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GI IMAGE

Tumor Symbiosis: Gastrointestinal Stromal Tumor as a Host for Primary Peritoneal Mesothelioma

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Case Presentation

A 57-year-old man with a history of polycythemia vera presented for routine primary care follow-up and was found to have anemia with hemoglobin level of 12 mg/dL from 16 mg/dL. He was referred to gastroenterology for upper and lower endoscopies, which revealed an ulcerated submucosal mass in the gastric antrum. Endoscopic ultrasound (EUS) with core needle biopsy revealed a spindle cell neoplasm on hematoxylin and eosin (H&E) staining. Immunohistochemical analyses were positive for CD117 (KIT) and DOG-1, consistent with a gastrointestinal stromal tumor (GIST). Staging computed tomography (CT) of the abdomen/pelvis demonstrated a 15 × 12 × 13 cm gastric mass with effacement of the left liver. He was started on neoadjuvant imatinib (Gleevec, Novartis). Follow-up CT after 3 months of therapy demonstrated a 19% increase in tumor volume and new omental nodules (Fig. 1a). Tumor sequencing revealed a *PDGFRA* D842V mutation, which is known to be imatinib resistant. Thus, he was switched to dasatinib, but this was poorly tolerated. Therefore, he underwent diagnostic laparoscopy and peritoneal biopsies, which revealed primary peritoneal mesothelioma in addition to the known gastric GIST. He was then referred to our center for possible cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) to treat his mesothelioma. To determine his candidacy for this approach, repeat diagnostic laparoscopy was performed. This revealed the large gastric GIST with invasion, rather than abutment, of hepatic segments 2 and 3. Moreover, there were numerous peritoneal implants coating the surface of the GIST (Fig. 1b). The peritoneal cancer index (PCI) regions of the upper abdomen (e.g., regions 1–3) and along the small bowel (e.g., regions 9–12) were most affected. As compared to the upper abdomen, the pelvis and lower quadrants were essentially spared of mesothelioma. The patient had a PCI score of 17. We proceeded with an exploratory laparotomy, subtotal gastrectomy with an en bloc left lateral sectionectomy and omentectomy for the GIST followed by complete peritoneal cytoreduction (CC0) and HIPEC for the mesothelioma. Final histopathology (Fig. 2a) revealed numerous peritoneal calretinin immunostain-positive tumor deposits that were histopathologically consistent with epithelioid peritoneal mesothelioma (Fig. 2b) with an underlying highly vascularized KIT (C-KIT, CD117) immunostain-positive spindle cell tumor consistent with GIST (Fig. 2c).

Discussion

GIST is the most common sarcoma, although there are only about 3000–6000 cases per year in the USA.[1] The cell of origin for GIST is the interstitial cell of Cajal located within the submucosa of the gastrointestinal tract. Primary peritoneal

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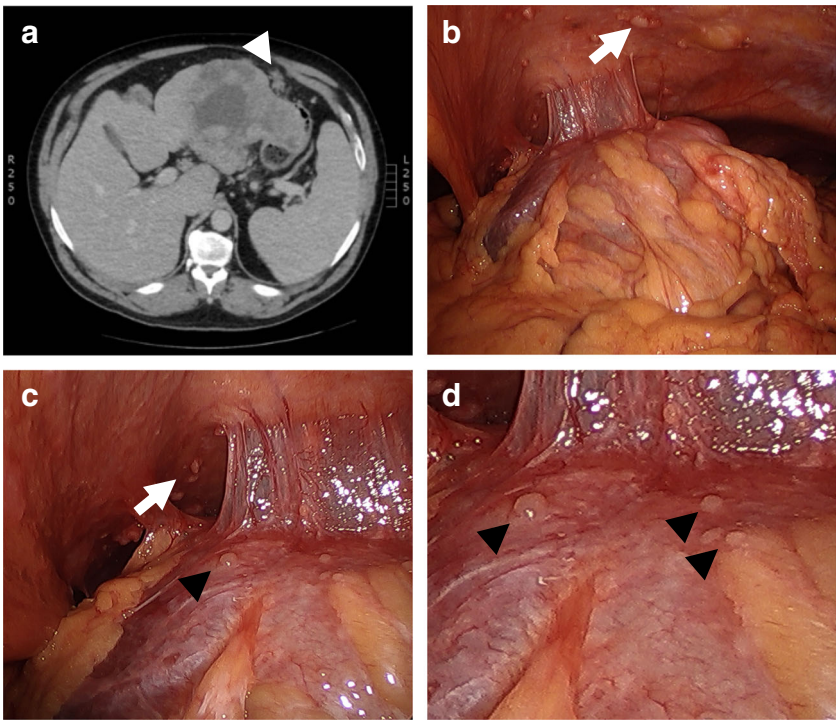

