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Case Report

Asymptomatic Left Ventricular Malignant Psammomatous Melanotic Schwannoma

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ABSTRACT

Malignant psammomatous melanotic schwannoma (MPMS) is a rare type of tumour, occasionally reported to occur with mediastinal involvement. Histopathologic similarities with melanoma may lead to a wrong diagnosis, but distinguishing between types of tumours is mandatory for adequate management and prognosis. MPMS may be aggressive and manifest unpredictable behavior, with a poor midterm prognosis despite benign histopathologic features. We discuss the challenges that come with a diagnosis of MPMS, and the rationale for our treatment strategy, in this first report regarding MPMS involving the left heart ventricle.

RÉSUMÉ

Le schwannome mélanotique psammomateux malin (SMPM) est un type de tumeur rare qui est à l'occasion observé au niveau du médiastin. Ses similitudes histologiques avec le mélanome peuvent conduire à un diagnostic erroné, mais il est impératif de savoir faire la distinction entre ces types de tumeur pour optimiser la prise en charge et le pronostic. Le SMPM peut être agressif et avoir une évolution imprévisible, avec un pronostic défavorable à moyen terme malgré des caractéristiques histopathologiques bénignes. Dans cette première étude de cas de SMPM présentant une atteinte du ventricule gauche, nous décrivons les défis posés par un diagnostic de SMPM et justifions notre stratégie de traitement.

Malignant psammomatous melanotic schwannoma (MPMS) represents 10% of all diagnosed schwannomas, with approximately 200 published cases.[1] Rarely, MPMS has been described as occurring in the mediastinum, with one report outlining a case of MPMS in the right atrium.[2] MPMS can be difficult to distinguish from melanoma because of histologic similarities. The management and prognosis differ greatly between these 2 tumours, thus necessitating an accurate final diagnosis. To our knowledge, this is the first report of MPMS involving the left ventricle (LV) of the heart. We aim to discuss the steps toward accurate diagnosis, treatment strategy, and long-term follow-up of left ventricular MPMS.

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Ethics Statement: The research reported has adhered to the relevant ethical guidelines.

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See page 979 for disclosure information.

Pathology

Originating from the neural crest, the histopathologic features of malignant melanotic schwannoma are extremely variable.[1] Malignant melanotic schwannoma is usually a grey-to-black tumour that exhibits psammoma bodies, a variable amount of melanin pigment, and similar morphology (spindled or epithelioid) to melanocytes and Schwann cells. Malignant melanotic schwannoma is divided into nonpsammomatous and psammomatous subtypes. The presence of psammoma bodies is not related to the metastatic potential of the tumour,[1] nor are the ploidy or size.[3]

Gene suppressor PRKAR1A is absent in most MPMS,[4,5] with a 95% penetrance at 50 years.[3] Interestingly, melanoma never loses the expression of PRKAR1A.[4] The BRAF V600E mutation is negative in MPMS, but it is typically positive in melanoma.[4] S100 protein, HMB45, and Melan-A are also consistent features of MPMS.[4,5]

Carney Complex

The Carney complex is an autosomal dominant syndrome usually described in young adults (median age of 20 years[5]). It is associated with melanotic schwannoma and skin pigmentary abnormalities (lentiginosis, blue nevi, cutaneous myxoma, and café-au-lait spots), endocrine tumours (or endocrine

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Novel Teaching Points

- This is the first report of a left ventricular malignant psammomatous melanotic schwannoma.
- The distinction between MPMS and melanoma is crucial for appropriate management.
- MPMS is a type of tumour with deceptive histologic features and unpredictable behavior. Therefore, it should be considered a malignant neoplasm and treated with total surgical resection when feasible.
- Further studies are needed to determine the role of longitudinal clinical and radiologic surveillance in improving the prognosis of these patients.

overactivity), and cardiac myxomas. Carney suggested that approximately 50% of cases of MPMS were associated with the complex.[5] However, recent studies have suggested that this is an overestimate, with the real association being less than 5%.[6] PRKAR1A is mutated in 50% of familial and sporadic Carney complex patients[1,5].

