A case of Type II Autoimmune pancreatitis in a patient treated with pembrolizumab adjuvant therapy

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Introduction

- Immune checkpoint inhibitor (ICI)-therapy can cause GI toxicity, affecting multiple systems including the pancreas.
- Pancreatic manifestations of ICI-toxicity are known, but its association with mass-forming Type II AIP has not been described.
- Here we describe a case where a patient developed a worrisome pancreatic mass during ICI-therapy. The mass was was not amenable to steroid treatment due to potential adverse oncological outcomes.
- We describe the pathological and imaging features of this entity of IC- associated mass-forming Type II AIP, so that others may consider this diagnosis in the future.

Case Report

A 59-year-old female with no significant medical history was diagnosed with stage IIIC clear cell ovarian cancer. Of note, her father had a history of pancreatic cancer diagnosed at age 58. The patient underwent optimal cytoreduction to no evidence of disease (NED) followed by adjuvant carboplatin/paclitaxel and bevacizumab maintenance. In addition, she was started on pembrolizumab therapy for two years to prevent disease recurrence. She tolerated this treatment regimen well besides development of mild diarrhea responding to loperamide and a mild grinding sensation in her upper abdomen for which she was started on pantoprazole. After 15 months on pembrolizumab a restaging positron emission tomography (PET) scan showed a fluorodeoxyglucose (FDG)-avid lesion in the region of the pancreatic head (Figure 1). MRI showed a 3.5cm hypoenhancing mass in the pancreatic head without vascular involvement and no pancreatic duct dilation. Labs included a lipase of 1014, normal liver function tests (ALT 17, AST 25, ALP 85, Tbili 0.3), normal tumor markers (CA 19-9 was 8, CEA 3.3 and CA-125 11) and normal IgG levels (IgG1 505, IgG2 340, IgG3 38.4, IgG4 38.3). Her physical exam was notable for a soft abdomen with mild tenderness to epigastric and right upper quadrant palpation.

Case Report (continued)

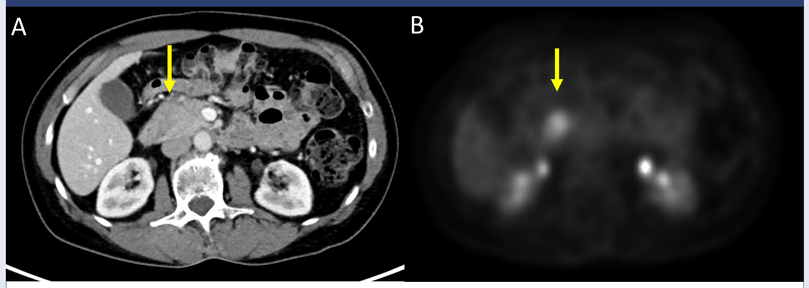

Figure 1. Contrast enhanced axial CT image shows hypo enhancing pancreatic head mass (yellow arrow) (A) which shows intense FDG avidity on the corresponding PET image (B).

The patient was referred for upper endoscopic ultrasound (EUS) which showed an irregular hypoechoic mass with a max diameter of 32mm in the uncinate process. Fine needle aspiration (FNA) demonstrated atypical cells and fine needle biopsy (FNB) showed features consistent with chronic pancreatitis with few plasma cells and negative STAT6 staining. A likely diagnosis of Type II AIP versus ICI-pancreatitis was made with decision to monitor patient with close surveillance imaging. Follow up CT showed increased size of the pancreatic mass to 4 x 2.7 cm with increased biliary duct dilation (Figure 2). Repeat EUS with FNB showed pancreatic parenchyma with cellular fibrosis and prominent periductal lymphohistiocytic and eosinophilic inflammation. SMAD4 expression was retained (normal) and ductal cells were positive for PD-L1 (Figure 3) consistent with Type II AIP.

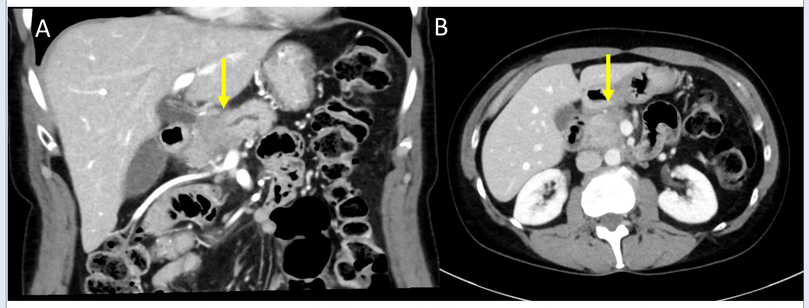

Figure 2. Contrast enhanced coronal (A) and axial (B) CT image shows interval enlargement of the hypo enhancing pancreatic head mass (yellow arrow) with pancreatic duct obstruction with dilatation of the main pancreatic duct.

Case Report (continued)

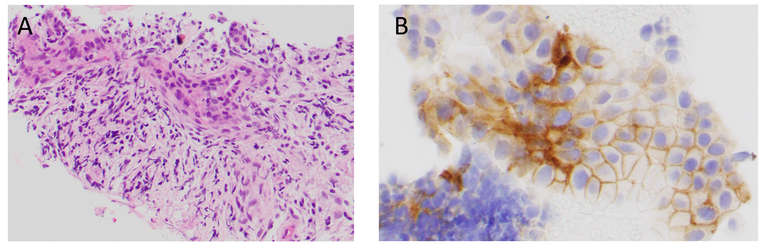

Figure 3. Autoimmune pancreatitis, type 2. The core biopsy shows the characteristic granulocytic epithelial lesion or "GEL" consisting of neutrophils infiltrating and injuring a duct (or acinus) surrounded by an inflamed fibrotic stroma (A, hematoxylin and eosin). Immunohistochemical staining with PDL1 shows membranous staining of the ductal epithelium, supporting the diagnosis of autoimmune pancreatitis (B).

The patient was not treated with steroids given the concern for negatively impacting her long-term oncological outcomes. She had repeat imaging following completion of her bevacizumab/pembrolizumab and there was complete resolution of mass lesion (Figure 4). Her symptoms improved, but she developed exocrine pancreatic insufficiency.

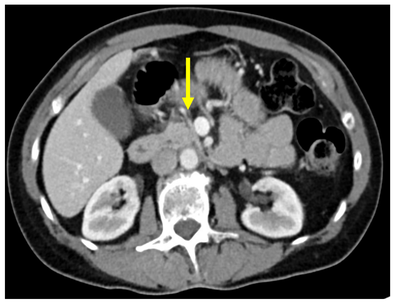

Figure 4. After 4 months of close monitoring axial contrast enhanced CT images show resolution of the mass with mild atrophy of the pancreatic head (yellow arrow).

CONCLUSIONS

To our knowledge, we describe the first case of mass-forming Type II AIP in the setting of ICI-therapy. While imaging and histology were consistent with Type II AIP, it is possible that this represents a new entity of ICI-mass forming pancreatitis. Here, we demonstrate that she was able to complete her ICI therapy while managed with short-interval imaging studies and pancreatic function monitoring. Additional studies are needed to determine the role of ICI-therapy in mass-forming AIP.