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Late-onset liver metastases from melanoma: two case reports and review of the literature

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Imaging Features of Fibrosing Mediastinitis: A Case Report

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Clinical case

Imaging Features of Fibrosing Mediastinitis: A Case Report

Aspects radiologiques de la médiastinite fibrosante : à propos d'un cas

Y Abdourabbih^{*1}, N Ennejari¹, I Chaouche¹, H Ouazzani², A Akammar², M Haloua², N El Bouardi¹,
MY Alaoui Lamrani¹, M Boubbou², M Maaroufi¹, B Alami¹

Résumé

La médiastinite fibrosante (MF) est une affection rare, bénigne mais potentiellement mortelle, liée à une réaction immunologique anormale entraînant une prolifération de tissu fibro-inflammatoire dans le médiastin. Les patients atteints sont généralement jeunes au moment de la présentation, mais une large tranche d'âge a été rapportée, sans prédominance de sexe. Deux types de médiastinite fibrosante ont été décrits : focale et diffuse. La forme diffuse peut être idiopathique ou associée à une maladie auto-immune ; elle touche habituellement des patients d'âge moyen et/ou âgés, et est plus fréquente chez l'homme. Les patients présentent des signes et symptômes liés à l'obstruction ou à la compression des structures médiastinales vitales. La tomodensitométrie (TDM) et l'imagerie par résonance magnétique (IRM) jouent un rôle essentiel dans le diagnostic et la prise en charge de la médiastinite fibrosante. Nous rapportons

un cas de MF chez un jeune patient de sexe masculin présentant un syndrome de la veine cave supérieure évoluant depuis cinq mois.

Mots-clés : médiastinite fibrosante, granulomateuse, idiopathique, IRM, TDM.

Abstract

Fibrosing mediastinitis (FM) is a rare, benign but potentially life-threatening process related to an abnormal immunologic reaction that results in the proliferation of fibro-inflammatory tissue in the mediastinum. Affected patients are typically young at presentation, but a wide age range has been reported, without a predilection for either sex. Two types of fibrosing mediastinitis have been described: focal and diffuse. The diffuse form may be idiopathic or associated with autoimmunity, usually affects middle-aged and/or elderly patients, and is more common in men. Patients present with signs and symptoms related

to obstruction or compression of vital mediastinal structures. CT and MR imaging play a vital role in the diagnosis and management of fibrosing mediastinitis. We present a case of FM in a young male patient with a five-month history of superior vena cava syndrome. Keywords: fibrosing mediastinitis, granulomatous, idiopathic, MRI, CT.

Introduction

Fibrosing mediastinitis (FM) is a rare, benign but potentially life-threatening process related to an abnormal immunologic reaction that results in the proliferation of fibro-inflammatory tissue in the mediastinum. Affected patients are typically young at presentation, but a wide age range has been reported, without a predilection for either sex. Two types of fibrosing mediastinitis have been described: focal and diffuse.

Clinical case

A 35-year-old male patient, chronic smoker, presented with a five-month history of swelling of the neck and face, associated with dyspnea, without fever or hemoptysis. Various investigations, including an electrocardiogram and routine blood tests, were unremarkable. He initially underwent a cervical echo Doppler, which revealed partial thrombosis of the right internal jugular vein, and a chest X-ray revealed superior mediastinal widening. A contrast-enhanced CT scan of the chest was performed for further evaluation and characterization of the chest radiograph findings.

Imaging findings

The CT scan revealed an ill-defined, hypodense, slightly enhancing soft-tissue attenuation lesion with amorphous calcification that encloses the superior vena cava, the right brachiocephalic arch, and the right pulmonary artery, causing their lumen to narrow. The lesion extends to the right hilum and encloses the

right bronchial stump (Figure 1).

An MRI was performed for further characterization. It demonstrated an upper mediastinal infiltrate extending to the right hilar level, with ill-defined margins, isointense on T1-weighted images with a hypointense T2 signal, and showing progressive and homogeneous enhancement after contrast administration, with marked enhancement at late phases, suggesting a fibrous component of the infiltrating tissue (Figure 2). Diffusion-weighted imaging did not show any restriction.

