CASE REPORT

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Left gluteal metastasis from a hepatocellular carcinoma – an unusual finding

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Abstract

Hepatocellular carcinoma (HCC) is the primary malignant tumor of the liver that is directly derived from parenchymal cells. It is usually encountered in patients already suffering from a long-established liver disease that has evolved past the stage of liver cirrhosis. It is usually associated with viral liver infections, alcohol consumption or other dietary habits that lead to liver damage. Metastases are not rare and are usually found incidentally after a period of monitoring the main liver disease. We present here a rare case of HCC metastasis found in the right gluteal region, in a hepatitis C virus-infected patient also displaying lung tumor lesions. Diagnosis of both the metastasis and of the primary tumor were found during the same hospital visit, employing contrast-enhanced computed tomography, magnetic resonance imaging and ultrasound (US), with positive biopsy of the metastatic lesion, performed under US guidance. The patient received oncological treatment, with good prognosis and stable evolution during the next eight months since diagnosis.

Keywords: hepatocellular carcinoma, gluteal metastasis, lung metastasis, immunohistochemistry, differential diagnosis.

Introduction

Hepatocellular carcinoma (HCC) is a malignant epithelial tumor with origins in the hepatic cells. It is the most frequent type of primary hepatic malignancy, occurring mostly in patients who suffer from hepatic cirrhosis [1, 2]. It is also one of the major causes of death among these patients. It is the sixth most frequent type of cancer worldwide (749 000 new cases/year) and the third cause of death by cancer (692 000 cases/year) [1–3].

The incidence varies from 3/100 000 in Western countries to more than 15/100 000 in certain endemic regions and it is directly correlated with the geographical distribution of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, recognized as the most important causes of chronic liver disease and consequently HCC [2–4].

The occurrence of the hepatocellular carcinoma is associated with a series of predisposing factors. HCC is more frequent among males, old age also being associated with an increase predisposition. Viral liver disease, exposure to exogenous toxins (aflatoxins or alcohol abuse), metabolic factors (obesity, hepatic steatosis, hemochromatosis, type 2 diabetes mellitus) or congenital disorders (either alpha-1 antitrypsin deficiency, Wilson's disease or hemophilia) are also strongly associated with HCC development [5–8].

The frequency of HCC among the patients who suffer from hepatic cirrhosis is reported to range between 1% and 7% [1–4, 9]. Hepatitis C chronic infections that are left untreated lead to hepatic cirrhosis in the majority of cases, and the risk of HCC is of 14.4%. Literature cites HCC development in approximately 20% of the patients diagnosed with liver cirrhosis, at an average time interval of 30 years and in 1–5% of the patients infected with the hepatitis C virus [9, 10].

A growing body of evidence directly correlates the "metabolic epidemic", an emerging threat especially in the Western countries due to unhealthy dietary habits, and liver disease. An interesting correlation was established between non-alcoholic liver disease leading to cirrhosis, diabetes and the early development of HCC [11, 12]. Mechanisms related to fibrosis, especially involving liver stellate cells and the altered environment created by pro-fibrotic conditions also seems to favor tumor development in the affected liver [13, 14].

The difficult differential diagnosis of the premalignant dysplastic lesions is usually aided by pathology. The invasion of the stromal cells or the invasion of the cancer cells inside the portal triads or inside the fibrous septa define HCC and are not found in the dysplastic lesions [15]. Nevertheless, other histological features can also be observed in dysplastic lesions [16]. Multiple immuno-histochemical (IHC) stainings are available and even computer-aided techniques have shown promising results

in diagnosing and establishing prognosis in HCC patients, especially when correlated with clinical and laboratory findings [17]. However, the latest protocols used for diagnosis and staging employ contrast-enhanced imaging methods, as obtaining positive biopsy from the liver may pose the risk of dissemination by needle or possible false-negative reports. Interpreting contrast uptake during the main physiological phases, either performed by the operator or aided by computerized semi-automatic techniques, can greatly enhance diagnostic accuracy, especially in centers that experience lower incidence of the disease [18, 19].

As modern diagnostic techniques and treatment options become increasingly available, the survival rate of HCC patients increases. Thus, a larger number of metastases are found, hence the possibility to encounter more unusual sites of extrahepatic dissemination [20]. Even in this context, muscle metastases remain rare, with only a few cases not related to needle dissemination being reported in cohort studies [21].

Aim

We present the rare case of a male patient diagnosed with a rare form of metastasis from HCC, highlighting the diagnostic procedures and the importance of immuno-histochemistry in establishing the origin of the secondary tumor.

Case presentation

We present the case of a non-smoking 69-year-old patient with rural residence. He provided informed consent in writing upon admission as part of the standard procedure, following the recommendations of the Ethical Boards of both the University of Medicine and Pharmacy of Craiova, and the Emergency County Hospital of Craiova, Romania. All relevant medical data, exclusive of any personal identifying information, were collected in accordance with national and international legislation and guidelines.

He was a former farmer, known with hepatitis C viral infection for 10 years and who underwent hepatoprotective treatment, with no other significant morbidities. He was referred to the Clinic of Gastroenterology accusing pain in the right hypochondriac region, tegumentary pruritus and asthenia.

