Rectal melanoma presenting as a solitary complex cystic liver lesion: role of contrast-specific low-MI real-time ultrasound imaging

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Abstract Cystic hepatic metastases arising from malignant melanoma are extremely rare, with the few such cases reported in the literature to date describing indeterminate imaging findings, being focused more on computed tomography. To the best of our knowledge, there is no prior report describing contrast-enhanced ultrasound findings of a solitary cystic liver metastasis from a primary rectal melanoma. We herein describe a case of a 41-year-old patient with a rectal melanoma, in whom the first manifestation of disease was a solitary complex cystic liver metastasis incidentally detected by ultrasound. On admission, our patient was free of specific symptoms and his laboratory test was normal. In this setting, contrast-enhanced ultrasound showed some distinctive features that helped us to make the correct diagnosis, confirmed subsequently by FNAC examination, thus allowing to provide the correct management for our patient. Although cystic metastases are rare, knowledge of CEUS imaging findings will be invaluable for radiologists and other medical subspecialties that may face such cases in the future in helping to provide adequate management for affected patients.

Keywords Contrast-enhanced ultrasound · Microbubbles · Rectal melanoma · Complex cystic focal liver lesions · Sonovue

Riassunto Metastasi epatiche di tipo cistico secondarie a melanoma maligno sono estremamente rare; ad oggi, i pochi casi riportati in letteratura descrivono reperti di imaging aspecifici, focalizzandosi quasi esclusivamente sul ruolo della Tomografia Computerizzata. Per quanto a nostra conoscenza, non ci sono precedenti lavori in letteratura che descrivano reperti eco-contrastografici di casi di metastasi cistiche solitarie epatiche a partenza da melanomi primitivamente rettali. Di seguito, descriviamo il caso di un paziente di 41 anni con melanoma rettale, nel quale la prima manifestazione clinica di malattia è stato il riscontro diagnostico di una lesione epatica cistica complex di natura metastatica, rilevata incidentalmente ad un esame ecografico di routine. Al momento del ricovero, il paziente era asintomatico e con profilo laboratoristico nella norma. In questo caso, l'eco-contrastografia ha mostrato caratteristiche semeiologiche peculiari che hanno permesso una corretta diagnosi presuntiva, confermata successivamente da un esame FNAC, consentendo un corretto management del paziente. Sebbene le metastasi cistiche rappresentino un'eventualità rara, riconoscerne i reperti CEUS è indispensabile sia per i radiologi sia per qualunque altro specialista che possa trovarsi ad affrontare tali casi in futuro, fornendo loro un valido strumento per la corretta gestione di questo tipo di pazienti.

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Introduction

Complex cystic focal liver lesions (FLLs) represent a wide spectrum of liver lesions that include both benign and malignant lesions. Discrimination between benign and malignant complex cystic FLLs is of fundamental importance since the management and prognosis vary greatly [1–3].

In our institution US is the imaging technique of first approach in the study of the liver and contrast-enhanced ultrasound sonography (CEUS) is usually chosen to characterize FLLs indeterminate at the conventional ultrasound (US). However, conventional ultrasound has low ability in differentiating diagnosis between them and the patients usually have to be referred to other imaging modalities such as contrast-enhanced computed tomography (CT) or contrast-enhanced magnetic resonance imaging (MRI) for further characterization.

The development of low acoustic power contrast-enhanced ultrasound allows real-time depiction of dynamic blood flow perfusion throughout vascular phases and it has been documented that real-time CEUS greatly improves the diagnostic ability in characterization of FLLs [4, 5], whereas few data were available with regard to CEUS in characterization of complex cystic FLLs [2, 3].

We report a case of metastatic melanoma presenting as a solitary complex cystic liver lesion detected incidentally by ultrasound. We also focused the attention on the crucial role of CEUS as primary imaging modality in providing the information needed for management decision.

There are few prior cases describing the imaging findings of cystic liver metastases [6–10]. Most of these articles to date are based on CT findings, and to the best of our knowledge there are no articles describing CEUS findings of cystic metastases arising from malignant melanomas. We think that this report may be useful for early and correct diagnosis of similar cases.

Case report

A 41-year-old Caucasian man who had undergone excision for adenoid cystic carcinoma in the left parotid gland 3 years ago was admitted to our hospital for an incidental focal liver lesion detected by follow-up US examination.

