Hepatoid Adenocarcinoma Presenting as a Necrotizing Soft Tissue Infection of the Abdominal Wall

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Abstract

A 46 y/o presented with a necrotizing soft tissue infection of the anterior abdominal wall. She denied recent trauma. She had recently been treated for sciatica, but had not been on any long term medications. Her symptoms worsened over the last week. She had an abdominal mass with diffuse abdominal tenderness. Her initial treatment was consistent with principles for managing a complicated skin and soft tissue infection including resuscitation, broad spectrum antibiotics and excision and incision of tissues. Tissues removed included her abdominal mass. Her pathology eventually revealed a hepatoid carcinoma of unknown but likely gynecologic origin. While uncommon, an underlying malignancy is a consideration in a patient with a necrotizing soft tissue infection whose clinical presentation is not typical.

Introduction

While advanced neoplastic diseases of the abdomen occasionally present with invasion through the abdominal wall, it is less common to present with a necrotizing soft tissue infection of the abdominal wall. Perforated colon and rectal cancers are reported to present in this fashion, but never a hepatoid adenocarcinoma [1]. We present an interesting case of hepatoid adenocarcinoma (HAC) presenting as a necrotizing soft tissue infection.

Case Presentation

A 46 year old woman with a history of sciatica presented with 1 week of malaise and weakness. She had noticed worsening of her sciatica for the past month and was being treated by a chiropractor. Additional symptoms included leg swelling, loss of appetite, and shortness of breath with ambulation. She appeared ill, was jaundiced, tachycardic and tachypneic. She had an abdominal wall mass, pitting edema of the abdominal wall, and diffuses abdominal tenderness. Her hemoglobin was 4.6 g/dl, white blood cell count 42.3 × 103/µL, creatinine 1.5 mg/dL, sodium 135 mmol/L, bicarbonate 16 mmol/L, lactic acid 2.3 mmol/L and albumin 1.8g/dL. She underwent a computed tomography (CT) scan revealing a small bowel fistula from the right lower quadrant to the anterior abdominal wall with extensive air and fluid dissecting through the musculature and subcutaneous fat of the abdominal wall, inguinal adenopathy, 3.9 cm left ovarian cyst, and bilateral mild hydronephrosis (Figure 1). The initial differential diagnosis included inflammatory bowel disease and malignancy.

The patient was admitted to the surgical intensive care unit, administered broad spectrum antibiotics, and given a blood transfusion. She was taken to the operating room where diagnostic laparoscopy revealed mucopurulent material in the peritoneal cavity and the omentum and right colon adherent to the abdominal wall. An abdominal incision was made to debride the anterior abdominal wall mass during which copious purulent and dishwater-like fluid as well as necrotic fat and muscle was noted. The omentum was adhered to the peritoneal contents and there was a rock-hard mass in the posterior cul-de-sac. After a thorough washout, the patient’s abdomen was temporarily closed and she continued resuscitation in the intensive care unit. The following day she returned to the operating room for a sigmoidoscopy and extended right hemicolectomy as well as further debridement of necrotic skin, fascia, and fat from the abdominal wall.

Intra-operative cultures grew Escherichia coli, Streptococcus anginosus, Candida albicans, Bacteroides fragilis, and mixed anaerobic flora. Over the next week, she returned to the operating room multiple times for washouts, an end ileostomy, mucous fistula, colonoscopy, clinical breast examination, partial oophorectomy and closure of the fascial defect using Strattice™ reconstructive tissue matrix (LifeCell Corp, Branchburg, NJ). The enterocutaneous fistula was isolated from the...
wound using a drain. The tissue defect was covered with a negative pressure dressing (Figure 2). The right colectomy specimen had metastatic carcinoma in the terminal ileum, appendix, and cecum as well as 2 of 6 pericolonic lymph nodes. Extensive lymphovascular invasion was present. The carcinoma stained positive for HEPPAR-1 and CK AE1/AE3. The cells were negative for CK7, CK20, PAX-8 (paired box gene 8), mamoglobin, ER (estrogen receptor), TTF-1, S100, calretinin, and HBME-1 (anti-mesothelioma antibody). The ovarian specimen revealed sheets and nests of cells with abundant eosinophilic cytoplasm, pleomorphic nuclei with prominent nucleoli, brisk mitotic activity which was all consistent with HCC (hepatocellular carcinoma) (Figure 3). Additional staining revealed SALL-4, CDX-2, and GATA-3 negativity, and CK-19 positivity. This discounted the possibility of a yolk sac tumor and supported a hepatoid carcinoma of unknown but likely gynecologic origin.