Bronchial fibroscopy revealed extrinsic compression of the medial wall of the right and left main bronchi. An ultrasound-guided transbronchial biopsy of a right hilar and a subcarinal lymph node was performed. Histopathological examination revealed a histiocytic infiltrate with a granulomatous appearance on a necrotic background, with no signs of malignancy. The GeneXpert test was negative on transbronchial biopsy samples.

Given the presence of calcifications within the mediastinal infiltrate, the delayed enhancement indicating a predominantly fibrous nature, and the results of the transbronchial biopsy, a diagnosis of fibrosing mediastinitis of tuberculous granulomatous origin was made.

The patient began anti-bacillary treatment combined with corticosteroids, without significant clinical improvement.

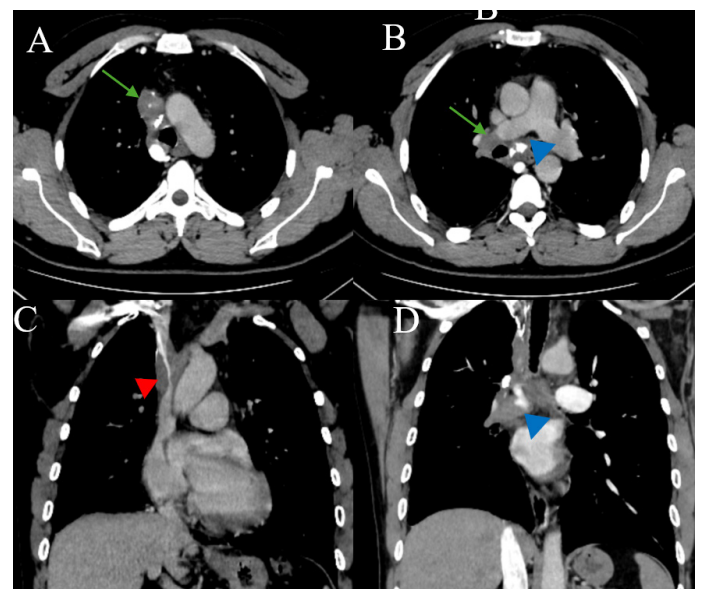


Figure 1 : A contrast-enhanced CT scan of the

chest in axial (A,B) and coronal (C,D) projections (mediastinal window) show an ill-defined, hypodense mediastinal mass (green arrow) in the pre tracheal and subcarinal spaces, extending to the right hilum, with no significant enhancement, causing narrowing of the superior vena cava (red arrow) and the right pulmonary artery (blue arrowhead).

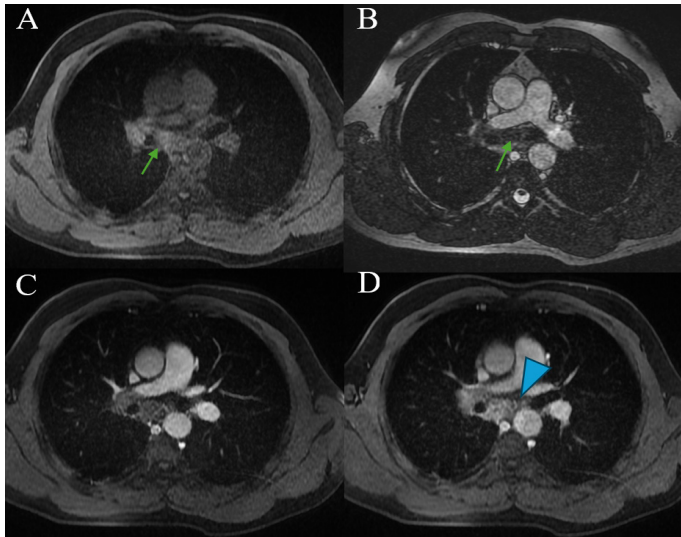


Figure 2: (A) Axial T1-weighted MRI showing an upper mediastinal infiltrative lesion with isointense signal relative to muscle (green arrow). (B) Axial T2-weighted MRI showing predominantly hypointense signal within the lesion, consistent with fibrous tissue (Green arrow). (C) Post-contrast T1-weighted MRI in the early phase demonstrating homogeneous enhancement. (D) Post-contrast T1-weighted MRI in the late phase showing marked persistent enhancement (Blue arrowhead), suggestive of a mature fibrous component.