The patient was asymptomatic, except a 3-month history of fatigue and moderate weight loss. His past medical history was clear of any other serious health problems. Physical examination revealed a fully alert patient with a soft and non-tender abdomen and normal bowel sounds. The remaining of the physical examination was unremarkable. Conventional laboratory evaluation was normal. His chest X-ray was normal and plain abdominal films were free of any pathology.

Abdominal ultrasound (US) was performed with a MyLab 70 XVG GOLD scanner (Esaote, Genoa, Italy) using multifrequency (2.5–5 MHz) convex probe. On US, the focal liver lesion appeared as a solitary hypo-anechoic complex cystic lesion with a thin internal septum in the left hepatic lobe (Fig. 1), but the differential diagnosis was

Fig. 1 Conventional US. Melanoma metastasis presenting as solitary hypo-anechoic complex cystic lesion with a thin internal septum in the left hepatic lobe, classified of uncertain diagnosis at conventional US (arrows)

considerably difficult exclusively on the US imaging. There were no other coexistent liver lesions or abnormalities.

To better assess the liver lesion, the patient was submitted to contrast-enhanced low-MI real-time ultrasound (CEUS) imaging with Sonovue® (Bracco, Milano, Italy). Sonovue® was injected into the antecubital vein in a bolus fashion of 2.4 mL, followed by a flush of 10 mL of 0.9 % normal saline solution. After contrast injection continuous scanning began immediately and lasted 4–5 min. On CEUS, the lesion revealed hyper-enhancement of the cystic wall and intra-cystic septation in the arterial phase (Fig. 2a, b). The enhancement washed out rapidly and depicted as hypo-enhancement in the portal and late phases (Fig. 2c, d). A schematic representation of enhancement features on CEUS was shown in Fig. 3. These features were heavily suggestive for malignancy.

Owing to the remarkable suspicion of the malignant nature of the cystic liver lesion, the patient underwent ultrasound-guided fine needle aspiration cytology (FNAC) with the evacuation of a brown fluid. Cytologic examination revealed a cell population showing melanin pigment in the cytoplasm and nuclei variable in size and shape (Fig. 4a). At immunochemistry, expression of S-100 and melanocytic markers (such as HMB-45) help in identifying melanoma metastasis (Fig. 4b).

Consequently, searching for the unknown primary tumor, dermatological and ophthalmological examinations were performed, but revealed no evidence of a cutaneous or an ocular primary lesion.

Whole-body contrast-enhanced computed tomography (CT) did not show any other liver lesion, except the heterogeneously low-density cystic lesion of left liver lobe previously detected on US examination. In addition, CT

Fig. 2 CEUS. **a, b** The lesion revealed hyper-enhancement of the cystic wall (*arrows*) and intra-cystic septation (*arrowheads*) in the arterial phase. **c, d** The enhancement washed out rapidly and depicted

as hypo-enhancement in the portal and late phases (images taken 25, 32, 81, and 148 s after the contrast injection)

Fig. 3 Schematic representation of malignant complex cystic FLLs enhancement features. In our case, hyper-enhancement of the cyst wall and internal septation in arterial phase (**a**) with portal wash-out

(**b**) on CEUS provide helpful findings leading to the suspicious of a malignant nature of the cyst because they reflect viable cancerous tissue

revealed an aspecific thickening of the rectal wall suggesting to better investigate the gastrointestinal tract. No other abnormalities were identified.

MRI of the pelvis confirmed the presence of the thickening of the rectal wall and revealed also multiple enlarged regional lymph nodes.

Subsequently, a colonoscopic examination was performed for a better characterization of the rectal lesion. Colonoscopy clearly showed a polypoid lesion about 3 cm in size, which was located on the right wall of the lower rectum, about 30 mm from the anal verge. Biopsy of the rectal mass was performed and

Fig. 4 Fine-needle aspiration cytology in diagnosis of liver metastasis from malignant melanoma. **a** The smear shows a dispersed cell population. The nuclei vary in size and shape. Some of the cells show

melanin pigment in the cytoplasm (Diff-Quik, $\times 40$). **b** Immunohistochemical confirmation of metastasis was obtained with cellular positivity for HMB-45

histopathological examination demonstrated a malignant rectal melanoma.

The clinical diagnosis was rectal melanoma and the tumor was staged as stage IV according to the tumor-node metastasis (TNM) classification.

