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Case Report

Metastatic melanoma presenting as rapidly enlarging hepatic cysts ☆

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ABSTRACT

Malignant melanoma is a highly aggressive disease with a propensity for metastatic spread. Although recent advances in targeted therapies have improved outcomes, effective screening for metastasis remains an important area of further research. We present a case of a man in his 70s who was recently diagnosed with recurrent, locally advanced melanoma. He presented with abdominal fullness, jaundice, and poor appetite. MR imaging of the abdomen revealed innumerable hepatic cysts with internal fluid-fluid levels which were markedly increased in size and number from recent imaging. These findings necessitated a broad differential that included parasitic or bacterial infection, metastases, or drug-induced polycystic liver disease. Subsequent biopsy revealed metastatic melanoma consistent with the patient's primary tumor. The patient was ultimately transitioned to comfort care measures due to the burden of the liver metastases and passed away shortly after presentation.

Introduction

Cutaneous melanoma accounts for 1.7% of newly diagnosed primary cancers and is increasing in incidence in countries with large populations of fair-skinned individuals such as the USA, UK, Australia, and countries in Northern Europe [1]. While making up only a small subset of cutaneous malignancies, melanoma accounts for a disproportionate amount of morbidity and mortality. This is attributable to its propensity for metastatic spread to local tissue or organs such as the lung, liver, brain, and intestine [2]. Historically, patients with metastatic melanoma had a 5-year overall survival rate of less than 10% but recent advances in targeted therapies have dramatically improved outcomes with 5-year survival rates now standing at 40%-50% in patients with locally advanced disease [1,3].

Here we present a unique imaging presentation of metastatic melanoma to the liver. The case required a broad differential due to the patient's complex history of melanoma and multiple myeloma, antineoplastic therapy, and remote travel. This case illustrates the wide range of imaging presentations that can be seen with metastatic melanoma and highlights the high degree of suspicion needed when evaluating liver lesions in patients with recurrent metastatic disease.

☆ Competing Interests: The authors have declared that no competing interests exist.

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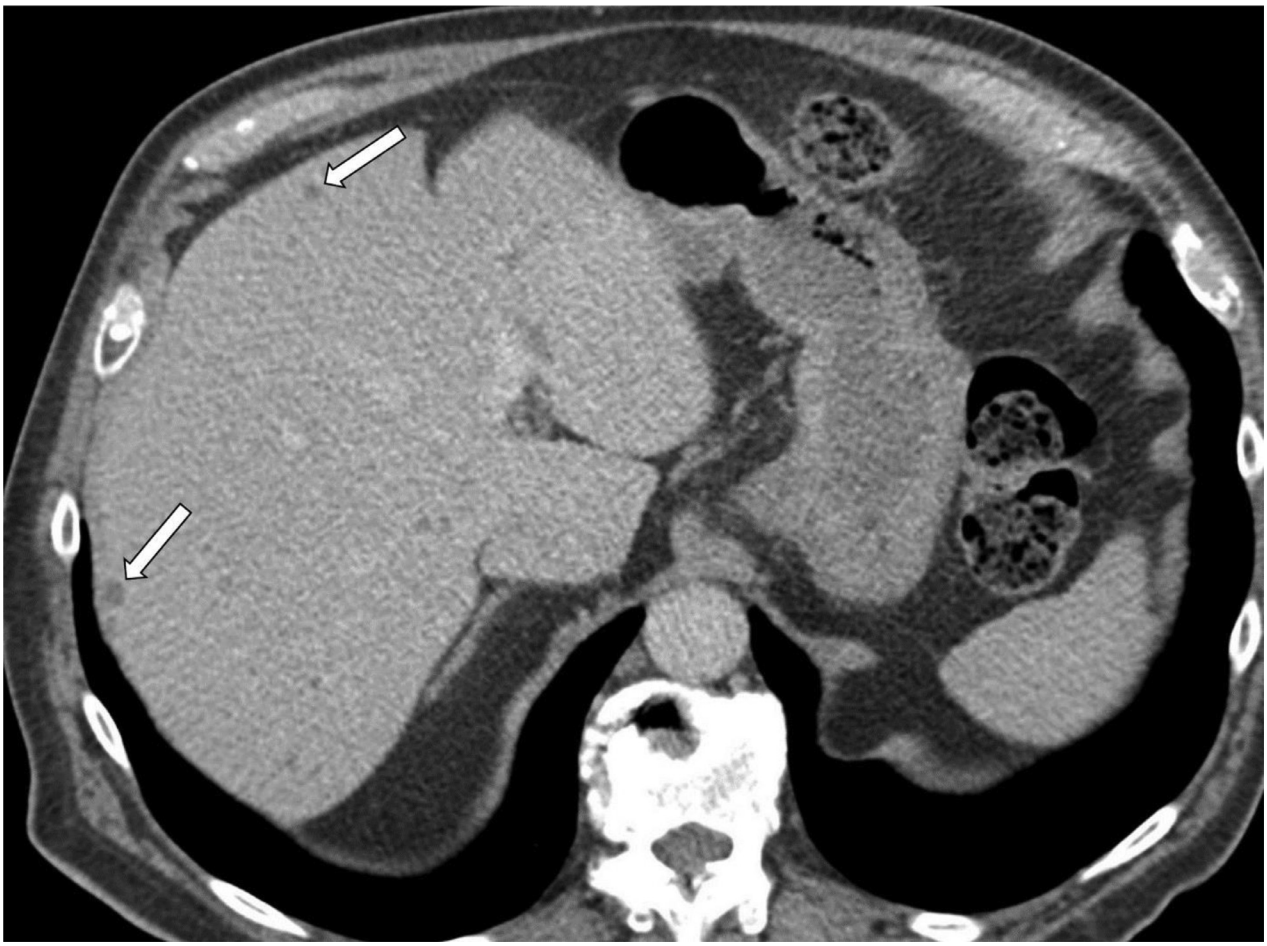