Discussion

Fibrosing mediastinitis (FM), also referred to as sclerosing mediastinitis or mediastinal fibrosis, is a rare benign fibroinflammatory condition in which normal mediastinal fat is gradually replaced by dense infiltrative fibrous tissue, which may encase mediastinal and hilar structures. Important mediastinal structures, especially the superior vena cava, are often progressively compressed when the disease first appears. In most cases, the exact etiology and pathophysiology of fibrosing mediastinitis are

unknown, and there is ongoing conjecture regarding both infectious and noninfectious causes (1).

Two distinct subtypes of FM are generally described: the granulomatous subtype, also referred to as the focal subtype, and the non-granulomatous subtype, usually referred to as the diffuse or idiopathic subtype. Most studies show a high incidence of granulomatous mediastinitis (localized form of FM) compared with the relatively few cases of diffuse FM in which tuberculosis has been identified as the cause (2). The granulomatous variety is primarily caused by tuberculosis and histoplasmosis; however, it is occasionally linked to other inflammatory or infectious diseases (3). This allows the pulmonary infection to spread to the mediastinal lymph nodes, leading to their calcification, followed by the release of fungal or mycobacterial antigens into the mediastinal space, triggering a hypersensitivity reaction and ultimately fibrosis (4). The non-granulomatous subtype may be idiopathic or fall within the IgG4-RD spectrum, including conditions such as retroperitoneal fibrosis or Riedel's thyroiditis (5).

The early signs and symptoms of FM vary depending on the specific anatomical structures affected by the fibrotic reaction. The superior vena cava (SVC) is the most frequently affected structure, as in our case, which is consistent with the observations of Schowengerdt and colleagues (6). When bronchial structures are affected, patients may present with progressive dyspnea, cough, and hemoptysis. There may also be less typical systemic signs, including chest pain, fever, and weight loss.

While radiographic techniques often suggest the diagnosis, thoracotomy and histological analysis remain necessary for confirmation in many cases. The chest radiograph has low sensitivity and specificity for diagnosing FM and may show mediastinal enlargement and enlarged lymph nodes, which may exhibit calcification.

Because CT can precisely describe the location of abnormalities, the specific mediastinal and/or hilar structures involved, the severity of the disease, and the degree and extent of involvement, it is the

preferred modality for examining individuals with suspected FM. When illustrating the extent and length of tracheal and mediastinal vascular stenosis, multiplanar reformatted images are very useful. CT angiography can be used to accurately show the level of vascular involvement.

When it comes to determining the extent of the disease, MRI and CT are largely interchangeable. However, CT provides a better assessment of the airways and remains the best technique to identify calcifications. MRI, on the other hand, does not rely solely on intravenous contrast for demonstrating vascular patency and can frequently identify the fibrous characteristics of the lesion. On T1-weighted images, fibrous tissue typically shows intermediate signal intensity; on T2-weighted images, however, it displays variable signal intensity with both high and low signal areas. Contrast enhancement is variable and heterogeneous, as on CT. Hyperintense regions on T2-weighted images signify more active inflammation, whereas foci that appear hypointense on both T1- and T2-weighted images indicate calcification or dense fibrotic scar (7).

PET/CT is not frequently used to assess FM. Variable levels of FDG avidity, thought to correspond to the degree of inflammatory activity, have been reported in a few case studies. Granulomatous FM is not frequently assessed using this modality.

Fibrosing mediastinitis has a broad radiological differential diagnosis. Lymphoma, primary lung cancer, metastases, and Castleman disease are difficult to differentiate from FM in the absence of mediastinal calcifications, and a biopsy is usually required (8,9).