Shortly after diagnosis and clinico-radiological staging, the patient underwent an abdominoperineal resection (APR) with dissection of loco-regional lymph nodes. The resection specimen showed a black solid tumor that was covered with normal mucosa. Microscopic findings revealed infiltration of the wall with pleomorphic cells that contained melanin in the cytoplasm. Immunohistochemically, tumor cells were positive for the expression of S-100 and HMB-45. The final histopathologic diagnosis was a primary rectal malignant melanoma based on these histopathological features. Tumor cells were not seen in the resected margins of at least 2 mm. However, at pathological report 3 out of 6 regional lymph nodes included in the specimen were involved. After the intervention, the patient made an uncomplicated recovery and was discharged 16 days later.

Two months after the ABR, the patient underwent exploratory laparotomy with left hepatic wedge resection of segments 2 and 3. A solitary metastatic melanoma with extensive necrotic areas was found. The surgical excisional margins were free of cancer.

The patient is currently being followed up by the oncology team and will be considered for postoperative adjuvant chemotherapy.

Discussion

Metastases composed of large fluid-filled areas within the lesion are regarded as cystic metastases [8]. Although not frequent, cystic liver metastases usually arise from

colorectal cancers [6], whereas lesions from other neoplasms such as malignant melanoma are very rare, with few such cases reported in the literature to date describing indeterminate imaging findings, being focused more on computed tomography [6–10]. In fact, despite an extensive search, we were unable to find a similar case in literature in which a solitary liver metastasis from an unacknowledged primary malignant melanoma presented atypically with an almost totally cystic appearance and required a careful differential diagnosis from other cystic focal liver lesions.

The cause of the cystic change in these secondary liver tumors is not well understood. The pseudocystic appearance due to necrotic phenomena or cystic degeneration is typical of histotypes (colon cancer, breast or ovarian cancer, sarcomas, melanomas, etc.) in which the tumor grew rapidly, outstripping/depleting its blood supply. Alternatively, the pseudocystic appearance is the result of treatment, e.g., GIST after therapy with imatinib. Instead, a clearly cystic appearance is characteristic of primary histotypes (ovarian cystadenocarcinoma, pancreatic macrocystic mucinous adenocarcinoma, etc.) whose specific neoplastic cellular differentiation produces a cystic structure regardless of overlying necrosis or cystic degeneration [7, 8].

Identification and correct characterization of cystic metastases is fundamental, especially if the liver lesion is solitary. Final diagnosis is not difficult when complex cystic lesions with irregular septa or focal wall thickening and enhancing intracystic solid portions are diffusely distributed in the context of a high-risk oncologic scenario. However, distinguishing on the basis of imaging solitary cystic metastases from other complex cystic focal liver lesions, as in our case, can be problematic because the imaging findings are usually unspecific [8].

On CEUS, typical cystic metastases appear as partially enhancing lesions with a peripheral rim enhancement and

complete non-enhanced internal areas in the arterial phase. Hyper-enhancement of the internal septations and intracystic solid component in the arterial phase are also observed. During portal and sinusoidal phases, the hyper-enhanced areas wash out and show hypo-enhancement [10].

According to Lin et al. [2], the characterization algorithm of CEUS for solid FLLs (sustained enhancement in portal-sinusoidal phase indicates benign lesions and wash-out in portal-sinusoidal phase indicates malignancies) is also applicable for cystic FLLs. Therefore, regardless of the appearance in the arterial phase, a hypoperfused hepatic lesion in the portal-sinusoidal phase should be considered malignant until proven otherwise, both in case of cancer patients and when the lesion is an incidental finding, as in our patient [2, 3].

In our case, an enhanced cyst wall and an enhanced septum on CEUS provide helpful findings leading to the suspicion of a malignant nature of the cyst because they reflect viable cancerous tissue. In fact, because US contrast agent circulating in the microvessels of cystic wall and internal septa produces strong signal intensity when it is destroyed by ultrasound, CEUS imaging could allow both the cystic walls and the internal structures of cystic lesions to be evaluated [3].

In conclusion, even though metastatic cystic hepatic lesions are rare and the differential diagnosis is not easy, the malignant nature should be always suspected in presence of a solitary complex cystic liver lesion, especially in the context of a high-risk oncologic scenario. In these cases, CEUS may provide an added diagnostic value, potentially avoiding the use of more invasive and expensive imaging modalities. The correct diagnosis leads to the best management for the patient.

Compliance with ethical standards

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). All patients provided written informed consent to enrolment in the study and to the inclusion in this article of information that could potentially lead to their identification. The study was conducted

in accordance with all institutional and national guidelines for the care and use of laboratory animals.

Conflict of interest The authors have no conflicts of interest.

Informed consent Written informed consent was obtained from patient according to the Ethical Committee of our Institution.

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