Case

An asymptomatic 74-year-old male, with no past medical history, was diagnosed with a nonspecific conduction abnormality on a preoperative electrocardiogram prior to hand surgery. Subsequent 2D transthoracic echocardiography showed a 21 x 17 mm endocardial mass within the LV (Fig. 1, E and F) and a normal LV ejection fraction. Subsequent transesophageal echocardiography (Fig. 1, G and H) and magnetic resonance imaging were performed to further characterize the tumour (Fig. 1, A and B). The lesion appeared to be encapsulated, without invasion of surrounding tissues, such as the mitral apparatus or papillary muscles. The lesion was immobile, and it was attached on one-fourth of its surface on the anteroseptal LV wall, 20 mm from the LV outflow tract. Coronary angiography showed a minimal vascularization of the lesion (Fig. 1C). No other abnormal lesions were identified by computed tomographic scan or positron emission tomography (Fig. 1D). The lesion was not calcified on any imaging modalities. The patient did not experience chest pain, palpitation, dyspnea, or syncope. Physical examinatino was negative for cutaneous and ocular abnormalities, and Carney complex was ruled out. No cardioembolic symptom was noted, and cardiopulmonary auscultation was normal. An electrocardiogram showed 45 bpm sinus bradycardia, a 194-ms PR interval, a nonspecific conduction abnormality, and a late R wave progression. Blood samples, including hemoglobin, creatinine, T-troponins, and B-type natriuretic peptide, were all in the normal range. Leucocytes and high-sensitivity C-reactive protein were within the normal range as well. The clinical differential diagnosis included heart rhabdomyoma, angiosarcoma, and myxoma.

Twenty-nine days later, the patient was brought to the operating room, and a median sternotomy was performed. After cardiopulmonary bypass and aortic cross-clamping, the ascending aorta was transversely opened. Through the aortic valve, a yellowish mass of 30 x 25 x 19 mm was resected from the inferior part of the interventricular septum (Fig. 2, A-C). Specimens were sent to pathology to assess completeness of resection. Gross pathologic margins were free of tumour, but histologic features suggested an aggressive neoplasm. To ensure the completeness of resection and the absence of surrounding tissue invasion, endocardial biopsies were performed in the adjacent areas of the interventricular septum. Endocardial biopsies were negative for neoplasm on frozen section. Total clamping time was 77 minutes, and total cardiopulmonary bypass time was 100 minutes.

Postoperative transesophageal echocardiography showed an intact interventricular septum. The patient had an uneventful recovery, except for the development of a left bundle branch block. The patient left the hospital in New York Heart Association Functional Class I. No adjuvant therapy was given because of complete excision. At 22 months postoperatively, a permanent pacemaker was implanted for transient complete atrioventricular block with syncopal episodes. No local recurrence could explain the atrioventricular block. At 3 years of follow-up, there was no sign of local or distant recurrence on clinical examination and multimodal imaging (chest X ray, echocardiography, and magnetic resonance imaging).

Histopathologic Analysis

Histologic examination showed a highly pleomorphic population of spindle-shaped and multinucleated neoplastic cells, arranged in fascicles with abundant melanin pigment (Fig. 2D). The tumour had minimal stroma and low vascularity. Psammomatous calcifications were present, and necrosis was not observed. Fourteen mitotic figures were identified on a total of 30 high-power fields (HPFs), on a microscope equipped with 22-mm diameter oculars. The overall mitotic count adjusted for soft tissue tumours was 3.4 / 10 HPF (HPF = 0.1734 mm^2). The highest value was 1 per HPF, with an average of 0.47 mitotic figures per HPF. On immunohistochemistry, tumour cells were positive for melanocytic markers (S100, HMB45, and MelanA), and negative for CD31, ERG, FVIII, and actin.

