Experimental and Molecular Pathology 106 (2019) 60–62

Contents lists available at ScienceDirect

Experimental and Molecular Pathology

journal homepage: www.elsevier.com/locate/yexmp

Short report

An unexpected diagnosis of histiocytic sarcoma

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1. Presentation

A 50 year-old male with cirrhosis secondary to hepatitis C produced ascetic fluid with ~5 l of fluid drained at weekly visits to the emergency department. The initial diagnosis of cirrhosis was made at an outside hospital only 3 months before this presentation. The patient was found to have hepatitis C, likely from a previous tattoo, but he had no history of heavy drinking and reported only a previous cholecystectomy for past medical history.

The patient began to have worsening abdominal pain along with his accumulation of ascites, and at his most recent drainage, the patient's GI doctor gave him an antibiotic and told him to visit the emergency room for possible peritonitis. The patient continued to have increased abdominal pain over baseline and watery, dark red diarrhea that changed to bright red, and the patient was admitted for workup. Radiologic imaging including non-contrast CT of the abdomen and pelvis showed evidence of cirrhosis and pulmonary hypertension with splenomegaly consistent with previous imaging. The patient did not have a mass lesion on non-contrast CT of the chest, abdomen, and pelvis. The patient was also noted to have inflammatory stranding and edematous changes throughout the mesentery. The patient was unable to receive contrast due to worsening renal function. Upper endoscopy identified esophageal varicies, but no other lesions were noted. Ascitic fluid was drained and submitted for cytologic analysis revealing only reactive cells.

The surgery team was called for a possible acute abdomen and during exploratory laparotomy the patient was found to have diffuse peritoneal studding consistent with carcinomatosis, but with no apparent perforation or discrete masses. Endoscopic gastroenteroscopy found only small gastric varices. The patient developed hepatorenal syndrome and multisystem organ failure soon after. The patient was transitioned to comfort care measures and died soon thereafter.

Given the patient's age and past medical history, our differential initially weighted heavily toward carcinoma, especially those of gastrointestinal origin. The initial H&E slides showed a network of malignant cells surrounded by inflammation. The cells could be seen as epithelioid, but the architecture did not contain glands or resemble GI mucosa. The fragments of tissue from the patient's abdomen showed a network of malignant histiocyte-like cells surrounded by a mixture of inflammatory cells (Fig. 1). The malignant cells have abundant eosinophilic cytoplasm, prominent nucleoli, and significant pleomorphism (Fig. 1). Malignant multinucleated giant cells were also identified (Fig. 2A).

In typical fashion, diagnostic immunohistochemical staining was performed by our CAP certified pathology lab, with appropriate controls for each antibody (See Table 1 for stains and results). The IHC for cytokeratins (AE1/AE3, CAM 5.2, CK7, CK20) did not highlight any of the tumor cells, effectively ruling out a carcinoma. Stains for microorganism (gram, GMS, PAS) were negative for microorganisms. Other GI related IHC stains including CA 19.9, CEA, hepPAR, arginase, and AFP were also negative. Rare positive cells were identified on a Pax5 stain while the IHC stain for desmin highlighted septa within the lesion. Stains for alpha-actin highlighted small vessels within the lesion, and S-100 highlighted rare scattered cells. The lesion showed weak patchy staining for CD45, no staining for CD21 and CD30 with rare positive staining for CD20. Both CD3 and CD4 showed scattered strong positive staining around the malignant cells. The malignant cells stained positive for CD163, CD68, and lysozyme, but did not stain for langerin or CD1a, which is consistent with other reports of histiocytic carcinoma (Fig. 2).

2. Discussion

Histiocytic sarcoma is a rare malignancy composed of mature histiocytes (Hornick et al., 2004; Pileri et al., 2002; Swerdlow et al., 2008; Swerdlow et al., 2016; Skala et al., 2018). Only a few hundred cases have been reported in the literature, and a recent review in the Archives of pathology and Laboratory Medicine highlights many of the key features of this rare entitiy (Kommalapati et al., 2018; Skala et al., 2018). An analysis of the SEER database has shown this malignancy to occur more often in Caucasians and slightly more often in men, but no known predisposing factors exist (Kommalapati et al., 2018). Histiocytic sarcoma can occur sporadically or arise from another hematopoietic malignancy (Skala et al., 2018). If histiocytic sarcoma arises from the monocyte/macrophage lineage and is not a true sarcoma (Castro et al., 2010; Wang et al., 2010). No characteristic genetic alterations have been identified, but many other histiocytic lesions harbor BRAF mutations with the V600E mutation seen most commonly. (Chen et al., 2009; Go et al., 2014; Liu et al., 2016) The tumor

