

# Primary pulmonary malignant meningioma with lymph node and liver metastasis in a centenary woman, an autopsy case

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**Abstract** Primary meningiomas arising outside the central nervous system are very rare. They have been reported in the head and neck region, in the thorax, the retroperitoneum, and the pelvis. Usually, they behave as slow-growing tumors with a good prognosis. Herein, we report an autopsy case of a 108-year-old woman, known for a right-sided slowly growing lung nodule for 39 years. Death was attributed to cachexia. At post-mortem, a 15-cm mass was present in the right inferior lobe of the lung, associated with an ipsilateral hilar lymphadenopathy, and another 10-cm mass in the liver. Histology revealed a WHO grade III meningioma. No tumor was observed in the cranial cavity. This case illustrates a rare location of meningioma and highlights its biological behavior, with a very slow progression from a most probably benign tumor to a malignant lesion with metastasis over four decades.

**Keywords** Meningioma · Extracranial · Malignant · Lung · Liver

## Introduction

Meningiomas account for about 25–30 % of primary intracranial tumors [1]. They most commonly occur in middle-aged and elderly patients, with a peak during the sixth and seventh decades. Women are more affected than men, with a ratio of 1.7:1 [2]. The vast majority of meningiomas arise in intracranial, intraspinal, and orbital locations, but rare cases have been reported in almost all organs. Most tumors are well-demarcated on macroscopy, and invasion of adjacent structures (i.e., brain parenchyma) is seldom observed. The previously reported cases of primary pulmonary meningioma are mainly benign.

In this article, we present the case of a centenary woman, known for an uncharacterized lung tumor for nearly 40 years, and a newly diagnosed hepatic mass.

## Clinical history

A 108-year-old woman, a retired translator, was hospitalized in the division of palliative medicine for a decline of her general condition with asthenia, lack of appetite, loss of weight, and anxiety. Her medical history included minor orthopedic interventions, a mastectomy for a benign tumor, and an atrial fibrillation since the previous year. She was also known for a lung nodule in the right inferior lobe that was discovered 39 years earlier (25 mm in 1972). She accepted a radiological follow-up but declined more invasive investigations. The reports of the successive chest X-rays demonstrated a very slow growth (approximately 1–2 mm/year).

The chest X-ray performed at admission demonstrated a large opacity of the right lung associated with bilateral pleural effusions. In addition, the abdominal ultrasound highlighted a 9 cm hepatic mass. Results of the blood

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exams showed hypochromic normocytic anemia (hemoglobin 106 g/l), increased fibrinogen (5 g/l), and severe malnutrition (albuminemia 24 g/l).

According to the wishes of the patient, a palliative approach was adopted. The general condition of the patient gradually worsened and she died 70 days later. The family gave permission for an autopsy.