Fig. 1 A 57-year old anemic male presented with biopsy proven gastrointestinal stromal tumor (GIST) of the stomach, as well as primary peritoneal mesothelioma (PPM). **a** Abdominal computed tomography images demonstrated omental nodules (white arrowhead) adjacent to the gastric GIST. **b**–**d** Upon laparoscopy, diffuse PPM implants (white arrows) were noted in the upper abdomen and several were growing on the surface of the gastric GIST (black arrowheads)

mesothelioma (PPM) is even rarer and has an incidence of approximately 200–300 cases per year in the USA. Here, we present the first report of a synchronous presentation of these two rare cancers.

Prior work by our group has shown that patients with GIST are at additional risk for certain cancers either before or after the development of GIST.[1] In this study, GIST patients were found to have a 7.3-fold higher risk of mesothelioma than the average population. Despite this association, the uniqueness of this presentation is the focused distribution of PPM throughout the upper abdomen and in the vicinity of the gastric GIST. By contrast, PPM typically occurs uniformly and diffusely throughout the abdominal cavity. This asymmetric distribution suggests the interesting possibility that the GIST may promote a favorable biological environment facilitating the growth of the PPM. The cellular interface seen on histopathologic examination supports the possibility of a commensalistic, or symbiotic, relationship in which the PPM gains a growth advantage from the GIST, while not harming the GIST. The ecology of these cancers could explain a possible cooperation between clonally distinct tumor cell types (i.e., sarcoma and carcinoma) that has been reported in other malignancies to involve the sharing of diffusible growth factors.[2] For instance, vascular endothelial growth factor (VEGF) is often highly expressed by GIST cells and has been shown to support the growth of PPM cells.[3] Although the occurrence of such a commensal relationship is clinically rare, it is interesting to consider that this interaction, and the factors involved in it, may provide more general insights about tumor growth and metastases. In conclusion, because adult patients

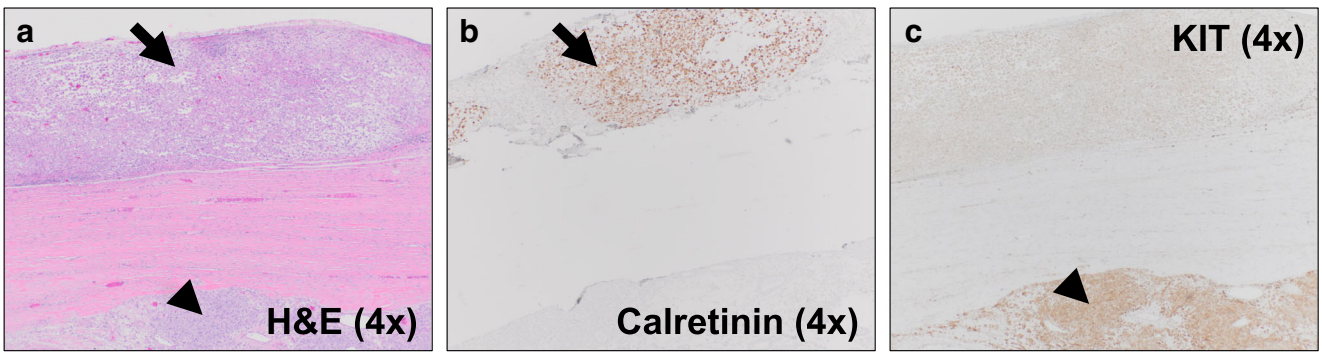

Fig. 2 Histopathologic analysis consistent with primary peritoneal mesothelioma (PPM) growing on the surface of a gastric GIST. **a** Photomicrographs of hematoxylin and eosin (H&E, × 4) staining of tumor interfaces demonstrating spindle cells and prominent thin capillaries (arrowhead) and epithelioid type cells forming clusters on peritoneal surface (arrow). **b** Photomicrographs of immunohistochemical staining for calretinin consistent with PPM (× 4). **c** Staining for KIT (c-KIT, CD117) consistent with GIST (× 4)

with GIST are at increased risk for other cancers, the identification of atypical sites of disease, such as lymph nodes, thoracic masses, or peritoneal disease, should not be presumed to be disease progression. In these settings, additional confirmatory workup should be performed before diagnosing treatment failure.

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Sudeep Banerjee - Contributed to the acquisition, analysis, and interpretation of patient data and the drafting of the manuscript. He approves of the final version to be published. He agrees to be accountable for all aspects of the work in ensuring that questions related to any part of the work are appropriately investigated and resolved.

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