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Partial Response to Carboplatin, Etoposide posphate and Atezolizumab in a Pediatric Patient with High-grade Metastatic Tumor with Rhabdoid and Focal Neuroendocrine Features

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To the Editor:

Metastatic solid tumors remain challenging to diagnose[4] and cure.[1–3] We present the case of a child with an undifferentiated, metastatic malignancy showing rhabdoid and neuroendocrine features exhibiting a partial response to carboplatin, etoposide phosphate and Atezolizumab.

A 7 year old male presented with a large retroperitoneal mass with liver metastases and gastric outlet obstruction. Pathology revealed rhabdoid histology with uniform cells, focal nuclear pleomorphism, and large central nucleoli though expression of INI-1 and BRG1 were retained, making a diagnosis of malignant rhabdoid tumor unlikely.[5] The tumor expressed epithelial and mesenchymal markers including diffuse positivity for cytokeratin Cam 5.2, and focal staining for cytokeratin AE1/AE3, pancytokeratin, and vimentin. Patchy positive staining for synaptophysin and chromogranin implied features of neuroendocrine differentiation.[6] Beta-catenin staining was membranous only excluding a primary liver tumor and negative trypsin staining indicated an unlikely origin from pancreatic acinar cells. Staining was negative for desmin, MyoD1, S100-protein, ALK-1, SMA, CD134, CD117, CD30, Arginase, WT1, SOX10, OCT3/4, Myf-4, EMA, PGP 9.5, alpha-fetoprotein, and

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CONFLICT OF INTEREST STATEMENT

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alpha-1-antitrypsin excluding most sarcomas and primary liver tumors. FISH was negative for *CIC, NUT* and *EWS* rearrangement. A diagnosis of an undifferentiated high-grade neoplasm with rhabdoid and focal neuroendocrine features was rendered.

Based on the retroperitoneal primary as well as tumor imaging, there was suspicion for pancreatic origin, and we decided to treat as a pancreatic carcinoma with rhabdoid phenotype which has been previously described, with similar histopathology.[7–9] A pediatric protocol was developed based on National Comprehensive Cancer Network guidelines as well as several studies in adults reporting good response rates to platinum-based agents combined with etoposide.[10–13] Chemotherapy was administered in four 21-day cycles and included etoposide phosphate (100mg/m^2) given on days 1–3 and carboplatin (5 Area Under the Curve) on day 1. The tumor expressed *PD-L1*, so a *PD-L1* antibody, Atezolizumab, was given on the first day of each cycle (15mg/kg).[14] Following 4 cycles of chemotherapy, the patient continued maintenance Atezolizumab every 21 days. Palliative radiation was administered to the primary tumor and liver metastases. The regimen was well tolerated; expected side effects including myelosuppression and electrolyte derangements were observed. The patient also experienced coagulopathy and hyperbilirubemia which were presumed secondary to progressive liver dysfunction rather than a chemotherapy side effect.

Aftertwo cycles of chemotherapy, the gastric outlet obstruction resolved and imaging showed interval decrease in size of the primary tumor (15 × 8cm, previously 16.4 × 10cm) and liver metastases (Fig. 1A and 1B). Following this partial response, the child returned home for nearly two months. As described in the adult literature, this patient had a significant but not sustained response. Five months after initial diagnosis the child's disease progressed, and an invasive fungal infection precluded further systemic chemotherapy. His overall survival was almost 6 months.

Undifferentiated tumors with rhabdoid phenotype remain challenging to classify and treat. Our experience highlights a rare subset of pancreatic neuroendocrine tumors that display rhabdoid morphology. The treatment regimen described in combination with palliative radiation was well tolerated, resulted in partial disease response and improved quality of life.