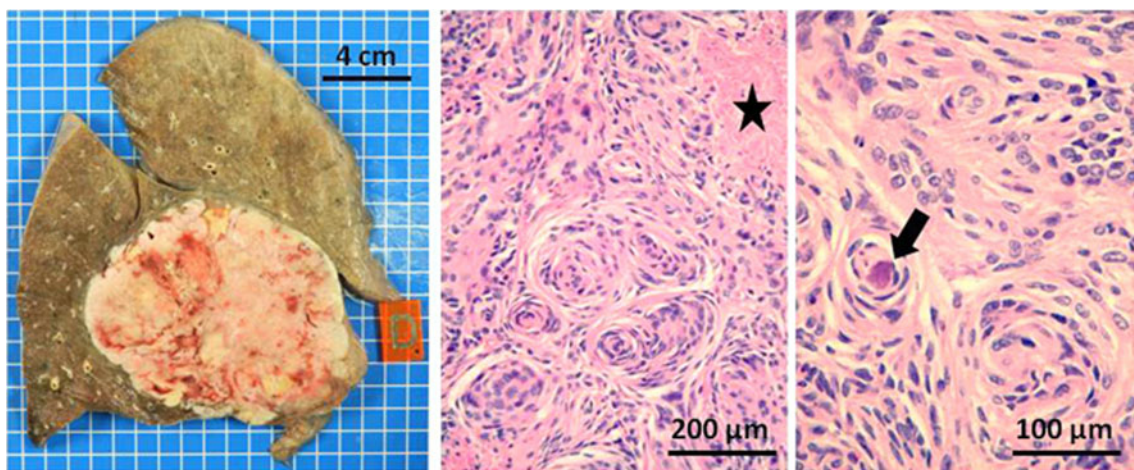
## Materials and methods

Complete autopsy, including brain examination, was performed 30 h after death. All internal organs were removed, and a macroscopic examination was done, with standard tissue sampling for histology. Brain, lungs, heart, a representative slice of the liver, a slice of the spleen, and one kidney were fixed in 4 % buffered formalin before dissection. All the samples were paraffin-embedded and 2- $\mu$ m thick slides were stained with H&E. Reticulin stain and immunohistochemistry according to standard protocols were performed on one block containing tumor tissue. The following antibodies were used: vimentin (DakoCytomation, dilution 1:40), MIB1/Ki67 (DakoCytomation, dilution 1:100), epithelial membrane antigen (DakoCytomation, dilution 1:100), Keratins (DakoCytomation & Biogenex, dilution 1:100 & 1:25), progesterone receptors (Ventana), TTF1 (DakoCytomation, dilution 1:100), S100 (DakoCytomation, dilution 1:2,000), chromogranin (Novocastra, dilution 1:20), synaptophysin (DakoCytomation, dilution 1:20), calretinin (Immunotech, dilution 1:600), smooth muscle actin (DakoCytomation, dilution 1:300), Ber-EP4 (DakoCytomation, dilution 1:50), CD34 (DakoCytomation, dilution 1:50), collagen IV (DakoCytomation, dilution 1:100), and Glut-1 (Thermo Scientific, dilution 1:100).

## Results

External examination showed signs of dehydration and a large sacral bedsore. The woman was 150 cm tall and weighed 35 kg (body mass index: 16 kg/m<sup>2</sup>). At internal examination, no pleural, pericardial, or peritoneal effusions were found. Heart and large vessels were unremarkable, except for mild atherosclerosis. The weight of the lungs was normal, and there was no emphysema or anthracosis. On cut sections, a unique large polycyclic and well-demarcated mass was observed in the right inferior lobe, measuring 15×10×7 cm (Fig. 1). The mass was firm, yellow to white, with foci of necrosis. In the ipsilateral hilum, a 2 cm lymphadenopathy was present. Neck and mediastinum dissection did not reveal other tumor. A second large mass with a similar macroscopic aspect was observed in the left lobe of the liver, measuring 10×10×5 cm (Fig. 2). Besides small uterine leiomyomas and atrophy of the renal and adrenal cortex, no other abnormalities were found in the abdominal cavity, retroperitoneum, or pelvis. At examination of the cranial cavity, no tumor was observed, especially in the dura mater. The brain weighed 1,080 g, without macroscopic lesions besides atherosclerosis of the large vessels. Histology revealed two old microscopic infarcts of the entorhinal area and the occipital cortex on the left side. The spine was not dissected.

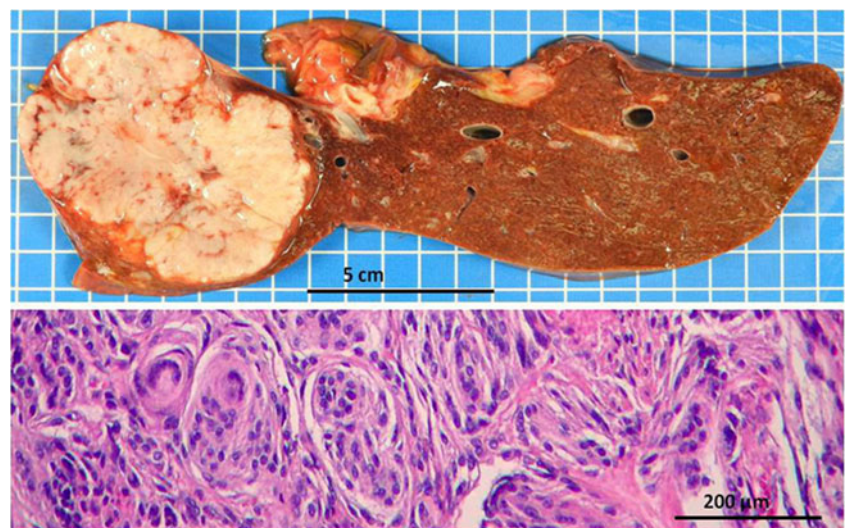
Microscopically, the right pulmonary mass, the ipsilateral hilar lymph node, and the hepatic mass appeared similar (Figs. 1 and 2). The tumors were well-demarcated from the adjacent lung and liver parenchyma. The cells were oval to spindle shaped. They had round or oval monomorphic nuclei and poorly defined cytoplasmic borders. They were arranged in lobules and interlacing bundles, with the formation of many whorls, not centered by a vessel. Some