Fig. 1 – CT image performed 2 months prior to presentation. Multiple sub-centimeter hypodense hepatic cysts were noted (arrows).

Table 1 – Laboratory tests evaluating liver function during the patient's hospitalization. All tests included in the table are noted to be elevated from the laboratory's reference range.

Laboratory test	Measured value	Reference range
Alanine aminotransferase	427 U/L	<40 U/L
Aspartate aminotransferase	323 U/L	<37 U/L
Alkaline phosphatase	568 U/L	30-120 U/L
Bilirubin - Total	9.2 mg/dL	<=1.2 mg/dL
Bilirubin - Direct	7.5 mg/dL	<=0.4 mg/dL
Gamma-glutamyl transferase	339 U/L	12-55 U/L

Case report

We report the case of a man in his 70s with a history of locally advanced melanoma and multiple myeloma who was admitted to the oncology service in 2022 with abdominal fullness, jaundice, and anorexia. His melanoma was initially diagnosed in 2017 with the primary tumor on his right lower extremity as stage IIIc (T4b, N1a, and M0) and determined to be SOX10 and S100 positive. At that time, he was treated with local excision and 1 year of adjuvant nivolumab. In 2021, the patient was diagnosed with multiple myeloma and begun on a combination regimen of bortezomib, lenalidomide, and dexamethasone. One month before presentation to the hospital, he developed inguinal lymphadenopathy and was diagnosed with recurrent melanoma. He was started on temozolomide rather than his original anti-PD-1 therapy due to evidence that anti-PD-1 treatment is associated with an increased mortality rate in those with co-existing multiple myeloma [4]

Two months before presentation, an abdominal CT revealed sub-centimeter hypo-attenuating foci of indeterminate etiology (Fig. 1).