The patient also described a self-perceived subcutaneous tumor mass in the left gluteal region, measuring approximately 8/11/13 cm, solid upon local examination, painless on palpation, with irregular margins, adherent to subjacent textures and having normal covering tegument. Affirmatively, the tumoral development appeared after intense physical effort that the patient had performed eight months before and showed some improvement after self-administered anti-inflammatory therapy. The patient noticed not only the decrease in the painful lumbar symptomatology, but also a decrease in the dimensions of the tumor and in the local inflammatory phenomena.

Clinical examination showed normally hydrated, slightly pallid teguments, with skin lesions located on the front and back of the chest, on the abdomen and inferior limbs, the left gluteal tumor previously described, balanced cardiorespiratory system, liver with the inferior margin at 3 cm under the costal margin, of slightly increased consistency, sensitive on palpation, impalpable spleen and reported polakiuria.

The biological examination revealed increased values for aspartate transaminase (AST) 133.9 U/L, alanine aminotransferase (ALT) 127.5 U/L, gamma-glutamyl-transferase (GGT) 148 U/L, alkaline phosphatase 111 U/L, an inflammatory syndrome – erythrocyte sedimentation rate (ESR) at one hour 50 mm/h, with no anemic syndrome – hemoglobin (Hb) 13.6 g/dL, and with thrombocytopenia – 86 000/μL. The anti-HCV antibodies had a titer of 26.38 cutoff index (COI), and from the tumor markers we retain the alpha-fetoprotein (AFP) of 3577 ng/mL, neuron-specific enolase (NSE) 15.34 ng/dL and CYFRA 21-1 (cytokeratin 19 fragments) 2.96 ng/mL.

Abdominal ultrasound highlighted within the liver segments VII/VIII, near the inferior vena cava, an oval area with a hyperechoic, inhomogeneous structure, with peripheral halo of 3/2.4 cm that seemed to invade the right hepatic vein. The left liver lobe was 10 cm, right lobe 16 cm, irregular margins, with intensely diffuse inhomogeneous structure, aspect specific of cirrhosis. We decided to follow with abdominal contrast-enhanced ultrasound (CEUS); after the administration of 2.4 mL contrasting agent (SonoVue, Bracco Imaging, Switzerland), the hepatic tumor showed inhomogeneous and complete early arterial contrast uptake, more intense and precocial than the hepatic parenchyma. In the portal phase, the tumor was isocaptant, and in the tardive phase, it presented incomplete tardive "wash-out", suggestive aspect for HCC.

We performed a magnetic resonance imaging (MRI) of the abdomen and pelvis to evaluate the gluteal tumoral formation. After injecting the contrast agent, we found an inhomogeneous, gadophil tissue mass in the left gluteal region measuring 8.8/11.3/13.2 cm, with edema and osteolysis in the sacrum and on the same side of the wing of ilium. It also showed infiltration of the adjacent soft parts, prevertebral muscles and gluteal muscles (Figure 1, A and B). The liver had an irregular form, and showed two rounded focal tumors measuring 5.76 cm and 2.93 cm. We found normal signal and heterogeneous signal after the injection of the contrast agent, with hemorrhagic areas inside the larger lesion, with an intense collection in the arterial phase and washout in the tardive phase, with aspect of a possible HCC (Figure 2). We could not exclude the secondary hepatic determinations and the presence of adenopathy in the hepatic hilum with a maximum dimension of 1.69/0.7 cm.

Consequently, this was a diagnostic challenge as the differential diagnosis between a HCC with secondary hepatic determinations or a gluteal sarcoma had to be established.

In the aid of giving the diagnosis, we performed musculoskeletal echography that highlighted in grayscale a hypoechoic, multilobated image, well delimited, with sharp edges inside the *gluteus maximus* muscle, close to the iliac crest, which was deforming the superficial soft tissues (Figure 3A). Power Doppler examination revealed intense, diffuse, anarchic signal inside the lesion (Figure 3B). Puncture–aspiration–injection followed by reaspiration revealed no significant information, thus automatic core needle biopsy using a Bard® Magnum® gun (Bard, Arizona, USA) was performed, obtaining four samples from the gluteal lesion for histopathological (HP) and IHC examination. The biopsy was performed with local anesthesia, both at the skin entry and near lesion, with a 14G needle, after preliminary scanning the area of

entrance to identify the appropriate approach. The skin was cleared using specific asepsis protocol and then was cut using a disposable surgical blade No. 24, to introduce the needle tip, which was advanced into the lesion under US guidance. The position of the needle tip was confirmed at the level of the lesion by US examination in two planes and the cutter was then deployed. We harvested four tissue fragments and placed them in a formalin container for the HP and the IHC stainings. We fixated the bioptic material with 10% formalin and included in paraffin.

The HP evaluation highlighted tissue fragments of variable dimensions (from 1 to 6 mm) with a microscopic structure of hepatic parenchyma. Enlarged epithelial cells displayed slightly rounded or polygonal shapes, with eosinophilic cytoplasm, rounded nucleuses and dispersed chromatin. We observed tumoral cells laid in trabeculae or islands, separated by a conjunctival richly vascularized capillary stroma. Further examination revealed relatively rare mitoses and fibrosis that shaped a nodular structure with reduced focal chronic infiltrate (Figure 4, A–D).