**Fig. 1** Right lung pathology. On the *left side*, macroscopic section of the formalin-perfused lung, demonstrating a 15-cm large well-demarcated white–yellow mass, with foci of necrosis, located in the inferior lobe. In the *center*, H&E-stained histological section of the tumor, demonstrating

typical whorl formations, and a focus of necrosis (*asterisk*). On the *right side*, high power view of the tumor cells, with whorl formations and a beginning psammoma body (*arrow*)

**Fig. 2** Liver pathology. On the *top*, macroscopic section of the liver, with a 10-cm large mass in the left lobe, with same characteristics than the lung mass, although with less necrosis. On the *bottom*, H&E-stained histological section of the liver lesion, with transitional morphology and whorl formations



psammoma bodies were also seen. There was no reticulin mesh around tumor cells. In the center of the tumors, large areas of necrosis were present. In the lung mass, there was merging of the benign looking areas with the more anaplastic areas. In the latter, there were over 20 mitoses per 10 high-power fields.

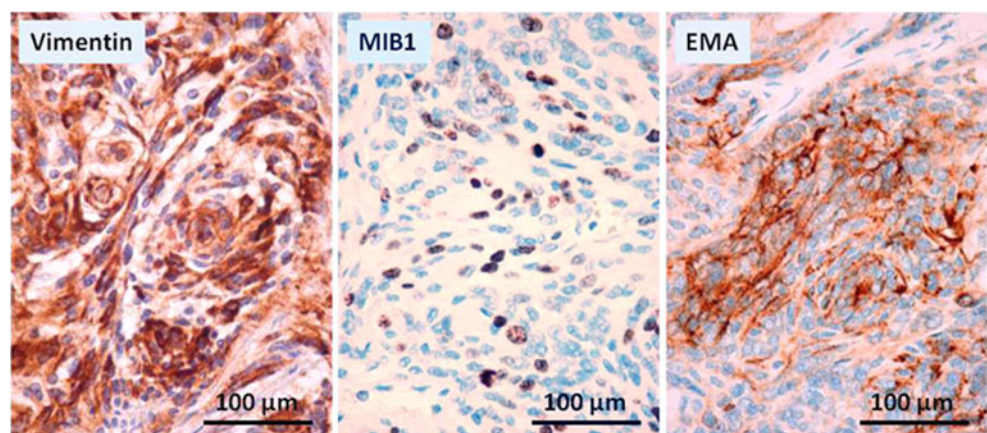
Immunohistochemically, the tumor cells were positive for vimentin, epithelial membrane antigen, and Glut-1 and weakly positive for keratin. They were negative for progesterone receptors, TTF1, S100, chromogranin, synaptophysin, calretinin, smooth muscle actin, Ber-EP4, and CD34. collagen IV did not show pericellular positivity. The proliferative index (MIB1/Ki67) was relatively high, with up to 15 % of tumor cells being labeled (Fig. 3).