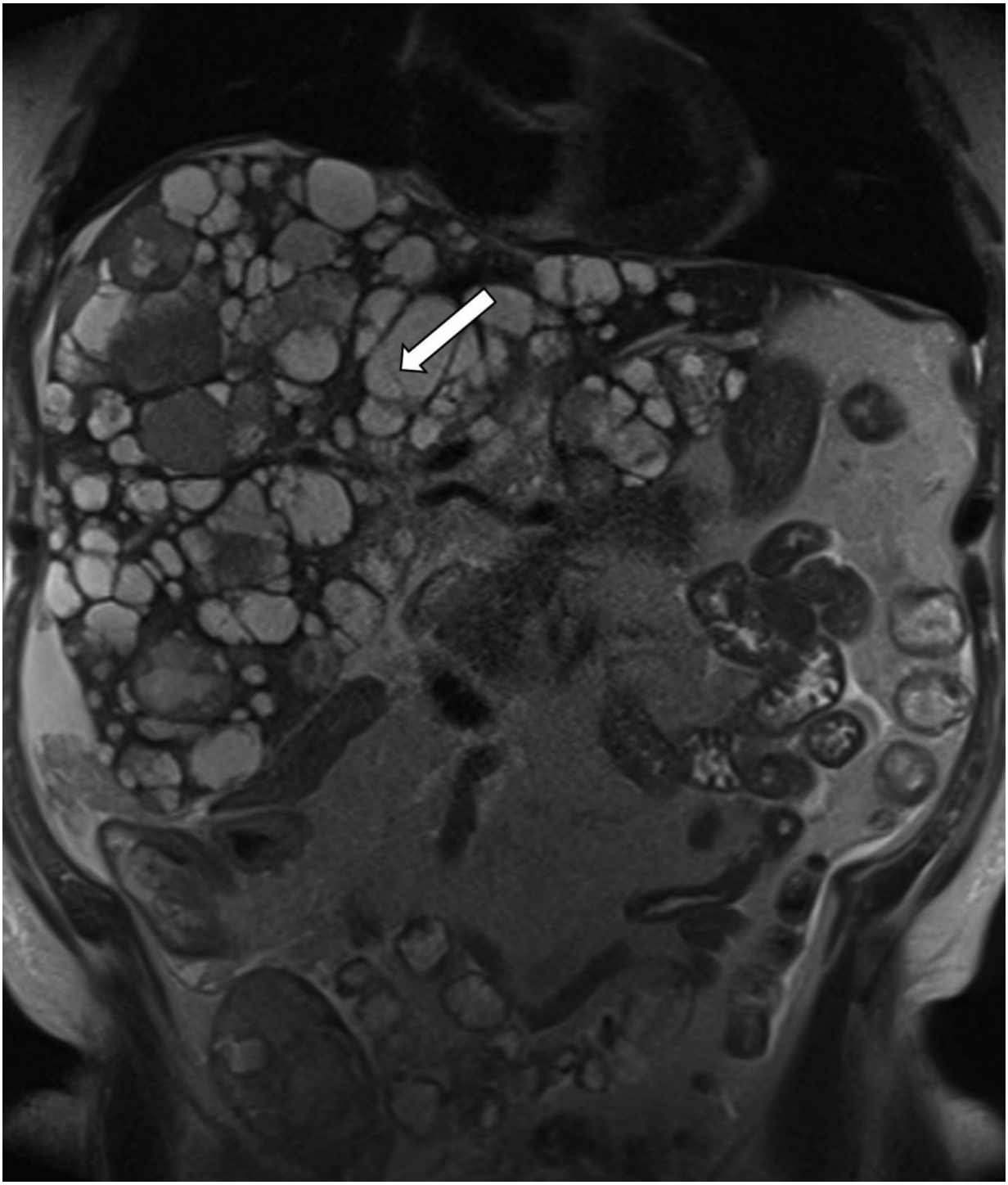

Fig. 2 – T2-weighted coronal MR image taken during the patient's hospitalization showing innumerable heterogenous cystic lesions in the liver. Some of the cystic lesions contain thin internal septations (arrow).