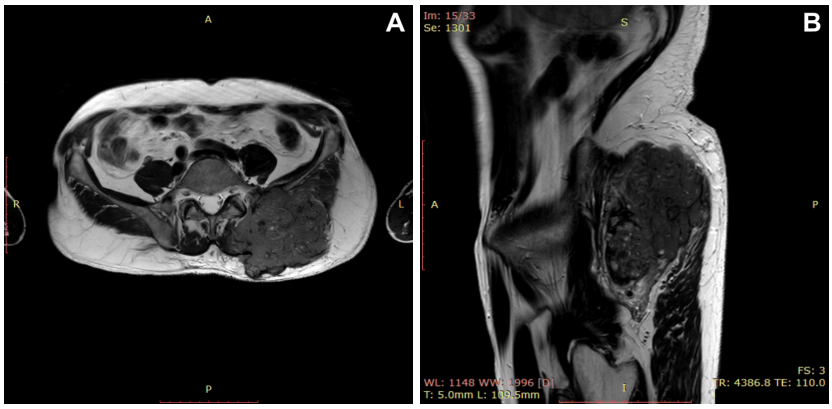

Figure 1 – ***MRI of the left gluteal mass, showing an inhomogeneous, intensely gadophil mass, displaying edema and osteolysis of the sacrum and iliac crest, with invasion of soft parts and paravertebral and gluteal muscles: (A) Cross-sectional image; (B) Sagittal view.***

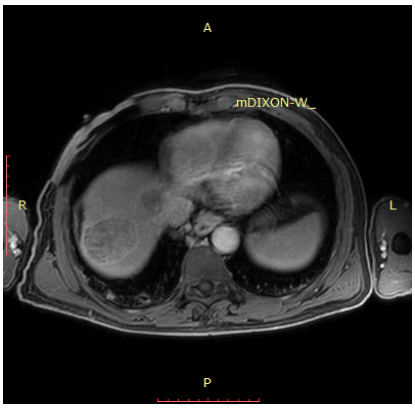

Figure 2 – ***MRI of the liver, showing the primary heterogeneous HCC lesions, arterial contrast uptake and late washout, characteristic of primary liver tumors derived from hepatocytes.***

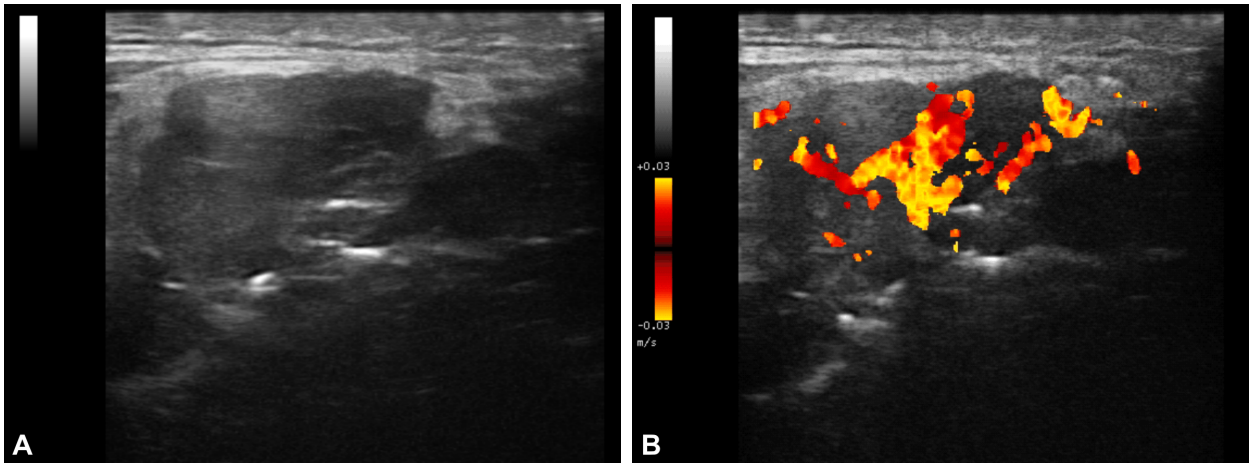

Figure 3 – ***Grayscale (A) and Doppler (B) ultrasound examination of the left gluteal mass.***

