

## CASE REPORT

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# Gallbladder Metastasis Presenting with Cholecystitis in a Patient with Malignant Melanoma

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**ABSTRACT** Melanomas are malignant tumors that thrive from melanocytes. Malignant cutaneous melanoma can metastasize to almost any organ. A 64-year-old male patient with cutaneous primary malignant melanoma who had gallbladder metastases and was treated with cholecystectomy is presented. In the literature, up to the present, only a few patients with metastatic melanoma of the gallbladder, who was surgically treated, have been reported. In such cases, the level of suspicion of the surgeons must be high as possible due to the fact that most metastatic melanomas with gallbladder metastases are asymptomatic. However, it should be stated that the surgical approach is still an argued issue and treatment of metastatic cutaneous malignant melanoma should be individualized.

**Keywords:** Gallbladder; melanoma; metastases

Melanoma develops as a result of the malignant transformation of melanocytes, which are pigment-containing cells.<sup>1</sup> Cutaneous malignant melanoma is one of the tumors with an aggressive clinical course and a high probability of metastasis. There are some genetic mutations and immunological factors in the development and spread of the tumor.<sup>2</sup> Mutations that activate the BRAF protein are the most important of these mutations.

Most frequently metastasized organs are soft tissue, lung, liver, skin, brain, and less commonly, the gastrointestinal system.<sup>3,4</sup> Metastases of cutaneous melanoma to the gallbladder and biliary tree are uncommon and usually clinically asymptomatic. Gold standard treatment of patients with metastasis to the gallbladder is still controversial. In the treatment of malignant melanoma and metastases; surgical, palliative local, and systemic treatments are applied. Advantages of long-term overall survival, response rates, and progression-free survival can be achieved in the light of new treatments.<sup>5</sup> We wanted to present

a patient with an extensive-stage disease, who was previously diagnosed with malignant melanoma and admitted to our clinic with signs of cholecystitis.

## CASE REPORT

A 64-year-old male patient consulted a doctor 4 years ago when a black scaly growing lesion was detected in the back region, and a biopsy was diagnosed as malignant melanoma and was followed up regularly after extensive excision and completion surgery (Stage IIA (pT2b, N0, M0)). During the external center follow-up of the patient, local recurrence and regional lymph node metastases were detected several times in a period of approximately 2 years, and intermittent surgical treatment was performed and the patient was referred to the oncology unit, and adjuvant interferon treatment (1 year) was administered. In the last evaluation of the patient who was followed-up, reoperation was planned due to findings consistent with local recurrence, and the operated patient was referred to our oncology unit when the

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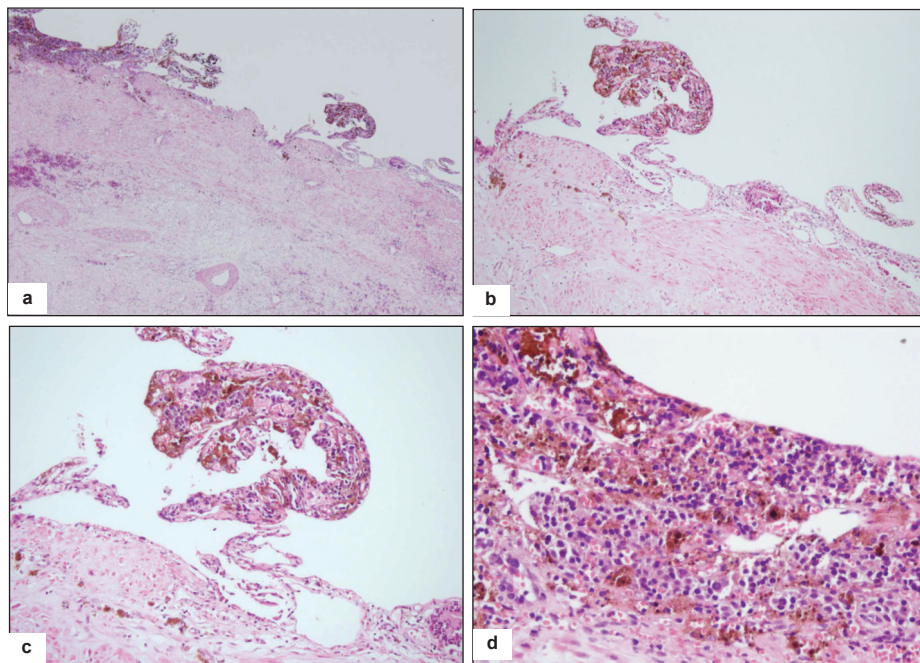
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pathology result was compatible with malignant melanoma. Positron emission tomography (PET) scanning of the patient, which was performed for staging, revealed post-operative changes in the lumbar region, parenchymal involvement suggesting metastasis in both lungs and liver, and signs of dilatation with positive  $^{18}\text{F}$ -fluoro-2-deoxy-D-glucose involvement accompanied by a marked growth in the gallbladder. The patient, who had abdominal pain and dyspeptic complaints, was firstly performed abdominal ultrasonography (USG) and in imaging; findings consistent with acute cholecystitis and lesions suspicious for metastasis in the liver were detected. Subsequently, the patient underwent contrast-enhanced abdominal magnetic resonance imaging, and a hydroptic, irregular gall bladder of large size extending to the pelvis with findings compatible with metastasis in the liver was detected. The patient's current blood tests were performed, BRAF mutation was requested, and the patient with signs of acute cholecystitis was consulted with the general surgery unit before systemic treatment. Cholecystectomy was performed and cholecystectomy material was compatible with malignant melanoma metastasis (Figure 1). The histopathological findings together with the im-