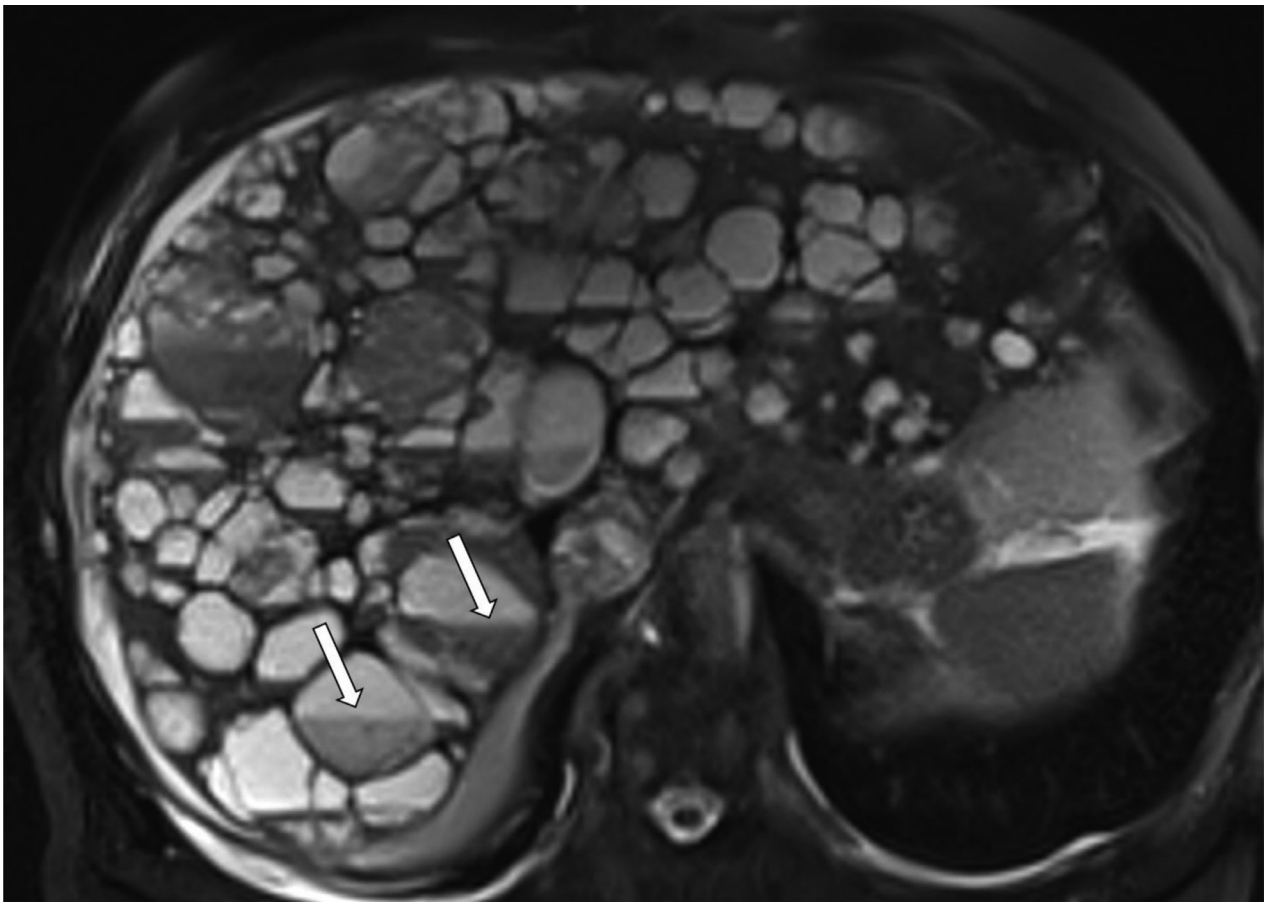

Fig. 3 – T2-weighted axial MR image of the abdomen demonstrating numerous hepatic cysts with internal fluid-fluid levels (arrows).

Two weeks before admission, laboratory tests reported a mild elevation in liver function tests. Subsequent ultrasound imaging showed interval increase in the size and number of the previously documented hepatic cysts. Upon admission to the oncology service, the patient's liver function tests were elevated beyond his previous values (Table 1).

MRCP showed innumerable nonenhancing, mildly complex cystic lesions with associated diffusion restriction, internal fluid-fluid levels, and thin septations, markedly increased in size and number from previous imaging studies. The lesions were hypointense on T1-weighted images and hyperintense on T2- weighted images which were taken shortly after admission (Figs. 2-4).

On initial presentation, the patient's liver function tests were concerning for a cholestatic process. This was initially attributed to either viral hepatitis or temozolomide induced liver injury [5]. The subsequent MRI findings narrowed the differential towards an infectious, drug-induced, or neoplastic etiology. Infectious abscesses were considered due to the patient's immunocompromised state secondary to his antineoplastic therapy and history of travel to South-East Asia and South America. However, the patient denied infectious symptoms and the imaging characteristics were less suggestive of abscesses which are typically thick walled with peripheral rings of enhancement [6]. The patient's history of rapidly enlarging hepatic cysts while on numerous antineoplastic medications raised consideration for drug-induced polycystic liver disease. While exceedingly rare, there has been a documented case of a patient with metastatic disease receiving checkpoint blockade and tyrosine kinase inhibitor therapy that developed rapidly growing, benign hepatic cysts [7]. Despite this, metastatic melanoma remained the most likely diagnosis given the patient's oncologic history and the tendency for melanoma to metastasize to the liver [3]. Although it would have been an unusual presentation, plasma cell infiltration also remained on the differential [8].

A viral hepatitis panel was sent and returned negative. Due to concern for a possible parasitic infection of the liver, echinococcal and entamoeba histolytica serology studies were also ordered. The patient was negative for entamoeba histolytica IgG and the echinococcal IgG study did not result before the patient passed away. Due to the patient's clinical decline, the team proceeded with an ultrasound-guided biopsy of the liver lesions prior to receiving the echinococcal lab results. Fine needle aspiration (FNA) biopsy revealed numerous individual moderate to large malignant cells including a few cells with bizarre, giant nuclei. The cells displayed a high nuclear to cytoplasmic ratio with 1 or 2 small nucleoli. The concurrent core biopsies showed small fragments of malignant cells. Immunostains were performed on core biopsy. The neo-