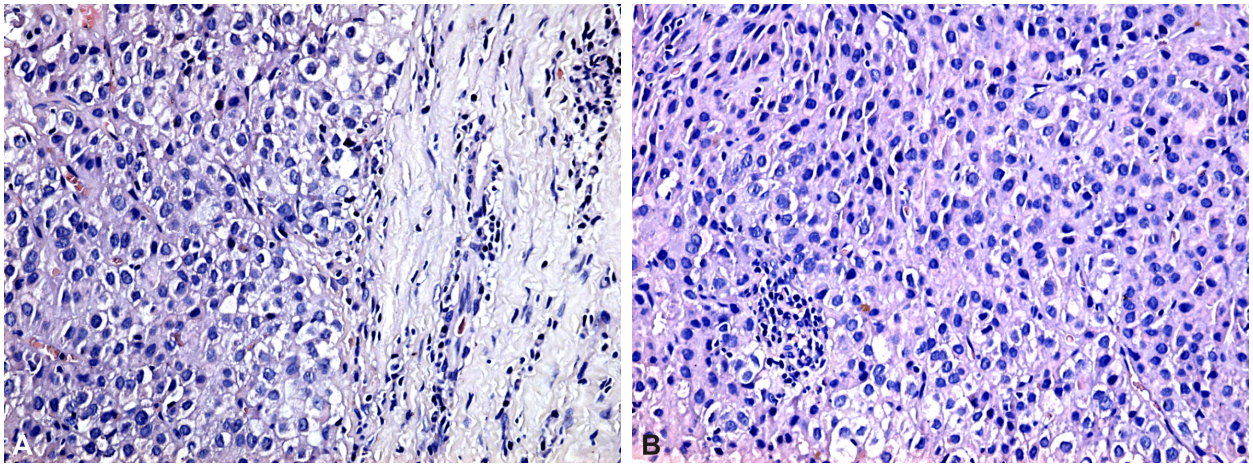

Figure 4 – ***We could observe the trabecular placement of tumoral cells (A) and islands (B), separated by a conjunctival richly vascularized capillary stroma (A). Hematoxylin–Eosin (HE) staining, ×100.***

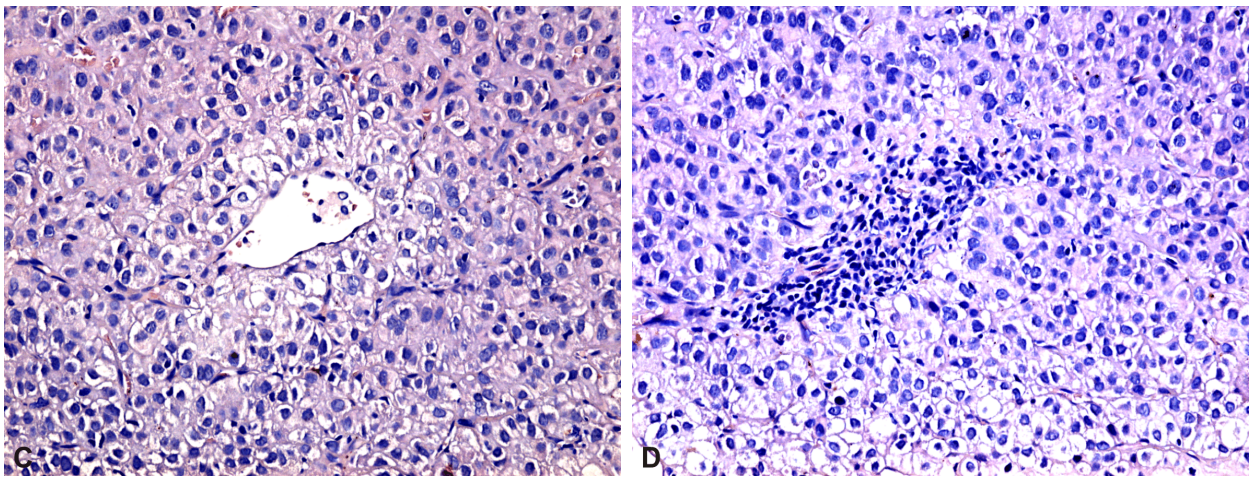

Figure 4 (continued) – ***We could observe the trabecular placement of islands (C and D), separated by a conjunctival richly vascularised capillary stroma (C). HE staining, ×200.***

We further performed IHC stainings, employing the Avidin–Biotin complex (ABC) method. We used the following antibodies: AFP, vimentin, carcinoembryonic antigen (CEA), Ki67, cytokeratin (CK) 8/18, CK7 and OCH1E5 (mouse monoclonal hepatocyte-specific antigen).

The IHC analysis showed negative AFP in the tumoral cells and positive vimentin in vessels. We found negative vimentin and CEA in the tumoral cells. However, we identified positive Ki67 signal in approximately 15% of the tumoral cells (Figure 5), diffuse positive OCH1E5 in the tumor cells (Figure 6, A and B), also diffuse positive CK8/18 within the tumor (Figure 7, A and B) and negative CK7 (Figure 8).

After microscopy examination, the diagnosis was of metastatic trabecular hepatocellular carcinoma.

A chest computed tomography (CT) scan was considered convenient for the evaluation of the neoplastic extension; this emphasized the multiple pulmonary bilateral nodules (Figure 9, A and B) with a maximum dimension of 1.12 cm, acknowledged as secondary pulmonary determinations, as well as an adenopathy of up to 12 mm (right paratracheal lymph nodes, the Barety segment, supracranial and infracranial).

Hence, taking into consideration the suggestive aspect of the multifocal HCC, emphasized by the MRI and by CEUS, AFP of 3577 ng/mL, and the pathology exam of the tumoral gluteal formation, we established a diagnosis of HCC with muscular and pulmonary determinations.