Currently, there is no curative treatment for fibrosing mediastinitis. Certain studies indicate positive outcomes with corticosteroids; however, their efficacy is limited in the granulomatous variant of FM. In our case, the patient received full-dose corticosteroids with gradual tapering, in conjunction with anti-bacillary therapy. Alternative treatment modalities may include percutaneous stenting of vascular structures or endoscopic stenting for airway obstruction and dysphagia. Palliative surgery is

reserved for limited disease. Bilateral mediastinal involvement contraindicates surgery because of the significant associated risks.

Conclusion

Fibrosing mediastinitis must be considered in cases of chronic superior vena cava syndrome or mediastinal compression syndrome, especially when calcifications and imaging characteristics suggestive of fibrosis are present. The presence of superior vena cava syndrome, upper mediastinal widening, amorphous calcifications, an infiltrative process surrounding vascular and bronchial structures, and delayed enhancement on MRI indicative of mature fibrous tissue strongly supports the diagnosis of fibrosing mediastinitis.

The confirmation of a tuberculous granulomatous condition through lymph node biopsy highlights the necessity of extensively investigating for an infectious cause—especially in regions endemic for tuberculosis—before determining that the disease is idiopathic or associated with IgG4-RD. This scenario underscores several issues from a therapeutic perspective. Despite a medical regimen that included antituberculous treatment and corticosteroid therapy, clinical improvement remained limited, indicating the poor reversibility of established fibrotic lesions. Furthermore, no pharmacological treatment has demonstrated reliable effectiveness in modifying the progression of fibrosis.

Endovascular interventional techniques (angioplasty, stenting of the superior vena cava or pulmonary veins) and endoscopic procedures (bronchial stenting) are important palliative measures to alleviate symptoms and enhance quality of life, especially when surgical intervention is considered excessively hazardous because of bilateral involvement or a highly infiltrative pattern. This case emphasizes the necessity of a multidisciplinary approach. Long-term follow-up is crucial to monitor the progression of vascular and bronchial stenoses, identify complications (venous hypertension, pulmonary hypertension, recurrent

respiratory infections), and reassess therapeutic options as necessary.

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Clinical case

Late-onset liver metastases from melanoma: two case reports and review of the literature

Métastases hépatiques tardives de mélanome : à propos de deux cas et revue de la littérature

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B Alami¹, M Boubbou², M Maaroufi¹, MYA Lamrani¹

Résumé

Le mélanome malin est la forme la plus agressive de cancer de la peau, en raison de son fort potentiel métastatique et de la possibilité de récurrences tardives, survenant parfois de nombreuses années après le traitement de la tumeur primitive. Ces métastases tardives sont souvent initialement asymptomatiques et peuvent se manifester par des signes cliniques non spécifiques, ce qui pose un problème diagnostique majeur. Parmi les sites viscéraux, l'atteinte hépatique est particulièrement importante en raison de sa gravité et de son impact pronostique. Nous rapportons deux cas de patientes ayant présenté une douleur de l'hypochondre droit, chez qui l'imagerie a révélé de multiples lésions hépatiques, et dont la biopsie hépatique a confirmé un mélanome métastatique concordant avec leurs tumeurs cutanée et choroïdienne initiales. Ces cas illustrent le phénomène des métastases hépatiques d'apparition

tardive, soulignent le rôle de l'IRM dans la détection des lésions contenant de la mélanine, et mettent en évidence d'importants pièges diagnostiques ainsi que les implications cliniques pour le suivi à long terme.
Mots clés: malignant melanoma, late metastases, liver metastases, MRI.

Abstract

Malignant melanoma is the most aggressive form of skin cancer, due to its high metastatic potential and the possibility of late recurrences, sometimes occurring many years after treatment of the primary tumor. These late metastases are often initially asymptomatic and may present with non-specific clinical features, posing a significant diagnostic challenge. Among visceral sites, hepatic involvement is particularly important because of its severity and prognostic impact. We report two cases of female patients presenting with right upper quadrant pain, in

whom imaging revealed multiple liver lesions, and in whom liver biopsy confirmed metastatic melanoma consistent with their initial cutaneous and choroidal tumors. These cases illustrate the phenomenon of late-onset liver metastases, underscore the role of MRI in detecting melanin-containing lesions, and highlight important diagnostic pitfalls and clinical implications for long-term follow-up.