The patient’s serum tumor markers revealed an elevated CEA of 6.6 (normal< 3), CA-125 of 310 (normal< 35), and CA 19-9 of 35, and a normal AFP of 7.1 (normal< 5.5). A tri-phasic contrasted CT study did not reveal any evidence of HCC. Given the aggressiveness of this rare tumor type, the widespread disease, and the patient’s ECOG status of 4, no chemotherapy was recommended. The patient transitioned to inpatient hospice and died of her disease less than one month later.

**Discussion**

Hepatoid adenocarcinoma is a rare extrahepatic neoplasm most often described as originating in the stomach. Other sites for this tumor include the ovary, duodenum, urinary tract, pancreas, gallbladder, testicle, uterus, or lung. This tumor type was first reported in 1970 by Bourreille et al. [2] and remains a diagnostic and treatment challenge. It is more common in men, and the average age of diagnosis is 64 years [3].
HAC morphologically displays hepatoid differentiation such as polygonal cells in trabecular or glandular formation, bile canaliculi or bile production, and sinusoidal formation [4]. HAC tumors have a propensity for lymphovascular invasion [5]. It is difficult to differentiate HAC from hepatocellular carcinoma, especially when HAC metastasizes to the liver. HAC tumors have differential immunostaining patterns, with multiple different patterns reported in the literature. Table 1 displays commonly used immunohistochemical markers for HAC versus HCC and HYST [6-13]. Typically, HAC stains positive for AFP, mCEA, glypican-3, TTF-1, napsin A, Hep par 1, HEA-125, and MOC-31 positive. PLUNC and CDX-2 (a marker of adenocarcinomas of intestinal origin) can be negative or positive [14,15]. The cytokeratin profile is usually CK 7, CK 8, CK 18, and CK 19 positive, and CK 5, CK 6, CK 14, and CK 20 negative [16,17]. In this patient, the immunostaining profile of CK-19, CK AE1/AE3 and HEPPAR 1 positivity directed our concern to either HCC or HAC.

In this patient, there was no radiologic evidence of hepatocellular carcinoma on CT imaging, and no evidence intraoperatively of HCC. Given the extensive amount of pelvic tumor, the direct extension into pelvic bone, and the worsening sciatic pain pre-dating other symptoms, it is likely that this patient’s carcinoma started in the pelvis. In hepatoid tumors possibly arising from gynecologic structures, it is important to rule out hepatoid yolk sac tumor, which is a distinct entity. While both yolk sac tumor and HAC stain positive for AFP and glypican 3, hepatoid yolk sac tumors will also stain positive for SALL 4. This patient’s tumor was SALL-4 negative, supporting the diagnosis of HAC over yolk sac tumor. Hepatoid yolk sac tumors generally occur in younger patients than HACs, with an average age of 22 years. Patients with yolk sac tumors often also have a diagnosis of gonadal dysgenesis [18].

The median survival of HAC is 11 months, and there is no standardized treatment approach. The recommended treatment of HAC of presumed gastrointestinal origin is surgical resection and adjuvant chemotherapy- FOLFOX (leucovorin calcium, fluorouracil, oxaliplatin) or FOLFIRI (leucovorin calcium, fluorouracil, irinotecan) with or without bevacizumab. Alternatively, capcitabine with a platinum agent (oxaliplatin or cisplatin) has been used for treatment [3,14]. Treatment of pulmonary HAC is resection followed by cisplatin and gemcitabine, and sometimes followed by localized radiation therapy [19]. Hepatoid carcinoma of the ovary is less common, and has been treated with carboplatin and paclitaxel, often in conjunction with surgical resection. Given the pathologic similarity to hepatocellular carcinoma, sorafenib has been used with variable responses [16]. Our patient had an unresectable tumor and a poor functional status precluding any chemotherapy. Alpha fetoprotein is usually elevated in the serum of patients with HAC and, if initially elevated, can be used as a tumor marker to monitor treatment response. However, not all patients display an elevated serum AFP.

**Conclusion**

It is important to keep neoplastic processes as a differential diagnosis in patients with necrotizing soft tissue infections, especially when presenting with systemic evidence of malignancy. While immunohistochemistry can assist in differentiating HAC from hepatocellular carcinoma, the most convincing evidence is a lack of radiologic or surgical findings of HCC. As this case appeared to have originated in the pelvis, immunohistochemical markers were used to exclude hepatoid yolk sac tumor. HAC is a rare tumor, with its treatment is often determined by the organ system which is involved. However, a combination of surgical resection and chemotherapy has been reported to have treatment efficacy in patients presenting with early stage disease.

**References**


