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Intraperitoneal seeding of a testicular mixed germ cell tumor following spontaneous intraperitoneal mass rupture with associated anti-NMDA paraneoplastic encephalitis

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ABSTRACT

A 25-year-old male was admitted to the neurological intensive care unit for neurologic deterioration, likely caused by a paraneoplastic syndrome secondary to testicular malignancy. He experienced spontaneous rupture and hemorrhage of his testicular mass arising from an undescended testis while admitted. The tumor was excised, revealing a mixed germ cell tumor. Serum tumor markers began to rise after 4 cycles of chemotherapy. Surveillance scans 32 weeks after mass rupture revealed numerous tumor deposits throughout his peritoneum concerning for teratoma. We review a case of intraperitoneal metastasis of a testicular mixed germ cell tumor following intra-abdominal mass rupture.

1. Introduction

Testicular cancer is the most common malignancy in males aged 15–35.[1] Tumor metastasis typically spreads to retroperitoneal lymph nodes, with visceral metastases to lungs, liver, bones, and brain. There have been several cases of atypical intraperitoneal metastasis of germ cell tumors (GCT).[2,3] Here, we review a case of testicular cancer seeding the peritoneal cavity after spontaneous intra-abdominal tumor rupture.

2. Case presentation

A 25-year-old male was admitted to the Neurologic Intensive Care Unit (Neuro-ICU) with neurologic deterioration and no known urologic history.

Cerebral spinal fluid evaluation was significant for lymphocyte predominant elevated white blood cell count (WBC 75–129, protein 22-27, glucose 80–107) and positive Anti-NMDA at 1:80. Patient was found to have recurrent mouth movements without ictal correlate on electroencephalograms which was felt to represent a manifestation of an underlying autoimmune encephalitis. The patient exhibited signs of sympathetic storming with elevated respiratory rate, elevated heart rate, and fever with normetanephrine 1.37nmol/L (normal 0.00–0.89nmol/L). MRI brain with and without contrast revealed bilateral cingulate gyral swelling with small region of left cingulate gyrus restricted diffusion, compatible with autoimmune/paraneoplastic limbic encephalitis (Fig. 1). A computed tomography (CT) of the chest, abdomen, and pelvis was obtained, revealing a 9.7cm mass near the left internal inguinal ring (Fig. 2A). Initial serum tumor markers (STMs) showed elevated AFP at 39 and LDH at 554 with normal bHCG <1. Testicular ultrasound revealed a normal right testis and unidentifiable left testis or spermatic cord within the scrotum.

Due to the presence of malignancy and positive anti-NMDA antibodies, the neurologic symptoms were believed to be caused by paraneoplastic anti-NMDA encephalitis secondary to germ cell malignancy arising from an undescended left testis. While the patient was in the Neuro-ICU, the mass ruptured leading to a hemoglobin drop and subsequent urgent laparotomy (Fig. 2B). Laparotomy revealed a large intraperitoneal hematoma and large pelvic mass arising from the left

Abbreviations: GCT, germ cell tumor; STMs, serum tumor markers; NMDA, N-methyl-D-aspartate receptor; RPLND, retroperitoneal lymph node dissection.