Keywords: malignant melanoma, late metastases, liver metastases, MRI.

Introduction

Malignant melanoma is the most aggressive form of skin cancer, due to its high metastatic potential and the possibility of late recurrences, sometimes occurring many years after treatment of the primary tumor. These late metastases are often initially asymptomatic and may present with non-specific clinical features, posing a significant diagnostic challenge. Among visceral sites, hepatic involvement is particularly important because of its severity and prognostic impact.

Clinical cases

Case n°1

The first case is a 55-year-old female who was admitted with pain in the right hypochondrium. She had a history of cutaneous melanoma of the peri-lachrymal region, which had been surgically treated 14 years earlier. No additional information regarding the initial stage or adjuvant management was available, and she had been considered disease-free since that time.

On current presentation, abdominal ultrasound revealed several hypoechoic liver lesions that were challenging to characterize, as well as a right subcapsular collection. To better characterize these findings, magnetic resonance imaging (MRI) of the liver was performed. MRI demonstrated multiple hepatic lesions exhibiting high signal intensity on T1-weighted sequences and predominantly low signal

intensity on T2-weighted sequences, with central hyperintensity in some lesions, and enhancement after contrast administration, suggestive of metastatic melanoma (Figure 1).

A percutaneous ultrasound-guided liver biopsy was performed. Histopathological examination revealed a malignant proliferation of epithelioid cells with prominent nucleoli and intracytoplasmic brown pigment consistent with melanin, confirming the diagnosis of metastatic melanoma compatible with the patient's previous cutaneous primary.

Case n°2

The second case is a 40-year-old female with a history of choroidal melanoma treated 10 years earlier. She had undergone local treatment of the ocular lesion (details of the initial staging and exact therapeutic modality were not available in the record), with no known evidence of metastatic disease during the subsequent years.

She presented with marked abdominal pain in the right hypochondrium and abnormal liver function tests. Initial abdominal ultrasound revealed infiltrative hepatic lesions that were difficult to delineate, with a heterogeneous echotexture. A contrast-enhanced CT scan was then performed, demonstrating diffuse, infiltrative low-density lesions throughout the liver with mild enhancement after contrast administration (Figure 2), raising suspicion of extensive metastatic disease.

A percutaneous ultrasound-guided liver biopsy was performed. Histology showed sheets of atypical melanocytic cells with nuclear pleomorphism and occasional intracytoplasmic melanin pigment, confirming metastatic melanoma consistent with the prior choroidal primary.