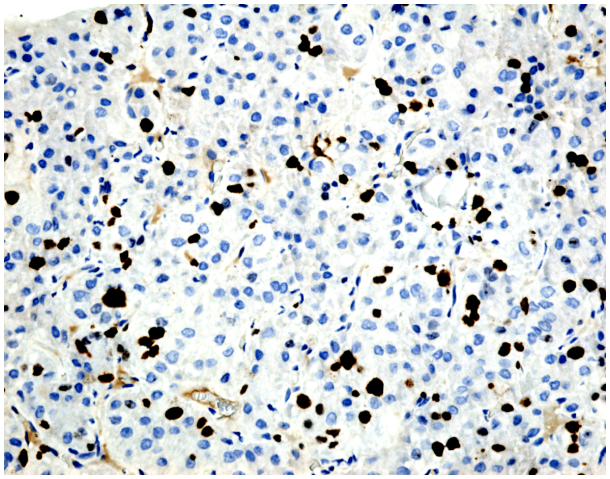

Figure 5 – ***We observed positive nuclear Ki67 signal in some of the tumor cells. Anti-Ki67 antibody immunostaining, ×100.***

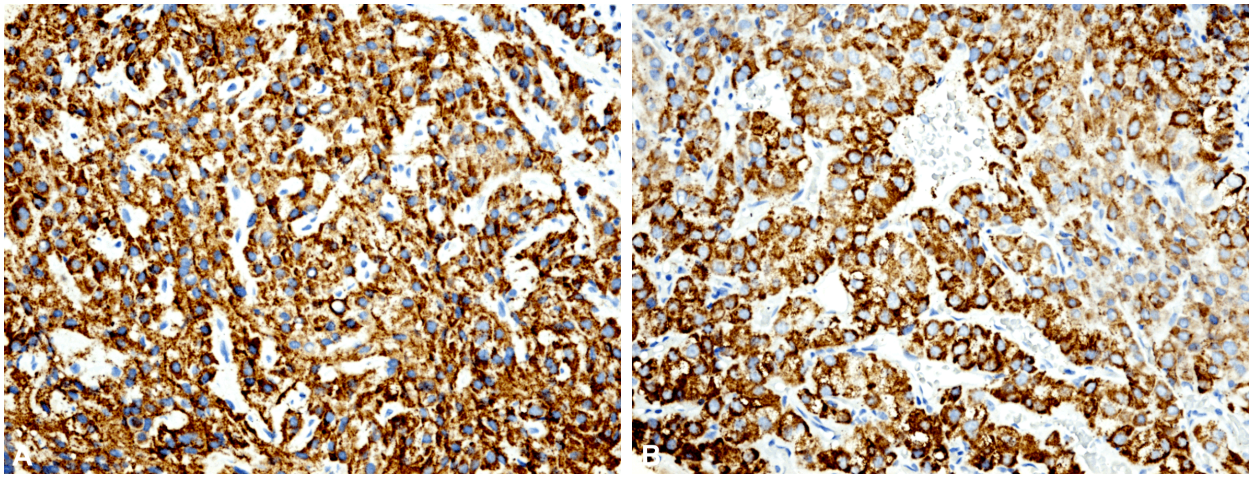

Figure 6 – ***(A and B) Immunostaining with OCH1E5 marker showing diffuse signal. Anti-OCH1E5 antibody immunostaining, ×100.***

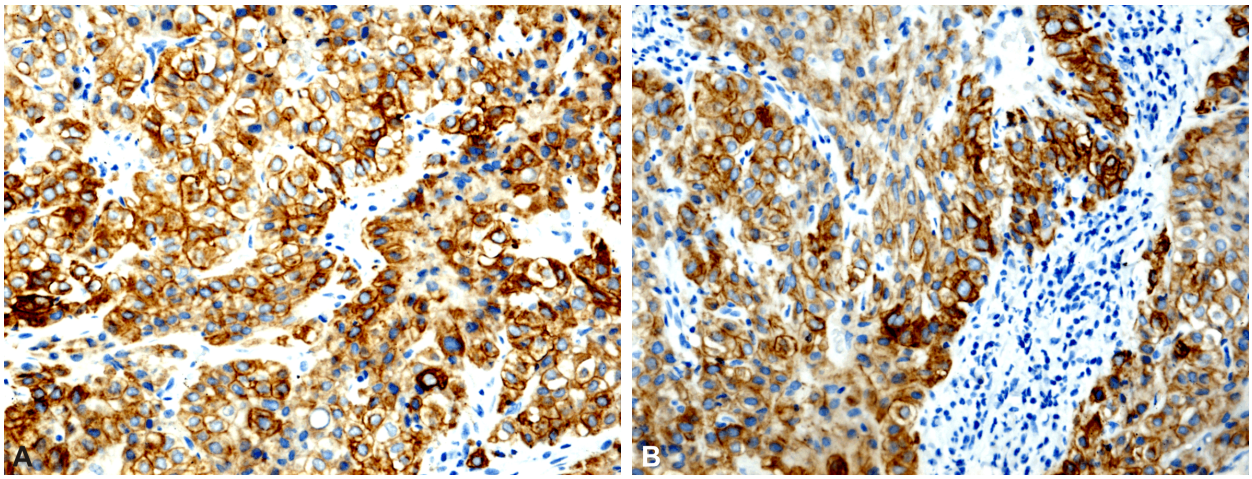

Figure 7 – ***(A and B) Diffuse immunostaining with CK8/18 marker. Anti-CK8/18 antibody immunostaining, ×100.***