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https://doi.org/10.1016/j.yexmp.2018.11.012
Received 28 September 2018; Received in revised form 20 November 2018; Accepted 25 November 2018
Available online 28 November 2018

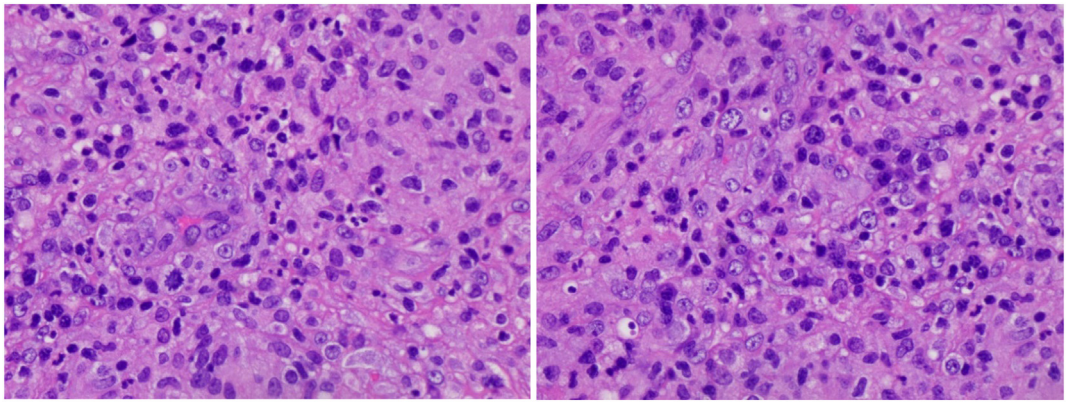

Fig. 1. H&E of peritoneal biopsy showing malignant cells (x693).

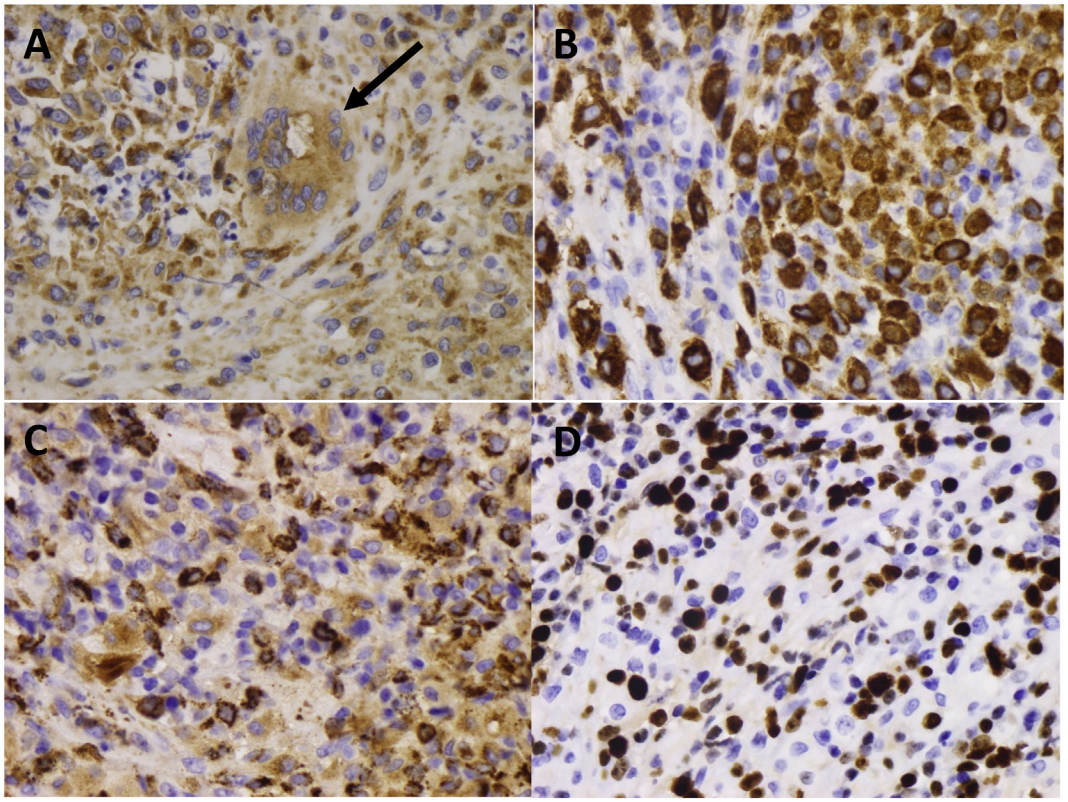

Fig. 2. Immunohistochemistry for histiocyte markers staining malignant cells A) CD68 with a multinucleated giant cell (arrow), 606×; B) CD163, 606×; C) Lysozyme, 606×; D) MIB-1, 606×.