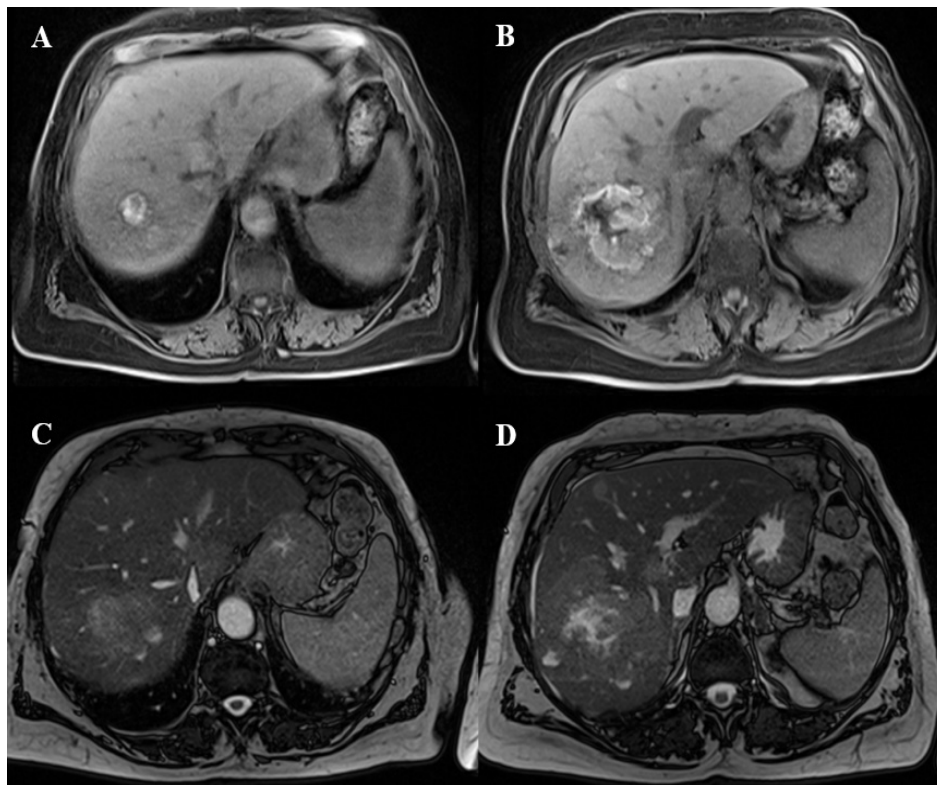


Figure 1: Hepatic lesions with high signal intensity on T1-weighted sequences (A, B), with central hyperintensity on T2-weighted sequences (C, D), consistent with melanin-containing metastases.

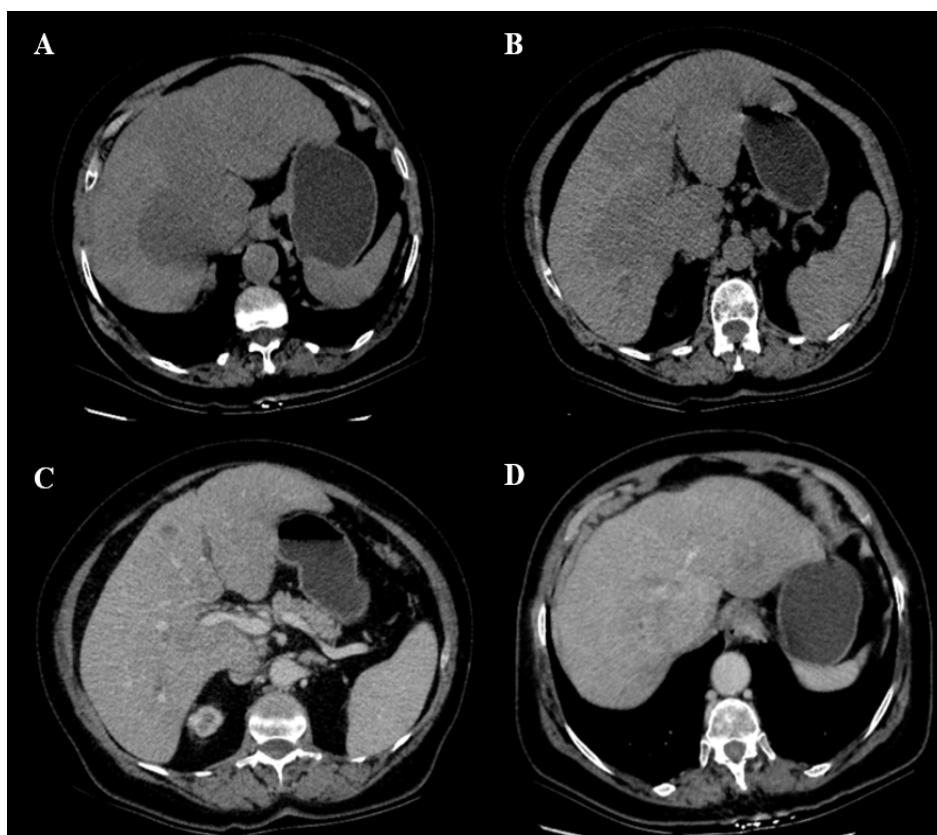


Figure 2: Contrast-enhanced abdominal CT scan showing low-density infiltrative liver lesions (A, B) with mild enhancement after contrast administration (C, D), compatible with diffuse metastatic involvement.