## Discussion

We report an unusual autopsy case of a 108-year-old woman, with a large tumor of the right lung, an ipsilateral hilar lymph node involvement, and a large liver tumor. Based on the histology and immunohistochemistry of the three lesions,

which were similar, and the fact that the lung tumor was present long before the liver tumor, we propose a diagnosis of lung primary malignant meningioma, with lymph node and liver metastasis. Morphologically, the presence of many whorls and psammoma bodies is suggestive of meningioma. The combined immunohistochemical positivity for epithelial membrane antigen and vimentin, although not specific, is also typical of meningioma. Perineurioma was considered as a differential diagnosis, since this tumor shares morphological and some immunohistochemical characteristics with meningioma [3, 4]. However, the absence of a reticulin mesh and immunoreactivity for collagen IV around the tumor cells argues against this diagnosis in our case [5]. Although Glut-1 positivity is typical for perineurioma, it has also been described in meningioma [6–8]. Concerning the histological grading, we applied the criteria from the 2007 WHO classification of brain tumors. Spontaneous geographic necrosis and more than 20 mitoses per 10 high-power fields were the two main criteria to classify this tumor as malignant. In the lung tumor, there were some more benign looking areas without cytological atypia, necrosis, or increased mitotic activity. These areas were merging with the anaplastic/malignant areas

**Fig. 3** Immunohistochemistry of the lung tumor



suggesting a malignant transformation of a preexisting benign tumor. The fact that the pulmonary tumor was known for a long time also supports this hypothesis.

Meningiomas are usually benign tumors with a slow-growing evolution (WHO grade I). However, 20–35 % of meningiomas are actually classified as atypical (WHO grade II) [9], whereas anaplastic/malignant meningiomas (WHO grade III) remain rare. Metastases rarely occur, involving lung, pleura, bone, and liver. The WHO grading system, according to the WHO Classification of Tumors of the Central Nervous System [10], is based on histological examination, the main criteria of grade progression being the mitotic count.

Primary extracranial meningiomas are rare neoplasms. In the only large clinicopathologic study published [11], all 146 cases were located in the head and neck region. Other sites, such as lung, mediastinum, retroperitoneum, and pelvis, were also mentioned in the literature, but only as case reports.

Extracranial meningiomas can be the result of four different mechanisms [12, 13]: (a) primarily intracranial tumors with extracranial extension through the holes of the base or the sutures of the skull, (b) tumor development from arachnoid cell rests of cranial nerve sheaths with extracranial growth, (c) tumor development from embryonic rest cells, and (d) extracranial metastases of an intracranial meningioma. In our case, since no intracranial tumor was observed, one can postulate the third mechanism, with tumor development from mesenchymatous multipotent cells or ectopic meningocytes/arachnoid cells, located in the lung [14, 15]. Derivation from perineurial cells rather than displaced arachnoid cells has also been suggested [16, 17]. Some reports suggested that pulmonary meningioma may arise from meningotheial-like nodules, named also chemodectoma or tumorlet [18–22]. This hypothesis was considered unlikely by other authors, because there was a great discrepancy between the incidence of meningotheial-like nodules (0.3–0.5 % autopsy incidence) and pulmonary meningiomas (0.05 % autopsy incidence) [23]. In our case, we did not find any meningotheial-like nodules after extensive histological sampling of the lung.

Less than 50 cases of primary lung or mediastinal meningiomas have been described in the literature [24]. These lesions were mostly benign, although a false-positive PET scan can mimic malignancy [25]. Less than five malignant cases were described, based on histological criteria of the local lesion, or on clinical suspicion of liver metastasis [26]. One case with histological proven parabronchial lymph node metastasis and a focus of metastatic tumor on the diaphragm was also described [27]. To our knowledge, this is the first case of primary pulmonary malignant meningioma with autopsy-proven liver metastasis.

Autopsy studies of centenarian patients are scarce and their contribution can be questioned. In one study of 40 centenarians, the cause of death was attributed to acute organ failure due to cardiovascular diseases, respiratory illnesses, gastrointestinal disorders, and cerebrovascular disease, and no neoplasm's were found [28]. Conversely, in another autopsy study of 3,000 geriatric patients (age range from 62 to 102 years), malignant neoplasm's were observed in 28.1 % of the patients, but only in one of the nine centenarians described in the study (Hodgkin's lymphoma) [29]. Still, as shown in our case, autopsies in centenarians should not be given up, since this category of patients may present different epidemiological data than younger patients and sometimes demonstrate unusual pathological conditions. Moreover, they provide unique data on the natural history of apparently benign neoplasms or other long-standing diseases.

**Conflict of interest** The authors declare that they have no conflict of interest.

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