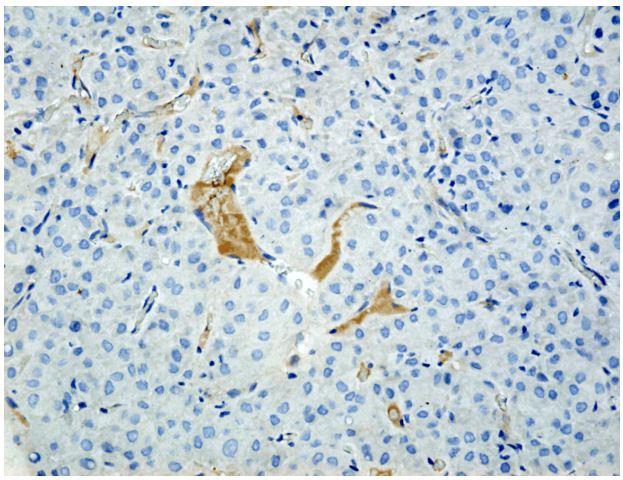

Figure 8 – ***We found negative CK7 signal within the tumor. Anti-CK7 antibody immunostaining, ×100.***

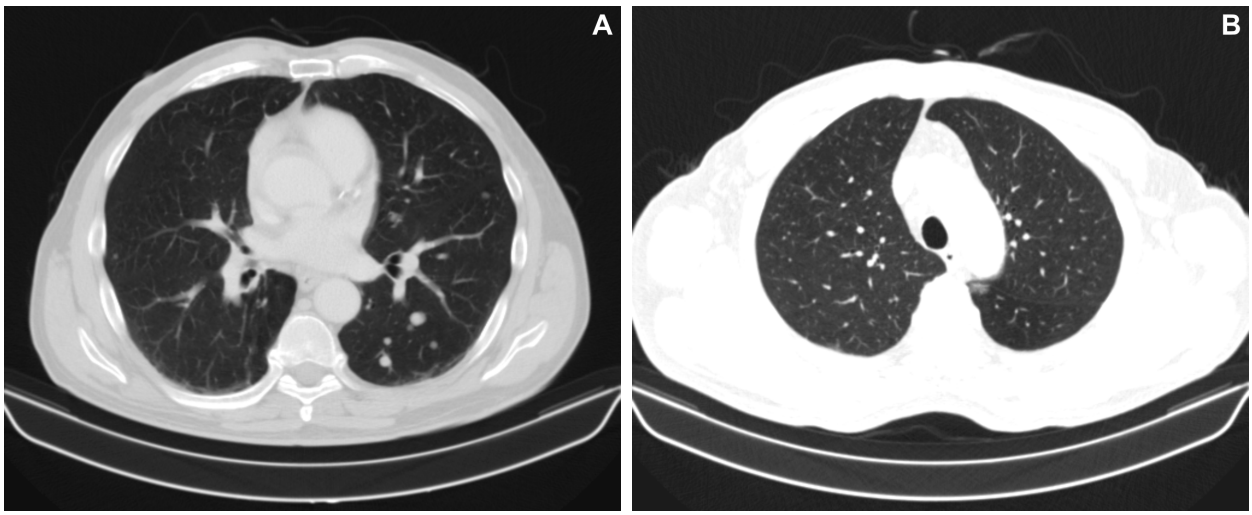

Figure 9 – ***(A and B) Chest CT showing multiple lung nodules and enlarged lymph nodes, suggestive of secondary dissemination.***

The patient was initiated in September 2017, with Sorafenib 200 mg film-coated tablets given at 800 mg/day – two capsules in the morning / two in the evening. Until now, the patient continues with Sorafenib without significant adverse events.

AFP levels progressively decreased over the course of nine months, down to a value of 130.3 ng/mL in June 2018. Regarding the biological condition, the latest results of the analysis performed on in June 2018 revealed ALT 131.01 U/L, AST 125.79 U/L, GGT 143.26 U/L and normal blood counts.

The patient so far tolerated the treatment well, without changing the general state. The last imagistic investigations carried out on March 2018 revealed the presence of

calcifications inside the gluteal tumor mass with initial dimensions of 11.5/10.3/15.7 cm. The pulmonary nodules are spread on both pulmonary fields, with maximum dimensions of 1.23/1.21 cm and 1.42/1.28 cm, respectively.

At the hepatic level, tumor formations with a size of 5.47/4.28 cm in segment VII/VIII and 3.14/2.82 cm, respectively, at the level of the IVa segment were maintained, with no other evolutionary lesions.

Discussions

A clear differential diagnosis between left gluteal sarcoma or hepatocellular carcinoma with muscular metastasis may pose a challenge, as it is an unusual dissemination. The sarcomatous aspect of the left gluteal formation presents a challenge; however, the biological status of the patient and the history of the chronic hepatitis C point to a different diagnosis. In such cases, both the HP and the IHC analysis are the ones to establish the diagnosis.

We used cross-sectional contrast-enhanced imaging to diagnose the primary liver tumor; as CEUS is available in our Center and no major side effects or contraindications exist for the contrasting agent, we decided to perform this investigation as well in order to confirm the diagnosis. The CT further aided in staging as it highlighted the secondary lung tumors.