Discussion

Malignant melanoma is an extremely aggressive disease characterized by a strong tendency for metastatic dissemination. The liver is a common site of visceral metastases, particularly in advanced cutaneous melanoma and in uveal (choroidal) melanoma, in which hepatic involvement is often the dominant site. The median time to metastasis has been reported around 2–3 years (1), but late recurrences are well documented. Several series have described metastases appearing more than 10 years after the primary diagnosis, with some cases occurring as late as 20–25 years (2,3,10,13). Our two cases, with intervals of 10 and 14 years, thus fall into the category of late-onset or “late” hepatic metastases. The occurrence of metastases after a long disease-free interval is generally attributed to tumor dormancy. Melanoma cells can disseminate early and remain as limited residual disease, regulated over time by immune monitoring, angiogenic equilibrium, or a dormant cellular state (10,11). Age-related immunological senescence, alterations in the hepatic microenvironment, or other genetic or epigenetic factors may subsequently disturb this equilibrium and let dormant micro metastases to reactivate growth. The liver, characterized by its dual blood supply and distinctive immunological environment, is regarded as a permissive niche for dormant tumor cells, potentially elucidating the tendency for late hepatic recurrences in certain individuals, especially those with uveal melanoma (12,13). These observations prompt the inquiry regarding the duration of follow-up for melanoma patients. Current guidelines typically advocate for increased clinical and imaging surveillance during the initial 3–5 years, when the recurrence risk is at its peak, followed by a reduction in frequency thereafter (14). Nonetheless, the potential for late visceral metastases, especially in high-risk populations, indicates that clinicians must maintain prolonged surveillance (10,12–14). A prior history of melanoma (cutaneous or choroidal) should consistently be investigated when evaluating new

hepatic lesions, even after several decades (10,12,13). In patients with established risk factors (such as thick primary lesions, uveal origin, or prior high tumor burden when required), prolonged clinical follow-up and a reduced threshold for imaging may be warranted, particularly if liver-related symptoms or abnormal liver tests occur (12–14). Our data demonstrate that, in symptomatic individuals with a remote history of melanoma, metastatic disease is a significant diagnostic concern. The text delineates the distinctions and similarities between cutaneous and choroidal melanoma: cutaneous melanoma predominantly metastasizes to regional lymph nodes, lung, skin, and soft tissue, with hepatic involvement being prevalent in advanced stages, while choroidal melanoma exhibits a pronounced affinity for the liver, with hepatic metastases manifesting in the majority of patients experiencing systemic dissemination, frequently serving as the initial or primary site. The timeframe for hepatic metastasis varies, with choroidal melanoma recognized for late hepatic recurrences, occasionally occurring over a decade post-ocular therapy, while cutaneous melanoma generally recurs sooner, but late occurrences are not uncommon (10,12,13). Melanoma cells can disseminate early and remain as limited residual disease, regulated over time by immune monitoring, angiogenic equilibrium, or a dormant cellular state (10,11). Age-related immunological senescence, alterations in the hepatic microenvironment, or other genetic or epigenetic factors may subsequently disturb this equilibrium and let dormant micrometastases to reactivate growth. The liver, characterized by its dual blood supply and distinctive immunological environment, is regarded as a permissive niche for dormant tumor cells, potentially elucidating the tendency for late hepatic recurrences in certain individuals, especially those with uveal melanoma (12,13). These observations prompt the inquiry regarding the duration of follow-up for melanoma patients. Current guidelines typically advocate for increased clinical and imaging surveillance during the initial 3–5 years, when the recurrence risk is at its peak, followed by a reduction