The initial histopathologic diagnosis was metastatic melanoma, with an occult primary lesion. Further clinical investigation did not reveal active melanoma. A second histopathologic opinion was obtained in this clinical setting. Additional examination showed positive SOX10 expression on immunohistochemistry, no PRKAR1A expression, and no BRAF V600 mutation. Overall, the clinical and pathologic findings were consistent with MPMS rather than metastatic melanoma. Due to the rarity of this tumour in this particular location, another opinion was sought from the Dana-Farber Cancer Institute (Boston, MA), which confirmed our findings.

Comment

MPMS is diagnosed at a mean age of 41 years,[1] whereas melanoma is found in older populations (median of 70 years). Heart involvement in metastatic melanoma usually arises in the context of stage IV widespread disease, with a survival rate as low as 23% at 6 months.[7] New kinase and immune checkpoint inhibitor therapies have significantly improved melanoma survival up to 37% at 5 years.[8] Melanoma and

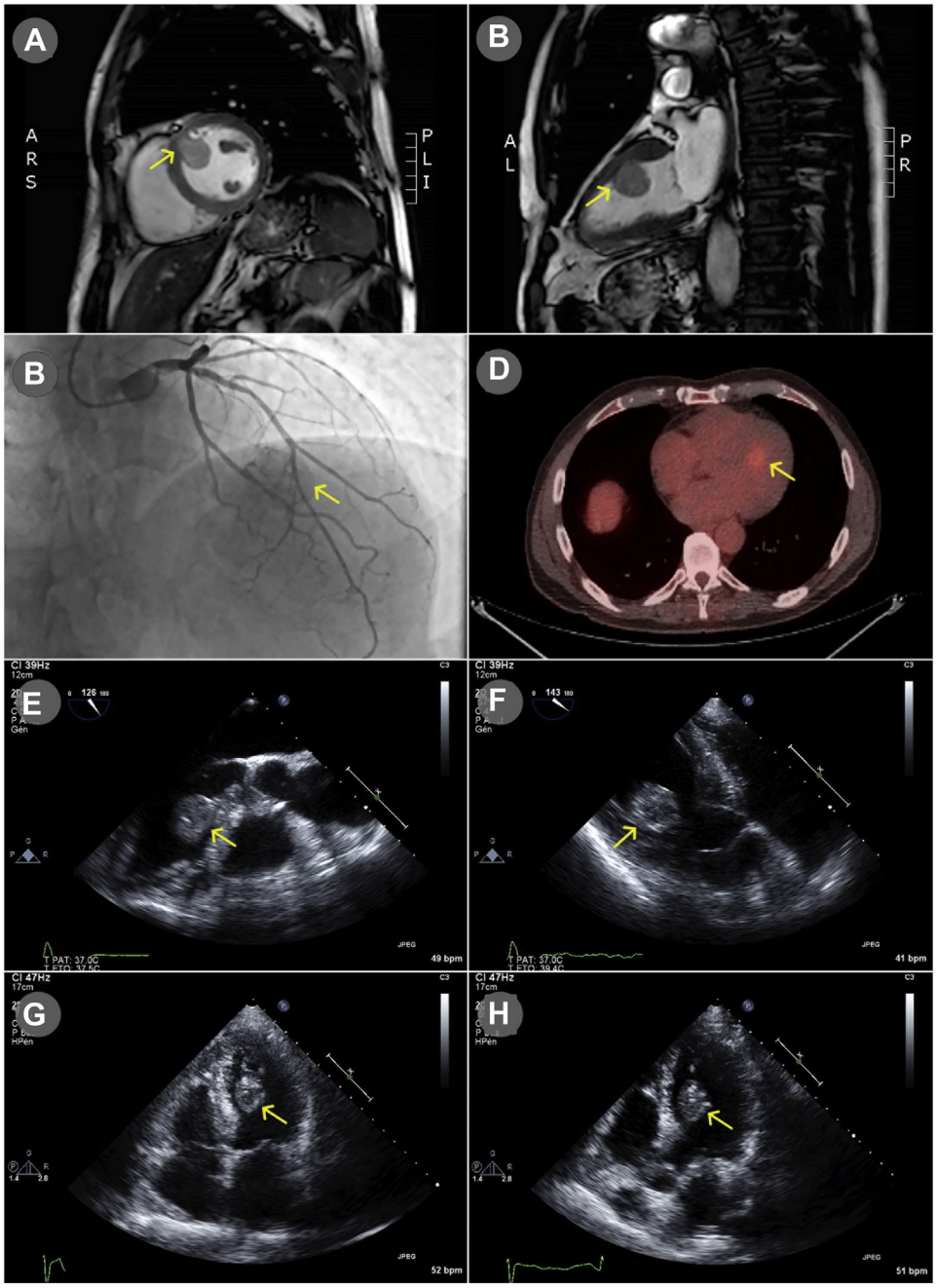

Figure 1. Preoperative imaging. (**A, B**) Magnetic resonance imaging showing a well-encapsulated tumour on the interventricular septum. (**C**) Coronary angiography showing mild vascularization of the tumour. (**D**) Positron emission tomography scan showing a hypermetabolic mass in the left ventricle with an standardize uptake value of 2.8. (**E**, **F**) Transesophageal echocardiography showing the tumour attached to the anteroseptal wall of the left ventricle. (**G**, **H**) Four-chamber view on transthoracic echocardiography showing the tumour of the left ventricle.

MPMS both express melanocytic markers, and both commonly show malignant features and necrosis.[1] Further histologic analysis allowed us to rule out metastatic melanoma with an occult primary lesion. The presence of psammoma bodies and the absence of PRKAR1A and BRAF V600 further suggested MPMS.[1,6] MPMS and melanoma both behave in a clinically malignant manner, but MPMS is associated with better survival.[4] Accurate final diagnosis is therefore crucial to ensure appropriate medical and surgical treatment and guide long-term clinical follow-up and imaging.

Due to the paucity of late data, no guidelines currently exist regarding MPMS management and surveillance.[4,6] Among 57 patients with MPMS, Vallat-Decouvelaere et al. reported a 26.3% risk of metastases, and a 53% likelihood of achieving disease-free status at 5 years.[6] Torres-Mora et al. reported a local recurrence rate of 35%, and a distant