suppressors PTEN and INK4A/ARF have been shown to prevent histiocytic sarcoma development (Carrasco et al., 2006). On histopathology histiocytic sarcomas show large, non-cohesive cells that may have abundant eosinophilic cytoplasm and are often ovoid but can appear spindled (Mikami et al., 2004). Giant tumor cells can be seen with engulfed red blood cells, i.e. hemophagocytosis (Shinoda et al., 2009). On immunohistochemistry, cells are typically negative for epithelial markers, S100, CD1a, B-cell, and T-cell markers (Pileri et al., 2002, Hornick et al., 2004, Vos et al., 2005, Yoshida and Takeuchi, 2008, Mikami et al., 2004, Lee et al., 2014). The cells of histiocytic sarcoma showed positive staining with CD163, lysozyme, and CD68 (Pileri et al., 2002; Hornick et al., 2004; Vos et al., 2005; Yoshida and Takeuchi, 2008; Mikami et al., 2004; Lee et al., 2014). Of note, histiocytic sarcomas occurring with acute monocytic leukemia are not considered histiocytic sarcoma (Shinoda et al., 2009; Johnson et al., 2013). Other diagnostic considerations would be Langerhans cell histiocytosis, hemophagocytic lymphohistiocytosis, or other lymphomas (Mikami et al., 2004; Johnson et al., 2013). In particular, Langerhans cell histiocytosis cells typically express CD1a and S100 (which our tumor did not) while hemophagocytic lymphohistiocytosis involves a proliferation of non-malignant histiocytes (Pileri et al., 2002; Vos et al., 2005; Yoshida and Takeuchi, 2008).

Our initial workup was negative for epithelial markers, desmin, alpha-actin, as well as B-cell and T-cell markers. As per a number of cases in the literature, our tumor showed patchy staining for CD45 LCA, CD68, CD163, and lysozyme (Pileri et al., 2002; Hornick et al., 2004; Vos et al., 2005; Yoshida and Takeuchi, 2008; Mikami et al., 2004; Lee et al., 2014). Proliferative index by MIB-1 was approximately 30–50% in tumor cells. On H&E stain there were occasional large cells and hemophagocytosis noted, also consistent with previous reports (Swerdlow et al., 2008, Shinoda et al., 2009, Takahashi et al., 2013, Swerdlow et al., 2016,).

Table 1
List of IHC Stains.

IHC stain	Result
AE1/AE3	Negative in malignant cells
CAM 5.2	Negative in malignant cells
CK7	Negative in malignant cells
CK20	Negative in malignant cells
Desmin	Negative in malignant cells
alpha-actin	Negative in malignant cells
S-100	Negative in malignant cells
Melan-A	Negative
Lysozyme	Positive in malignant cells
Langerin	Negative in malignant cells
CD45	Few scattered positive cells, Negative in malignant cells
CD3	Few scattered positive cells, Negative in malignant cells
CD4	Few scattered positive cells, Negative in malignant cells
CD20	Few scattered positive cells, Negative in malignant cells
CD21	Few scattered positive cells, Negative in malignant cells
CD30	Negative in malignant cells
CD34	Highlights vessels, Negative in malignant cells
CD68	Positive in malignant cells
CD163	Positive in malignant cells
CD1a	Negative in malignant cells

Often histiocytic sarcomas present with a single painless mass (Hornick et al., 2004; Swerdlow et al., 2008; Swerdlow et al., 2016). In addition to the somewhat rare diagnosis, we found the presentation of this case to be quite unusual. Of the between one and two hundred reported cases, most cases present with a solitary painless mass, and there is a chance of long-term survival with complete resection (Heath et al., 2014; Swerdlow et al., 2016). Many of the reported cases occur in association with a known hematopoietic malignancy and further transformation, but solitary cases do exist in the literature (Lee et al., 2014; Swerdlow et al., 2016; Kommalapati et al., 2018). The disease is known to often arise in the gastrointestinal tract, but it is quite unusual to see widespread carcinomatosis-like dissemination on presentation as in our case (Johnson et al., 2013; Lee et al., 2014; Swerdlow et al., 2016).

Our patient's tumor was found to not harbor the typical BRAF V600E mutation, but no further molecular testing was performed as the patient expired due to wide spread disease.

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