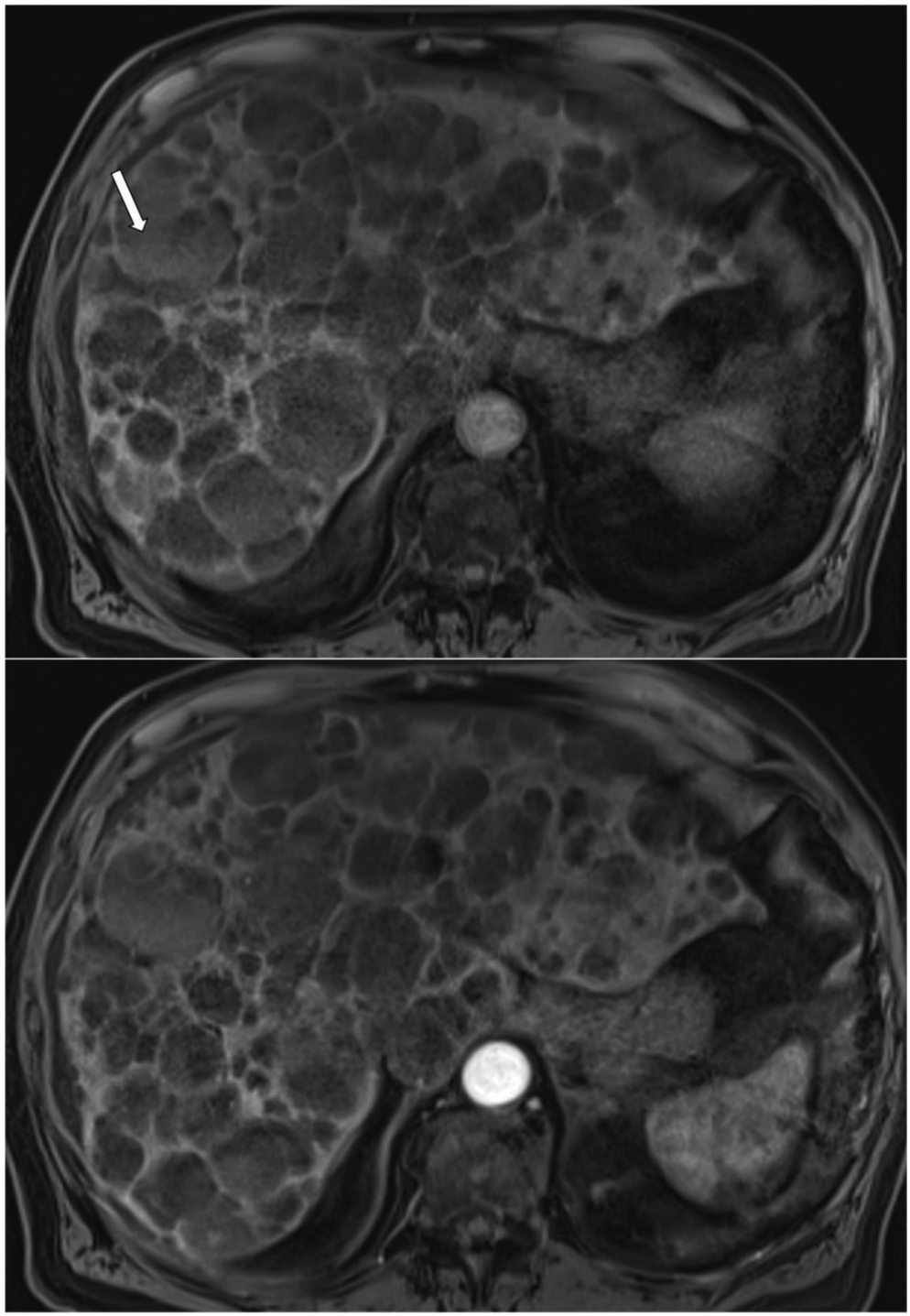

Fig. 4 – Noncontrast (top) and arterial phase postcontrast (bottom) T1 weighted MR image of the abdomen. Cystic lesions in the liver are hypointense in comparison to the background liver parenchyma with a small amount of layering T1 hyperintensity in a few of the lesions (arrow). Lesions are nonenhancing on postcontrast imaging.