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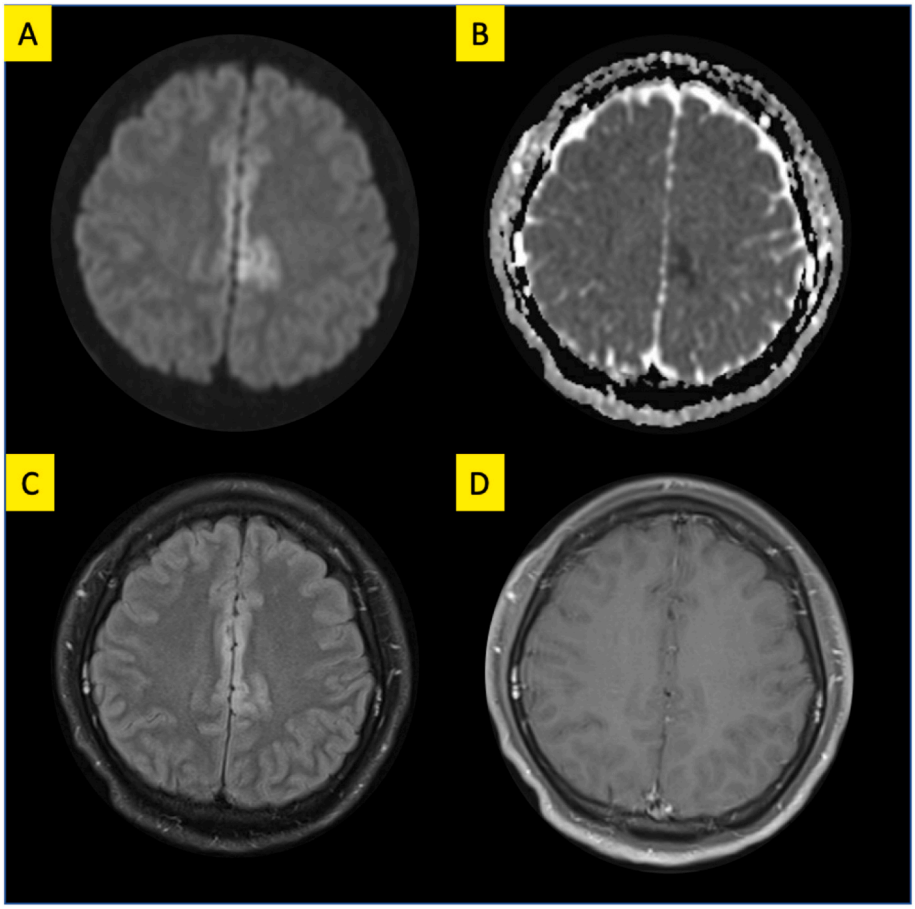

Fig. 1. A–D: MRI brain with and without contrast obtained in the Neuro-ICU.
Caption: Diffusion weighted imaging [(DWI), Panel (A)] showing an area of restricted diffusion in the bilateral cingulate gyrus with correlation on apparent diffusion coefficient [(ADC), Panel (B)] and fluid attenuated inversion recovery [(FLAIR), Panel (C)] sequences. T1 post contrast imaging (D) without an area of enhancement.