However, we diagnosed the left gluteal formation after we performed the pathology analysis on the biopsy specimens obtained under ultrasound guidance from the left gluteal formation of the patient, even though identified by imaging. This posed an important diagnostic challenge, as muscle HCC metastases are rare [22].

There are few reports in the literature of gluteal masses that were diagnosed as extrahepatic disseminations from HCCs. One such case was presented by Gilsanz Fernández *et al.*, in 1989 [23], and remains one of the few cases found in literature. Another case describes an unusual metastasis of the psoas muscle [24] and there is a report from Yau *et al.*, citing a late development of an intra-muscular metastasis in the left thigh [25], in a patient that progressed slowly and benefited from surgical treatment of the primary liver tumor. Recently, a group of authors report two musculoskeletal metastases of HCC, one of them at the *gluteus maximus* level [26]. Ours is, to our knowledge, one of the first reports that also shows data after initial treatment with Sorafenib for the primary lesion, initiated after the incidental discovery of the metastasis.

Some cohorts cite a very low incidence for muscle HCC metastases; for instance, one recent study on 995 consecutive cases diagnosed with HCC and followed at regular intervals only revealed one muscle metastasis from 151 patients that presented metastases (0.7% incidence) [27]. Another retrospective cohort that followed 482 HCC cases over a period of six years only identified one muscle metastasis [28]. Most of these studies link the increased number of metastases to increased survival due to modern treatment options and the refinement of protocols based on imaging; however, our case did not benefit from HCC or antiviral treatment. The gluteal self-perceived mass was one of the presenting symptoms, thus adding to the rarity of the finding and the need for thorough pathology investigation.

We promptly started the patient on systemic chemo-therapy with Sorafenib, an antiangiogenic therapeutic agent recommended by current guidelines [29]. Surgical management of extrahepatic metastases also ensures survival and quality-of-life benefits [30]. As our patient showed calcification within the gluteal mass, following treatment with Sorafenib, and his evolution seems favorable, surgical resection may be an option in the near future if the quality of life is severely impaired by the gluteal mass.

Conclusions

To sum up, the certain diagnosis of this patient was not possible without the myriad of clinical investigations, due to the fact that the main sign of HCC, in this case is represented by a tumoral gluteal formation. The patient considered it a result of physical effort, lacking any other significant symptoms. The difficulty in stating the diagnosis consists of the aspect of the MRI that initially states the sarcomatous aspect of this gluteal formation and the history of the patient that suffers from hepatitis C virus in association with the hepatocytolysis syndrome and the increased titer of the alpha-fetoprotein. The differential diagnosis was decided between left gluteal sarcoma and metastatic hepatocellular carcinoma, pathology and consecutive immunohistochemistry playing a key role.

Conflict of interests

The authors declare that they have no conflict of interests.

Author contribution

Alina-Maria Balea and Ananu Florentin Vreju had an equal contribution in preparing the manuscript and share first authorship.

References

[1] Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA Cancer J Clin, 2014, 64(1):9–29.
[2] Bodzin AS, Busuttil RW. Hepatocellular carcinoma: advances in diagnosis, management, and long term outcome. World J Hepatol, 2015, 7(9):1157–1167.
[3] Lowy DR, Collins FS. Aiming high – changing the trajectory for cancer. N Engl J Med, 2016, 374(20): 1901–1904.
[4] Sartorius K, Sartorius B, Aldous C, Govender PS, Madiba TE. Global and country underestimation of hepatocellular carcinoma (HCC) in 2012 and its implications. Cancer Epidemiol, 2015, 39(3):284–290.
[5] Streba LAM, Vere CC, Streba CT, Ciurea ME. Focus on alcoholic liver disease: from nosography to treatment. World J Gastroenterol, 2014, 20(25):8040–8047.
[6] Danaei G, Vander Hoorn S, Lopez AD, Murray CJL, Ezzati M; Comparative Risk Assessment Collaborating Group (Cancers). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet, 2005, 366(9499):1784–1793.
[7] Streba LAM, Cârstea D, Mitruţ P, Vere CC, Dragomir N, Streba CT. Nonalcoholic fatty liver disease and metabolic syndrome: a concise review. Rom J Morphol Embryol, 2008, 49(1):13–20.
[8] Thattil R, Dufour JF. Hepatocellular carcinoma in a non-cirrhotic patient with Wilson's disease. World J Gastroenterol, 2013, 19(13):2110–2113.
[9] Wang M, Xi D, Ning Q. Virus-induced hepatocellular carcinoma with special emphasis on HBV. Hepatol Int, 2017, 11(2):171–180.
[10] El-Serag HB. Hepatocellular carcinoma. N Engl J Med, 2011, 365(12):1118–1127.
[11] Forţofoiu M, Fortofoiu MC, Comănescu V, Dobrinescu AC, Pădureanu V, Vere CC, Streba CT, Ciurea PL. Hepatocellular