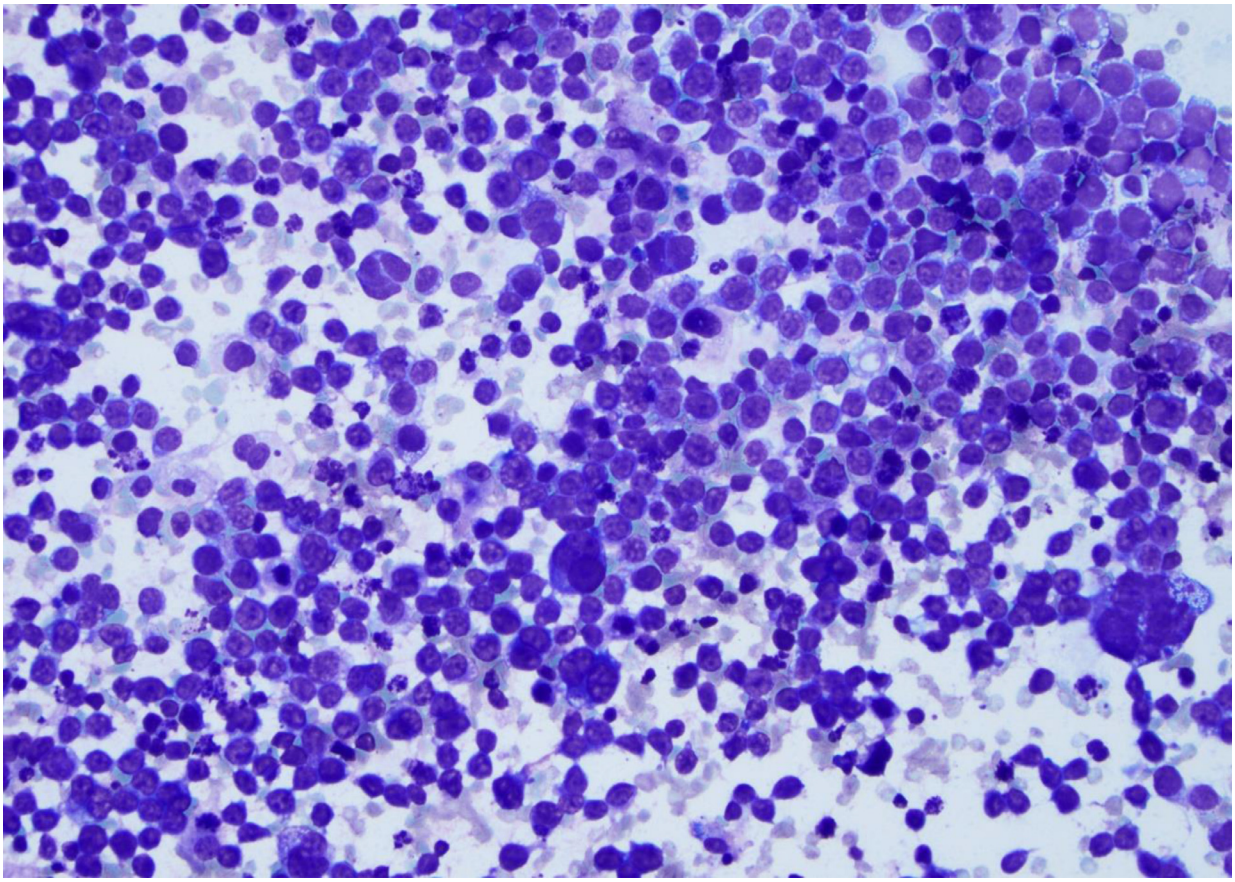

Fig. 5 – A smear of aspirated material showed numerous single cells with high nuclear to cytoplasmic ration. Note a few large cells with bizzare nuclei (Diff-Quik stain, X200).

plastic cells were positive for SOX10 and S100 and negative for CD138 which was consistent with the patient's known primary melanoma (Figs. 5–8).

During the patient's hospitalization, his abdominal symptoms worsened, and he began experiencing significant respiratory compromise. His care was primarily supportive during the diagnostic workup. Unfortunately, due to the burden of his metastatic disease there were no further treatment options available. The patient was transitioned to comfort care measures and passed away in the hospital soon after the final diagnosis was made.

Discussion

Malignant melanoma is a highly aggressive cancer with a strong propensity to spread hematogenously [1]. In 1 study, 31% of patients were diagnosed with metastatic disease during their initial presentation, and of these patients, the lung was the most common site of distant organ metastasis at 48%, followed by the brain at 29% and bone at 23% [9]. The aggressive nature of the disease is driven in part by the expression of cell-surface adhesion molecules on malignant cells. This allows malignant cells to clump in the bloodstream, protecting against shear stress and aiding in extravasation from the blood into solid organs [3]. The outcomes for patients with metastatic melanoma have dramatically improved with the advent of anti-BRAF and checkpoint inhibitor therapies. With these therapies in hand, early detection of metastatic disease is crucial for treatment. However, guidelines for screening remain controversial and range from CT or PET scans every 3-12 months to follow up with careful physical examination only [10].

Even in patients who undergo routine imaging, early metastases can sometimes be difficult to distinguish from other benign etiologies on cross-sectional imaging. This is particularly true within the liver as most small hepatic lesions are benign, even in patients with known extrahepatic malignancy [11]. Despite this challenge, a high degree of suspicion for metastatic malignancy must be maintained during the evaluation of new liver lesions in patients with an oncologic history. Suspected liver metastases are best evaluated with contrast-enhanced MRI. Metastatic liver lesions usually demonstrate diffusion restriction and are solid appearing, hypointense on unenhanced T1 weighted images, and enhance on postcontrast images [6]. While metastatic melanoma is often indistinguishable from other metastatic lesions, 20%-25% of melanoma-originating lesions can appear intrinsically hypertense on T1 weighted imaging due to high