in frequency thereafter (14). Nonetheless, the potential for late visceral metastases, especially in high-risk populations, indicates that clinicians must maintain prolonged surveillance (10,12–14). A prior history of melanoma (cutaneous or choroidal) should consistently be investigated when evaluating new hepatic lesions, even after several decades (10,12,13). In patients with established risk factors (such as thick primary lesions, uveal origin, or prior high tumor burden when required), prolonged clinical follow-up and a reduced threshold for imaging may be warranted, particularly if liver-related symptoms or abnormal liver tests occur (12–14). Our data demonstrate that, in symptomatic individuals with a remote history of melanoma, metastatic disease is a significant diagnostic concern. The text delineates the distinctions and similarities between cutaneous and choroidal melanoma: cutaneous melanoma predominantly metastasizes to regional lymph nodes, lung, skin, and soft tissue, with hepatic involvement being prevalent in advanced stages, while choroidal melanoma exhibits a pronounced affinity for the liver, with hepatic metastases manifesting in the majority of patients experiencing systemic dissemination, frequently serving as the initial or primary site. The timeframe for hepatic metastasis varies, with choroidal melanoma recognized for late hepatic recurrences, occasionally occurring over a decade post-ocular therapy, while cutaneous melanoma generally recurs sooner, but late occurrences are not uncommon (10,12,13). Imaging is crucial for the detection and characterization of hepatic metastases. CT is frequently employed as a first-line modality and is more sensitive than ultrasound, but it has limited specificity for melanoma metastases and may be insufficient in cases with subtle or infiltrative disease; in our second case, CT showed diffuse, infiltrative low-attenuation lesions with mild enhancement, a pattern that can be misinterpreted as other diffuse liver diseases or infiltrative tumors. Magnetic resonance imaging (MRI) is more sensitive than contrast-enhanced CT for the detection of hepatic metastases from melanoma and offers superior

soft-tissue contrast and functional information (4,5,6). The paramagnetic properties of melanin typically result in high signal intensity on T1-weighted images and low signal on T2-weighted images (7), as in our first case, where this classic pattern, combined with contrast enhancement, strongly suggested metastatic melanoma and guided the diagnostic work-up. When present, this T1 hyperintensity can be a useful imaging clue, but appearances are variable and several pitfalls must be considered: melanoma metastases may undergo cystic degeneration or necrosis, mimicking benign cysts or cystic neoplasms (8); they may infiltrate the liver diffusely or present as innumerable small nodules (miliary pattern), which can be difficult to distinguish from other diffuse infiltrative diseases (9); and they may show arterial phase hyperenhancement and washout, mimicking hyper vascular primary liver tumors such as hepatocellular carcinoma, while T1 hyperintensity may also result from hemorrhage or fat rather than melanin (6,9). In this context, MRI should be considered the preferred modality for further characterization of suspicious hepatic lesions in patients with a history of melanoma, especially when CT findings are equivocal, and correlation with clinical history, including remote melanoma, and histological confirmation by biopsy remain essential for accurate diagnosis. Finally, hepatic melanoma is overwhelmingly metastatic, whereas primary hepatic melanoma is exceedingly rare, with only isolated cases reported (7). Distinguishing primary from metastatic lesions relies on clinical evaluation, thorough search for an extrahepatic primary site, and histopathological correlation; in our patients, the presence of well-documented prior cutaneous and choroidal melanomas, together with compatible histology, clearly supported the diagnosis of metastatic disease.

Conclusion

These two instances of late-onset hepatic melanoma metastases exemplify the diverse imaging characteristics, ranging from multiple T1-

hyperintense nodules to extensive infiltrative liver involvement, and emphasize the notion of tumor dormancy, with metastases arising many years post apparent resolution of the primary tumor. MRI, due to its heightened sensitivity to melanin and exceptional soft-tissue contrast, is pivotal in the diagnosis and characterization of such lesions and should be favored when CT findings are equivocal.

Clinicians and radiologists must uphold an extensive differential diagnosis while assessing hepatic lesions, methodically contemplating metastatic melanoma in each patient with a present or past history of cutaneous or choroidal melanoma. Recognition of this potentiality has significant implications for the length of follow-up, the analysis of imaging investigations, and the prompt onset of suitable oncological treatment.

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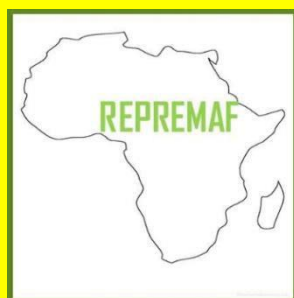
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RÉSEAU DE PROMOTION DE LA RECHERCHE MÉDICALE EN AFRIQUE

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