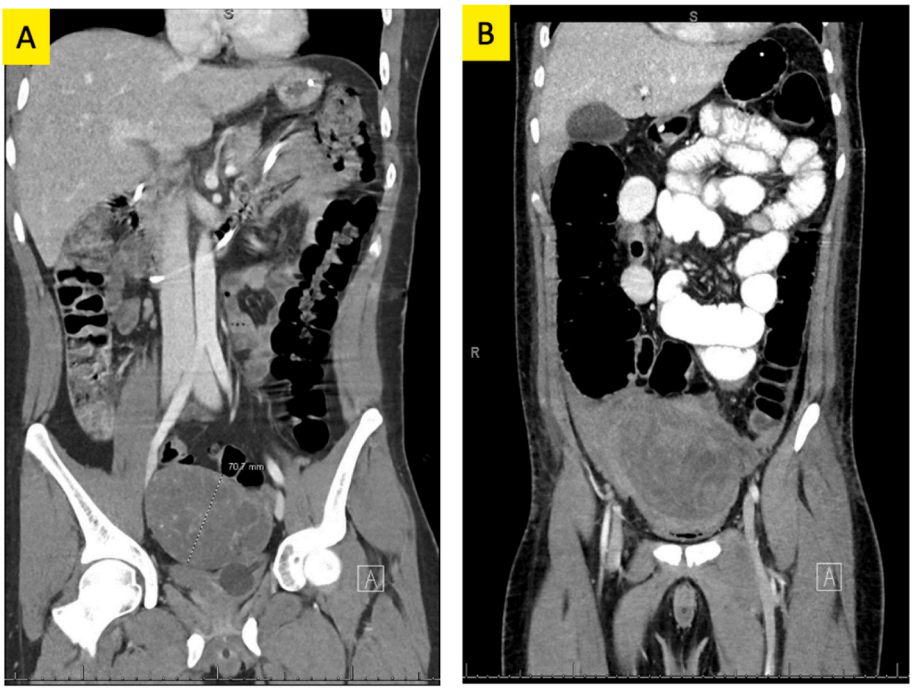

Fig. 2. A–B: CT imaging upon admission to the Neuro-ICU (A) and subsequent CT imaging 3 days after initial imaging (B).
Caption: Panel (A) shows the initial CT imaging upon admission to the Neuro-ICU revealing a sagittal view of the intra-abdominal testicular mass. Panel (B) shows subsequent CT imaging obtained 3 days after imaging shown in panel (A), which revealed a new mild to moderate hemoperitoneum with slightly increased massed size compared to initial imaging.

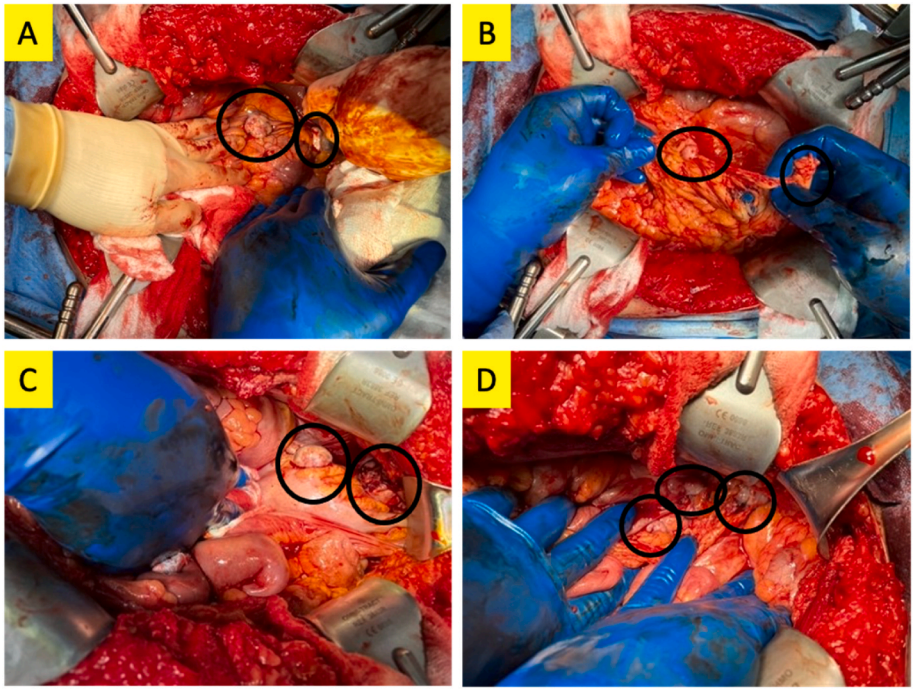

Fig. 3. A–D: Intraoperative images of select intra-abdominal masses 32 weeks after initial surgical excision of intra-abdominal testicular mass.
Caption: Black circles indicate masses. Panel (A) demonstrates masses in the left upper abdominal peritoneum, (B) demonstrates omental masses, (C) demonstrates masses in the pelvis along the peritoneum of the sigmoid mesentery and left lateral pelvic peritoneum, and (D) demonstrates a large conglomerate of masses in the pelvis along the sigmoid, rectum, and peritoneal surface of the bladder.

intra-abdominal testis. Gross spillage of dark appearing blood was noted within the abdomen. The mass was completely resected with no evidence of direct invasion into surrounding tissues. Pathology results showed a 12.5 × 9.5 × 6.5cm mass composed of 70% teratoma and 30% seminoma. Initial post-operative STMs were normal (AFP 3, LDH 219, bHCG <1). Initial staging was Clinical Stage IA (pT1bN0M0S0). The patient's neurologic symptoms improved after 5 rounds of plasma exchange, 5 days of 1g methylprednisolone, and one dose of 1000mg rituximab. He was discharged home on post-operative day 46.

11 weeks post-resection, STMs including AFP and LDH rose to 1416 and 240 with normal imaging and the patient was started on chemotherapy. He completed 1 cycle of bleomycin, etoposide, cisplatin ((BEP), discontinued due to pulmonary toxicity) and 3 cycles of etoposide, isofosfamide, and cisplatin (VIP). STMs then normalized (AFP 1, bHCG <1, LDH 226) and imaging remained normal.