**FIGURE 1:** Macroscopic appearance of melanoma metastasis of cholecystectomy material.

mune profile were consistent with melanoma (Figure 2). The patient's BRAF result was positive, BRAF and MEK inhibitor double combination therapy was started as treatment. The oncological follow-up and treatment of the patient, who has nearly complete



**FIGURE 2:** Atypic cell (melanoma cells) existence in the gallbladder epithelium: a) H&E x40, b) H&E x100, c) H&E x200, and d) H&E x400.

clinical and radiological responses during the treatment period of approximately 9 months, continues.

## DISCUSSION

Although cutaneous melanoma metastases can spread to almost any part of the body, they are most commonly found in the brain, lung, and liver.<sup>6</sup> Gallbladder metastasis is rare and part of a common disease. Some scientists reported many metastatic melanomas of the gallbladder as asymptomatic.<sup>7,8</sup> Patients with gallbladder metastases may present with epigastric or right upper quadrant pain that sometimes imitates acute cholecystitis.<sup>7,9-11</sup> Abdominal USG is the favorite imaging study to evaluate gallbladder metastasis in symptomatic and asymptomatic patients. Gallbladder masses having a lower density than gallstones are characterized by minimal or no acoustic shadowing. Besides, the existence of focal thickening of the gallbladder wall or intraluminal masses can possibly be determined, or even, if the mass contains the bile tree it is possible to determine the presence of ductal distension as well. Metastatic disease of the gallbladder as a single polypoid tumor or as an infiltrative and flat lesion can be observed. In order to highlight the existence of pathological blood flow, the Doppler is beneficial.<sup>6</sup>

The existence of the solid masses that are arisen from the biliary tract may be revealed by the computerized tomography/magnetic resonance scan of the abdomen. Consequently, a positivity at fluorodeoxyglucose PET scan may indicate the formation of suspected metastatic sites, and also, it may be helpful in the differential diagnosis of gallbladder lesions. However, the uncertainty in the gold standard treatment of gallbladder metastatic melanoma is maintained. The surgical treatment is indicated by taking into consideration the clinical condition of the patient as well as the spread of the disease.<sup>10</sup> On the other hand, minimizing complications, relieving symptoms, and enhancing overall survival are considered in the objectives of treatment.

For palliative aims, surgical removal appears to be a valuable procedure even in events of widespread disease. Because in some studies, open surgery rather

than mini-invasive techniques are favored to minimize port site recurrence, the surgical approach is considered still a questionable issue.<sup>12,13</sup>

As a result malignant cutaneous melanoma is a skin cancer with variable and unpredictable biology, characterized by the highest mortality since it has a high potential for common metastasis. Gallbladder involvement through metastatic cutaneous malignant melanoma is a quite rare finding that is observed at autopsy and broadly associated with extensive metastatic disease. Since gallbladder metastasis in malignant melanoma is rare and symptomless, its diagnosis is difficult. However, life can be limited by complications. Although the few available evidence suggests that the surgical approach appears beneficial in terms of improving prognosis and quality of life, there is no consensus on the appropriate management of this condition.

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### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Patient Consent

*Obtained.*

### Authorship Contributions

**Idea/Concept:** Gülhan İpek Deniz, Mustafa Özgüroğlu; **Design:** Gülhan İpek Deniz; **Control/Supervision:** Nuray Kepil, Mustafa Özgüroğlu; **Data Collection and/or Processing:** Gülhan İpek Deniz, Zeynep Hande Turna; **Analysis and/or Interpretation:** Gülhan İpek Deniz, Zeynep Hande Turna, Mustafa Özgüroğlu; **Literature Review:** Gülhan İpek Deniz, Nuray Kepil; **Writing the Article:** Gülhan İpek Deniz; **Critical Review:** Nuray Kepil, Mustafa Özgüroğlu; **References and Fundings:** Nuray Kepil, Mustafa Özgüroğlu; **Materials:** Nuray Kepil, Mustafa Özgüroğlu.

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