Malignant Melanoma of the Gall Bladder, A Case report and Literature Review.

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Citation

Abstract
Malignant melanoma is a highly unpredictable tumor, which can metastasize to any organ, including the gallbladder in 4–20% [1,2]. Grossly and histologically, the distinction between primary and secondary lesions can be difficult to differentiate because they share many similar characteristics [2]. Melanoma involving the biliary tree seldom causes relevant symptoms during life, and that is why few cases are reported in the literatures [2] and those documented in living patients are even fewer [3,5]. Herein, we present a case of a 75-year-old female with metastatic melanoma to the gallbladder and a brief review of the literatures.

CASE REPORT
Our patient was a 75-year-old female who had a history of Clark’s level IV malignant melanoma in her left forearm in 2001. In 2006, she had clinically palpable left axillary lymph nodes. She underwent right axillary dissection, and pathology confirmed multiple nodal metastases. Subsequently, she was followed with careful surveillance computed tomography (CT). In May, 2007, a suspicious 1.5 cm nodule in gallbladder was noticed. Due to paucity of symptoms and ambiguous radiological nature of this lesion, she was advised to follow with another surveillance CT scan in August 2007 which showed an increase in size to 2.5 cm (Fig 1) and she was advised to have cholecystectomy. Her complete blood count and liver function tests were within normal limits. The patient was taken to the operating room and underwent laparoscopic cholecystectomy.

Figure 1
Figure 1: computed tomography (CT) shows gallbladder nodule measures 2.5 cm

Gross examination revealed 6 pieces of gallbladder tissue which showed dark firm serosal mass that measured 2 x 1.2 x 1 cm. Microscopic examination showed ulceration of the surface mucosa with an underlying spindle cell proliferation extending to the serosal surface (Fig 2-a). These cells had hyperchromatic nuclei, prominent nucleoli and showed frequent mitotic figures (Fig 2-b). The histological differential diagnosis included malignant gastrointestinal stromal tumor (GIST), Leiomyosacoma, malignant peripheral nerve sheath tumor, poorly differentiated carcinoma, and metstatic melanoma.
**Figure 2**

Figure 2-a: shows ulcerated surface mucosa with underlying hypercellular spindle cell proliferation. (X4)

**Figure 3**

Figure 2-b: high power of the spindle cells shows hyperchromatic nuclei, prominent nucleoli, and brisk mitotic figures (X20).

Immunohistochemistry showed that the neoplastic cells were diffusely positive for S100, melan-A, and CD117, focally positive for HMB45, and negative for CD34 (Fig 3 A-E). In conclusion, the histological features and immunohistochemical profile supported the diagnosis of metastatic melanoma of the gallbladder.

**Figure 4**

Figure 3 (A-E): Immunohistochemical study shows that the spindle cells are diffusely positive for S100 (A), Melan-A, (B), and CD117(C), focally positive for HMB-45(D), and negative for CD34(E)

**Figure 5**

**Figure 6**
DISCUSSION

In the gallbladder mucosa, some melanocytes are present because of the migration of melanin-producing cells from the neural crest during embryological development, and this warrants the possibility of the development of primary gallbladder melanoma. Both primary and metastatic melanoma of the gallbladder are extremely rare, indeed, only 20 cases of primary and over 60 cases of malignant melanoma (MM) metastatic to the gallbladder had been reported worldwide. Melanoma metastatic to the gallbladder, although clinically rare, is the most common metastatic lesion involving this organ, and accounts for 30–60% of all gallbladder metastases. Gallbladder involvement has been found at autopsies in 15% of patients who died from disseminated melanoma. However, the clinical diagnosis is made only in less than 5% of patients. The majority of primary melanoma metastasizing to the gallbladder arises in the skin, but the primary lesion may also be in the oral cavity, anorectal region, uveal tract or meninges. Most patients with gallbladder metastasis have widespread diseases at the time of diagnosis. Our patient had only axillary lymph nodes metastasis.

The distinction between primary and metastatic lesions can be difficult to differentiate in terms of the histopathological features alone. Although metastatic disease tends to present as multiple, flat and infiltrative lesions, single polypoid lesions can occur. Some authors found that ‘junctional changes’ (intra-epithelial extension) in the mucosa overlying the tumor associated with primary gallbladder melanoma is an important finding and confirm the gallbladder origin of the neoplasm. However, other authors have also found junctional activity in metastatic tumors. In fact, most investigators believe that melanoma in the biliary tree is almost always metastatic and the majority of cases described as primary are secondary to an unrecognized or regressed extrabiliary site.

Clinically, these tumors are often pauci-symptomatic, as is shown by the discrepancy between the number of published cases and the rate of detection at autopsy. The most common presentation for gallbladder melanoma is cholecystitis with or without cholecystolithiasis, likely due to obstruction of the cystic duct by the tumour mass. Other reported symptoms and signs of gallbladder metastatic disease were weight loss, food intolerance, nausea, vomiting and diarrhea. Our case was asymptomatic.

The diagnosis is often not suspected preoperatively, because of the extreme rarity of gallbladder melanoma cases. Non-invasive radiographic studies rarely can be of help in uncovering the presence of gallbladder disease. Moreover, differentiation from chronic acalculus cholecystitis may be impossible in the majority of cases. Computed tomography (CT) or ultrasound may show focal thickening of the gallbladder wall or intraluminal masses. Computed tomography (CT) of our patient showed a well defined single nodule.

Because of the rarity of metastatic melanoma of the gallbladder, the optimal therapy is unclear. In many cases, the diagnosis is not made before surgery. Aggressive surgical therapy, including cholecystectomy, appears to prolong survival and improve the quality of life in many patients, even in the face of disseminated disease. The treatment options in metastatic cases depend on the extension of the disease and on the clinical status of the
patient. Although surgical management is often possible, complete excision of tumour metastases is feasible only in about one third of patients. Nevertheless, surgical removal, even in the presence of disseminated disease, seems to be a worthwhile palliative procedure.

The prognosis of primary and metastatic melanoma of the gallbladder is very poor. Only a few cases were alive at the time they were reported. Survival ranged from a few weeks to several years. The mean survival times for patients with primary and metastatic lesions are 20.1 months and 8.4 months, respectively.

In summary, melanoma metastatic to the gallbladder is usually asymptomatic. If symptomatic, it mimics cholecystitis. Moreover, gallbladder involvement is not uncommon at autopsy in patients who died from disseminated melanoma. So, we would recommend maintaining a high index of suspicion for metastases to the gallbladder and liberal use of abdominal ultrasound as an adjunct to CT for the evaluation of abdominal pain in these patients. Cholecystectomy is the treatment of choice for such lesions in the absence of widespread disease. Palliative surgical removal, even in the presence of disseminated disease, seems to be worthwhile.

References
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