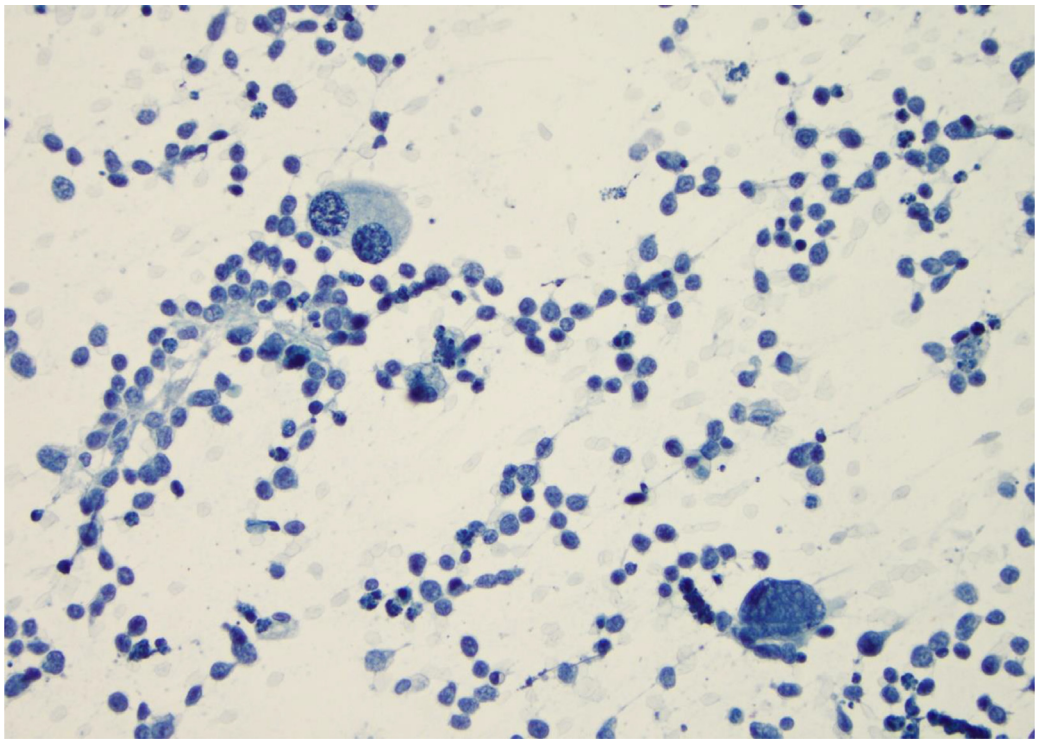

Fig. 6 – One large binucleated cell and 1 large cell with huge nuclei is noted while all cells are malignant in this field (Papanicolaou stain, X200).

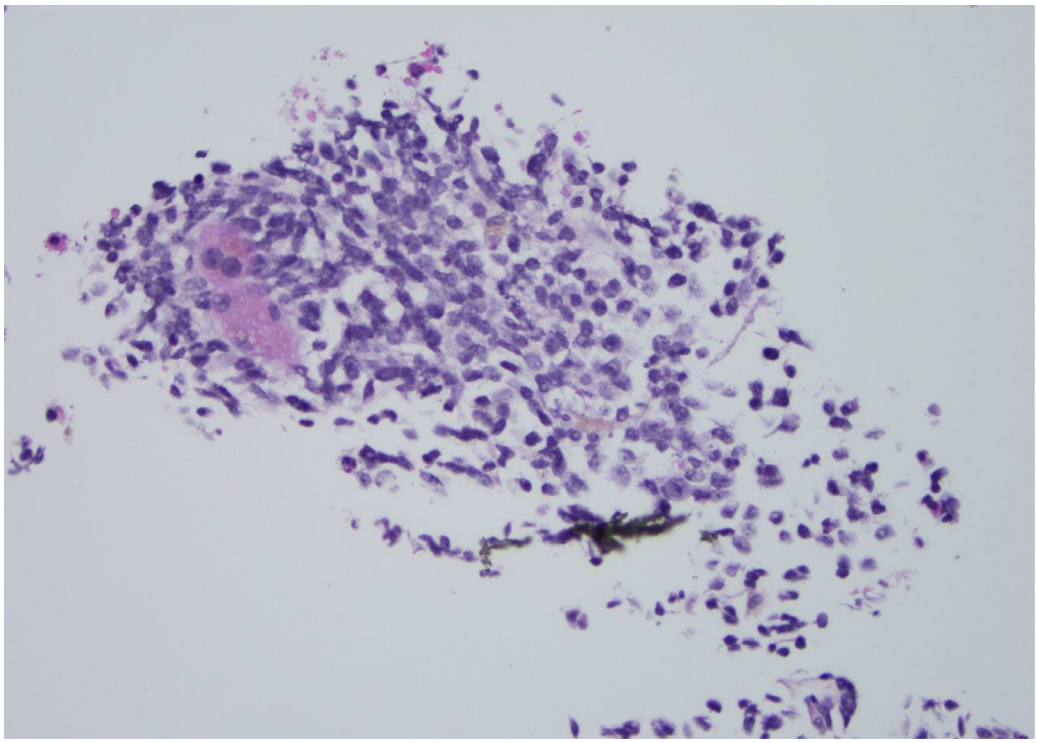

Fig. 7 – A concurrent small core biopsy shows a small fragment of malignant cells with round to oval nuclei (H&E stain, X100).