carcinoma and metabolic diseases – histological perspectives from a series of 14 cases. Rom J Morphol Embryol, 2015, 56(4):1461–1465.
[12] Băloşeanu CL, Streba CT, Vere CC, Comănescu V, Rogoveanu I. Association between liver histology, carotid ultrasonography and retinal vascular changes in patients with nonalcoholic fatty liver disease (NAFLD). Rom J Morphol Embryol, 2012, 53(3):609–614.
[13] Ionescu AG, Streba LAM, Vere CC, Ciurea ME, Streba CT, Ionescu M, Comănescu M, Irimia E, Rogoveanu O. Histopathological and immunohistochemical study of hepatic stellate cells in patients with viral C chronic liver disease. Rom J Morphol Embryol, 2013, 54(4):983–991.
[14] Ionescu AG, Cazacu SM, Streba CT, Forţofoiu MC, Ciurea ME, Ionescu M, Rogoveanu O, Comănescu V, Firu ŞG, Vere CC. Interrelations between hepatic stellate cells and immune system cells in patients with hepatocellular carcinoma. Rom J Morphol Embryol, 2015, 56(2):481–490.
[15] Gheonea IA, Streba CT, Cristea CG, Stepan AE, Ciurea ME, Sas T, Bondari S. MRI and pathology aspects of hypervascular nodules in cirrhotic liver: from dysplasia to hepatocarcinoma. Rom J Morphol Embryol, 2015, 56(3):925–935.
[16] Saftoiu A, Ciurea T, Georgescu C, Banita M, Comanescu V, Rogoveanu I, Gorunescu F, Georgescu I. Immunohistochemical assessment of proliferating cell nuclear antigen in primary hepatocellular carcinoma and dysplastic nodules. J Cell Mol Med, 2003, 7(4):436–446.
[17] Gheonea DI, Streba CT, Vere CC, Şerbănescu M, Pirici D, Comănescu M, Streba LAM, Ciurea ME, Mogoantă S, Rogoveanu I. Diagnosis system for hepatocellular carcinoma based on fractal dimension of morphometric elements integrated in an artificial neural network. BioMed Res Int, 2014, 2014: 239706.
[18] Ignee A, Jedrejczyk M, Schuessler G, Jakubowski W, Dietrich CF. Quantitative contrast enhanced ultrasound of the liver for time intensity curves – reliability and potential sources of errors. Eur J Radiol, 2010, 73(1):153–158.
[19] Streba CT, Ionescu M, Gheonea DI, Sandulescu L, Ciurea T, Saftoiu A, Vere CC, Rogoveanu I. Contrast-enhanced ultrasonography parameters in neural network diagnosis of liver tumors. World J Gastroenterol, 2012, 18(32):4427–4434.
[20] Terada T, Maruo H. Unusual extrahepatic metastatic sites from hepatocellular carcinoma. Int J Clin Exp Pathol, 2013, 6(5):816–820.
[21] Florimonte L, Iavarone M, Castellani M, Longo M, Pallotti F, Maffioli L, Orunesu E, Benti R. Uncommon extrahepatic metastases from hepatocellular carcinoma. Hepatology, 2017, 66(3):986–988.
[22] Takahashi K, Putchakayala KG, Safwan M, Kim DY. Extrahepatic metastasis of hepatocellular carcinoma to the paravertebral muscle: a case report. World J Hepatol, 2017, 9(22):973–978.
[23] Gilsanz Fernández C, García Castaño J, García Román M, Rodríguez Dorrego R, Cabrero Gómez F, López de la Riva M. [A gluteal mass as the initial manifestation of a calcified hepatocarcinoma]. Rev Esp Enferm Apar Dig, 1989, 76(2): 181–184.
[24] Wu MH, Wu YM, Lee PH. The psoas muscle as an unusual site for metastasis of hepatocellular carcinoma: report of a case. Surg Today, 2006, 36(3):280–282.
[25] Yau T, Wong H, Chan P, To M, Poon RT. Intramuscular recurrence in a hepatocellular carcinoma patient with indolent disease course. World J Surg Oncol, 2008, 6:42.
[26] Young C, Munk PL. Hepatocellular carcinoma presenting as musculoskeletal metastases: a report of two cases. Eur J Radiol Extra, 2007, 62(1):25–29.
[27] Uka K, Aikata H, Takaki S, Shirakawa H, Jeong SC, Yamashina K, Hiramatsu A, Kodama H, Takahashi S, Chayama K. Clinical features and prognosis of patients with extrahepatic metastases from hepatocellular carcinoma. World J Gastroenterol, 2007, 13(3):414–420.
[28] Natsuizaka M, Omura T, Akaike T, Kuwata Y, Yamazaki K, Sato T, Karino Y, Toyota J, Suga T, Asaka M. Clinical features of hepatocellular carcinoma with extrahepatic metastases. J Gastroenterol Hepatol, 2005, 20(11):1781–1787.
[29] Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, de Oliveira AC, Santoro A, Raoul JL, Forner A, Schwartz M, Porta C, Zeuzem S, Bolondi L, Greten TF, Galle PR, Seitz JF, Borbath I, Häussinger D, Giannaris T, Shan M, Moscovici M, Voliotis D, Bruix J; SHARP Investigators Study Group. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med, 2008, 359(4):378–390.
[30] Verhoef C, Holman FA, Hussain SM, de Man RA, de Wilt JH, IJzermans JN. Resection of extrahepatic hepatocellular carcinoma metastasis can result in long-term survival. Acta Chir Belg, 2005, 105(5):533–536.

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