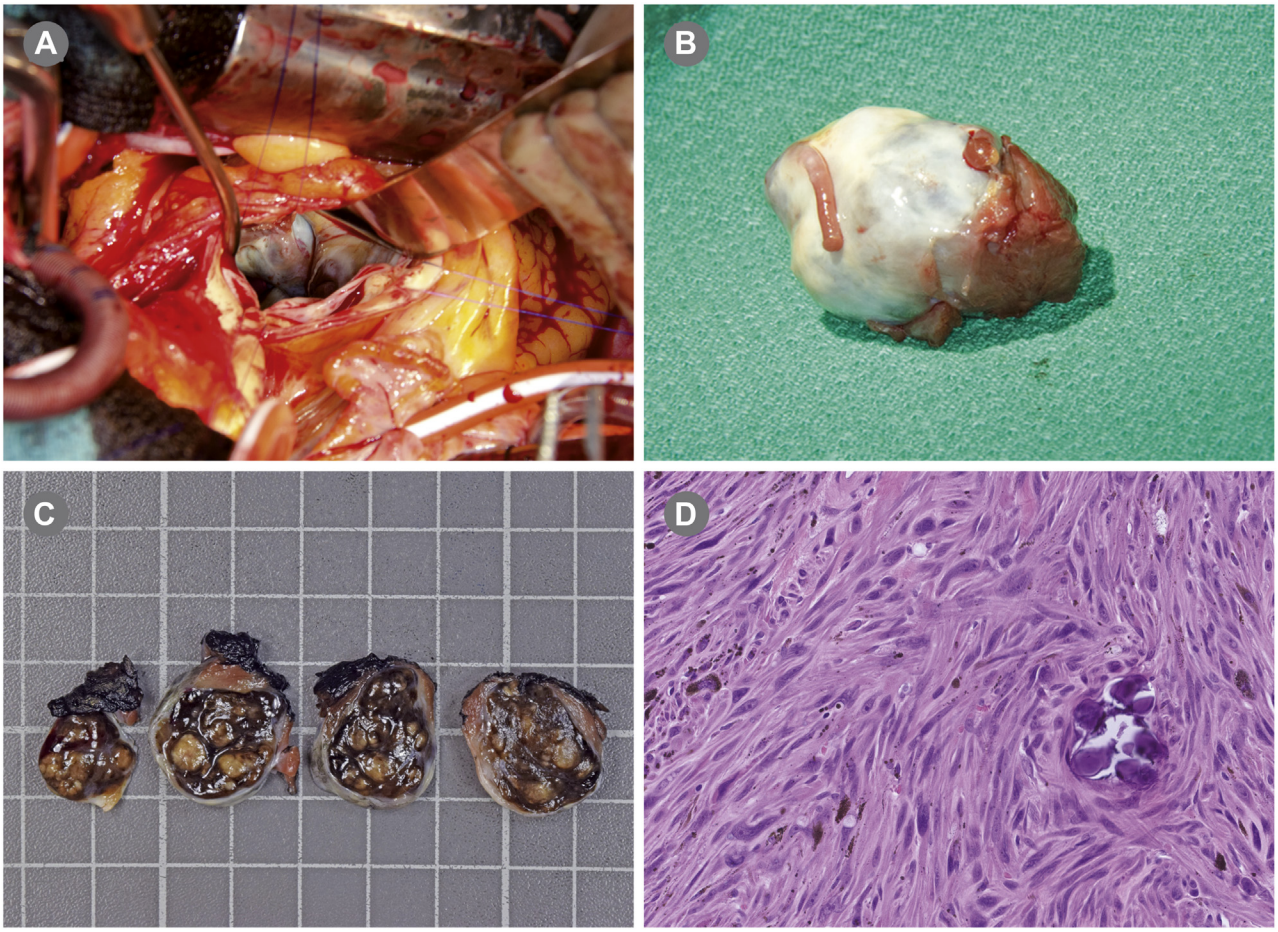

Figure 2. Malignant psammomatous melanotic schwannoma. (**A**) Intraoperative picture of the tumour location in the left ventricle. (**B**) Left ventricular mass resection showing a sessile tumour with an endocardial sclerotic capsule (cm scale). (**C**) Gross specimen cut showing lobular yellowish-to-black tumour. Black ink is applied to the surgical margin (cm scale). (**D**) Microscopic examination: cluster of psammomatous calcifications with epithelioid and spindle-shaped neoplastic cells arranged in fascicles with abundant eosinophilic cytoplasm and melanin pigment (hematoxylin & eosin, x22 magnification).

metastasis rate of 42% in their 40 consecutive MPMS cases, and most patients had recurrent disease within 4 years after the initial diagnosis.[1] Lungs and pleura are the most common locations for metastatic disease.[1] Clinical and histopathologic characteristics are poor predictors of prognosis in MPMS. Only a mitotic rate greater than 2/10 HPF has been suggested as being predictive of malignancy, but the absence of mitotic figures does not completely rule out malignant potential. MPMS should be considered an aggressive type of tumour because of a high risk of local recurrence and metastatic potential.[1] The dearth of long-term follow-up data in MPMS may have led to the underestimation of its malignant potential, and contributed to perpetuating the notion that MPMS is a benign tumour. Therefore, we suggest that all patients with MPMS be given close clinical and radiologic longitudinal follow-up, with a high index of suspicion for local disease recurrence and distant metastases, independent of the presence or absence of malignant microscopic features.

The optimal management of MPMS is complete surgical resection. Adjuvant therapy may be needed for cases of subtotal excision, positive margins, local recurrence, or distant metastases, although its role has not been clearly elucidated for MPMS.[6] The impact of adjuvant therapies in the presence of total resection with negative surgical margins (as in our patient) remains unknown. Further studies are needed to determine the role of longitudinal clinical and radiologic surveillance in improving the prognosis of these patients.

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