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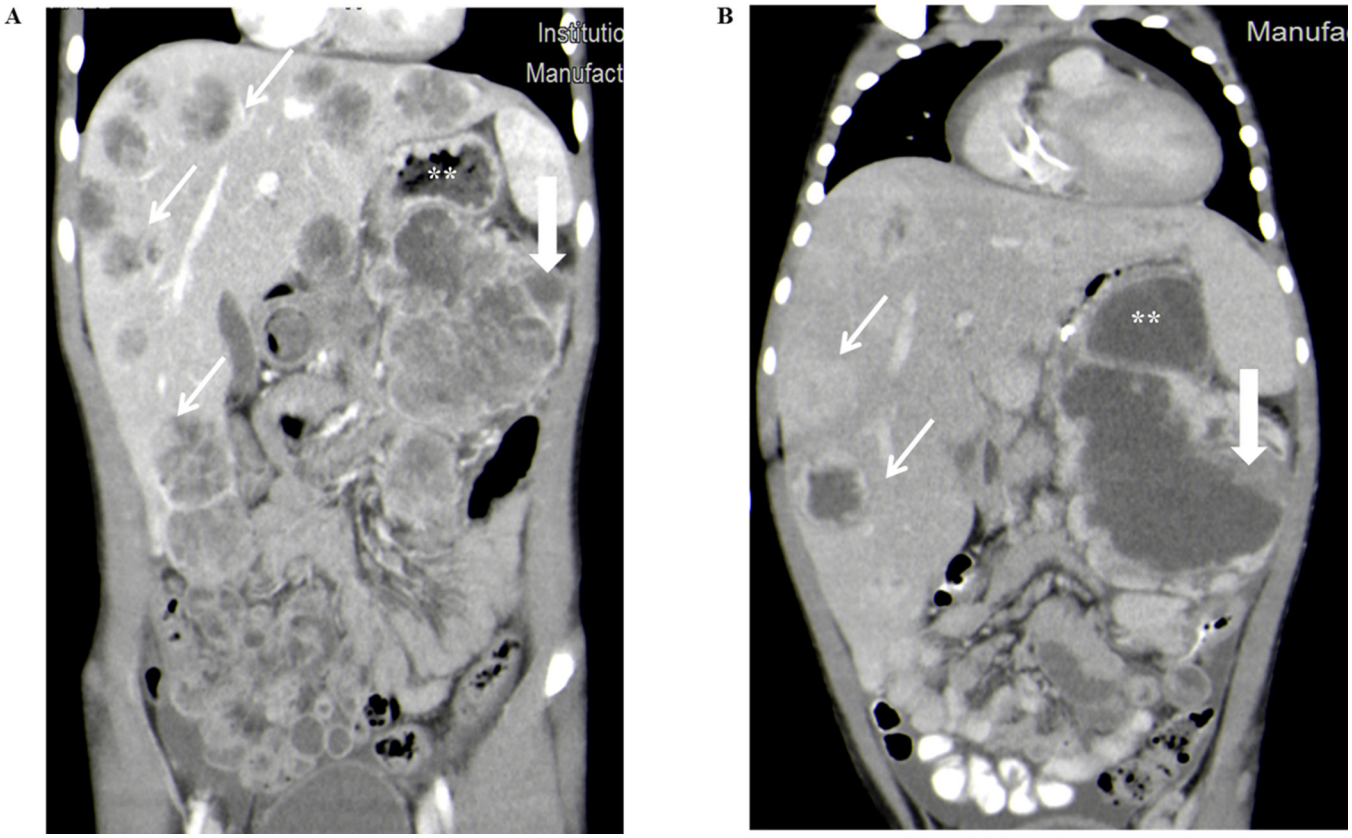

FIGURE 1.

Patient imaging demonstrated a marked tumor response to therapy. (A) CT scan prior to initiation of treatment with multiple liver masses (*open white arrows*) and large retroperitoneal mass (*closed white arrow*) compressing stomach (**). (B) CT scan showing marked decrease in tumor burden in both the liver metastases (*open white arrows*) and retroperitoneal tumor (*closed white arrow*) following two cycles of chemotherapy with carboplatin, etoposide phosphate and Atezulizumab. The gastric obstruction was also improved (**).