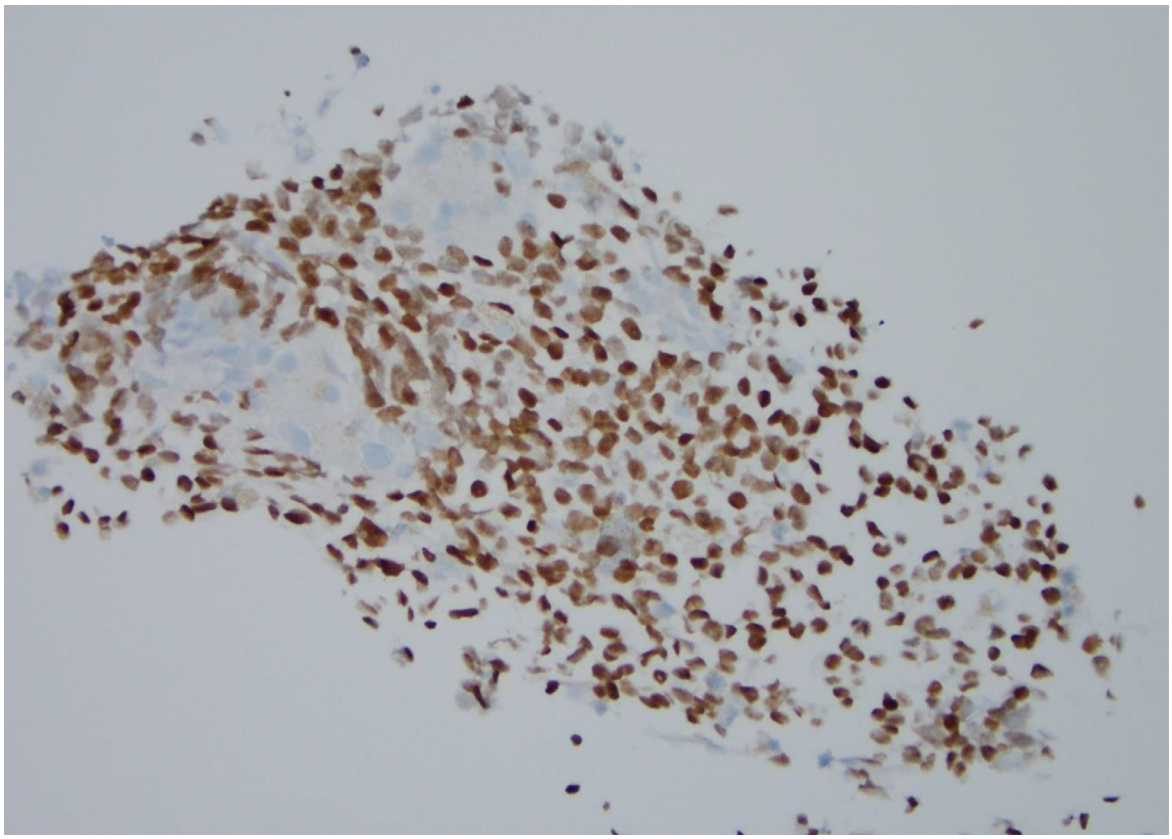

Fig. 8 – The malignant cells expressed nuclear staining for SOX10 confirming the diagnosis of melanoma (immunostain, X100).

concentrations of melanin or hemorrhage [11]. However, due to the unique properties of each patient's malignancy, hepatic melanoma can also present with a range of unusual imaging features. Previously published literature described a case of diffuse metastatic melanoma presenting with no distinguishable nodules with MR imaging [12] and a case of primary hepatic melanoma appearing as an irregularly hypointense, lobular mass on T1-weighted imaging with irregular contrast enhancement [13]. In this case, we present another unique presentation of hepatic melanoma to further demonstrate the wide range of imaging characteristics.

Conclusion

Here we report a case of an atypical imaging presentation of hepatic metastatic melanoma. In this patient's case, the rapid growth in the size and number of lesions and cystic appearance were uncharacteristic of typical melanoma metastases. The rate of growth also raised concern for a rare, cystic liver disease process such as one previously documented in response to antineoplastic therapy [7]. Overall, the imaging findings in this case serve as an example of the variable appearance of metastatic melanoma and the importance of maintaining a broad differential in the workup of hepatic lesions in patients with known malignancy.

Patient consent

The patient reported in the manuscript signed the informed consent/authorization for participation in research which includes the permission to use data collected in future research projects including presented case details and images used in this manuscript.

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