CT surveillance imaging 32 weeks after the first resection demonstrated enlargement of multiple soft tissue nodules in the abdomen, with normal STMs. Patient returned to the operating room for a retroperitoneal lymph node dissection (RPLND) and exploratory laparotomy with excision of suspected tumors. Over 30 masses were excised throughout the peritoneum, omentum, small and large bowel mesentery, perisplenic area, and bladder peritoneum with pathology results consistent with metastatic teratoma (Fig. 3). At least 2 additional masses were excised from the large bowel mesentery with pathology revealing metastatic mixed germ cell tumors. Mass size ranged from 2.0cm to 5.2cm. RPLND revealed 1 out of 17 paraaortic lymph nodes positive for metastatic teratoma, with remainder of lymph node dissection negative including 13 paracaval lymph nodes and 8 interaorotocaval lymph nodes. None of the peritoneal nodules were invasive into adjacent viscera.

Subsequent surveillance imaging after mass excision has been stable for 12 months following the second surgery and STMs have remained within normal limits (AFP 1, LDH 153, bHCG <1).

3. Discussion

In this case, we suspect the intraperitoneal rupture of the primary mixed GCT led to intraperitoneal metastases. We also present an unusual presentation of anti-NMDA encephalitis. Testicular cancer is well documented to follow a predictable lymphatic spread.[2] The ability of testicular cancer to directly seed the peritoneum due to tumor violation is less well documented. Several case reports have reported atypical spread to the peritoneum and two mechanisms have been suggested as causes of peritoneal seeding.

First, it has been hypothesized that peritoneal metastasis arises from tumor disruption during RPLND. A 2019 study found 4 out of 5 studied patients had atypical tumor recurrence in the abdomen after RPLND.[3] However, a 2022 retrospective study found that in 28 out of 3767 (0.74%) patients with initial testicular GCT and subsequent peritoneal carcinosis, only 45% underwent RPLND prior to the development of peritoneal carcinosis.[2] Patients developed peritoneal carcinomatosis at a median of 15 months after initial diagnosis and two lines of cisplatin based chemotherapy, suggestive of aggressive baseline disease. This data suggests that peritoneal carcinomatosis is a rare event in the natural history of GCTs.

Second, several case reports support the suggested mechanism that GCT violation (open or minimally invasive approaches) may directly lead to peritoneal seeding.[2,3] Li et al. postulated that it is possible for microscopic tumor cells to be the drivers of atypical metastasis.[4] Our case also supports this mechanism. Peritoneal seeding in our patient may have been caused by tumor rupture and release of microscopic tumor cells into the peritoneal cavity.

This case is a notable example of a patient with testicular GCT developing Anti-NMDA encephalitis. This condition is rare in men and more commonly occurs in women of child-bearing age with GCTs. It has been suggested that certain tumor types, including testicular GCTs, exhibit cell surface NMDA receptors that can lead to anti-NMDA encephalitis.[5] In reviewing the literature, there are very few documented cases of anti-NMDA paraneoplastic syndromes associated with testicular cancer. This case adds further evidence of this phenomenon.

4. Conclusion

Tumor violation of a GCT may lead to atypical peritoneal seeding and metastases. This case study and others suggest that this may occur from spreading of microscopic tumor cells. Further research is needed to better characterize this pathway.

Authors and contributions to manuscript

Morgan B Marshall: Conception and Study Design; Writing – original draft; writing – reviewing and editing; Final Approval.

Kassandra Dindinger-Hill: Conception and Study Design; Writing – original draft; writing – reviewing and editing; Final Approval.

Umang Swami: Analysis and Interpretation of Data; Writing – reviewing and editing; Final Approval.

Stephanie Lyden: Analysis and Interpretation of Data; Data Acquisition; Writing – reviewing and editing; Final Approval.

Alejandro Sanchez: Conception and Study Design; Analysis and Interpretation of Data; Data Acquisition; Writing – Reviewing and Editing; Final Approval.

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