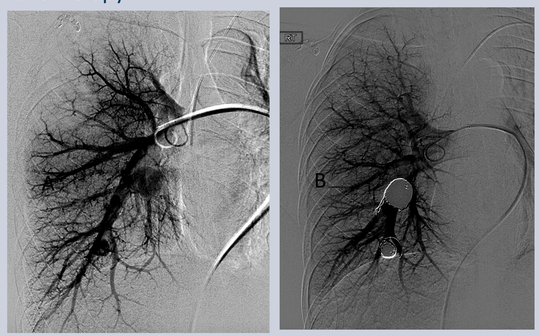

Figure 4. IR embolization of right lung AVMs A) pre and B) post embolization

CASE CONCLUSIONS

- Completed 10 cycles of EP/EMA and remains on pembrolizumab
- Final PET/CT demonstrated continued treatment response and beta-HCG currently remains undetectable (Figure 5)
- Genetic testing confirmed that antecedent pregnancy was the source of the tumor

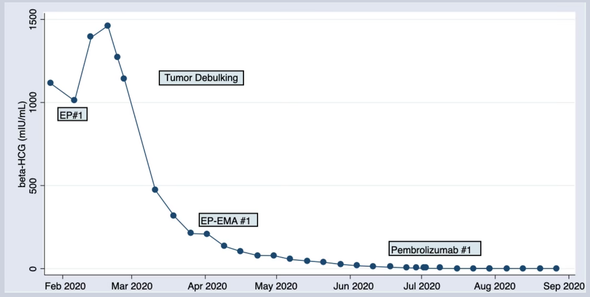

Figure 5. Beta-HCG trend over treatment course

DISCUSSION

- Management of primary disease
  - Surgery is mainstay of treatment for localized disease, but given disease burden in the pelvis, the patient underwent debulking surgery
  - Adjuvantly, patient started on EP/EMA the chemo regimen traditionally used in advanced PSTT (Gadducci 2019)
- Maintenance treatment
  - Given high PDL1 expression, the patient was additionally started on pembrolizumab (anti-PD-1) which has recently been shown to be effective in chemo-resistant GTN (Ghorani 2017, Clair 2020, Huang 2017)
- Management of AVMs
  - GTNs known to form uterine AVM, but development of pulmonary AVMS in the lungs following treatment has only been reported rarely (Yamanari 2017, Cain 2020, Choi 2003)
  - These AVMs likely formed in the setting of metastasis that regressed rapidly with treatment and in the setting of superinfection
  - AVMs can cause significant complications including pulmonary hemorrhage. They can be treated with surgery or embolization

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