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Miliary brain metastases from papillary adenocarcinoma of the lung – unusual MRI pattern with histopathologic correlation

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Summary

Miliary brain metastases are very rarely described in the literature but if they are, they are quite obvious on magnetic resonance imaging (MRI) and enhance after intravenous administration of the contrast medium. The authors presented a case of miliary metastatic spread to the brain which was invisible on computed tomography and hardly visible on MRI, i.e. as countless, tiny, slightly T1-hyperintense foci that did not enhance. The authors discussed a few T1-hyperintense brain lesions which did not include metastases (except for metastatic melanoma which was a radiological suggestion after brain MRI). Autopsy revealed papillary adenocarcinoma of the lung with numerous metastatic lesions in both cerebral and cerebellar hemispheres and the meninges.

Key words: brain • metastases • miliary • magnetic resonance imaging (MRI) • lung • adenocarcinoma

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Background

Miliary brain metastases are very rarely described in the literature. E.g. Iguchi et al. reviewed 13 cases published before their paper from 2006 [1]. Most of them are related to the lung cancer and papillary adenocarcinoma is the most frequent histopathologic diagnosis [1,2]. In most of those reports brain lesions were quite obvious on magnetic resonance imaging (MRI) and enhanced after intravenous administration of the contrast medium. We presented a case of miliary metastases of the papillary adenocarcinoma of the lung to the brain which were hardly visible on MRI and did not enhance.

Case Report

A 52-year-old man was admitted to the Neurology Department because of decreased contact, severe cognitive dysfunction, aphasia, adynamia and behavioral disorders. Computed tomography (CT) of the head was normal. The patient was then referred for an MRI which revealed

countless, very tiny lesions, hardly visible on T1-weighted images, i.e. as weakly hyperintense foci. They were disseminated both in the supra- and infratentorial compartment as well as in the meninges (Figure 1A–1C). Only very few of them were noticeable on FLAIR images (Figure 2) and GRE/T2*-weighted images (Figure 3). The degree of their hyperintensity on T1-weighted images did not change after intravenous administration of contrast medium. The radiological suggestion was: metastases, most likely of melanoma. However, no suspicious pigmented lesions were found on the skin or mucous membranes. Since the patient was under long-term care of the Institute of Tuberculosis and Lung Diseases due to sarcoidosis, he was referred there for a consultation. CT of the lungs was performed there and it revealed numerous nodular lesions in the lungs and osteosclerotic foci in the bones. Metastatic spread of unknown origin was diagnosed. Lung biopsy disclosed only fibrous and inflammatory changes. Neurosurgeons resigned from brain biopsy because of the diffuse nature of the changes. Two months later the patient died of cardiorespiratory failure. The autopsy revealed generalised neoplastic

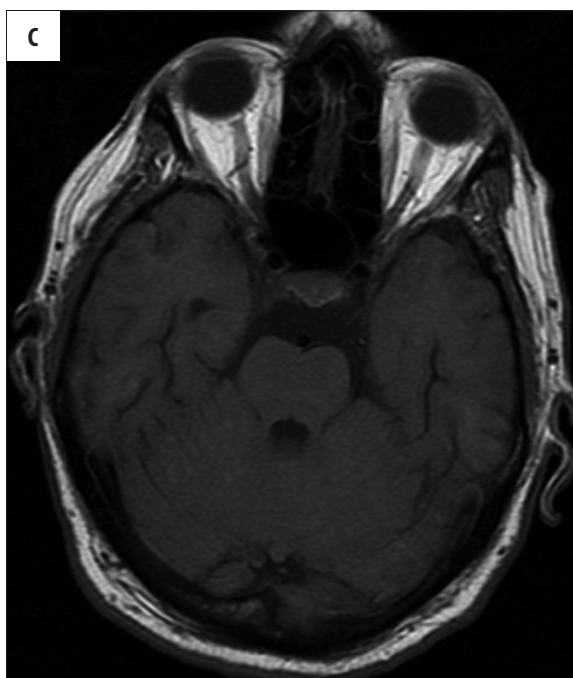
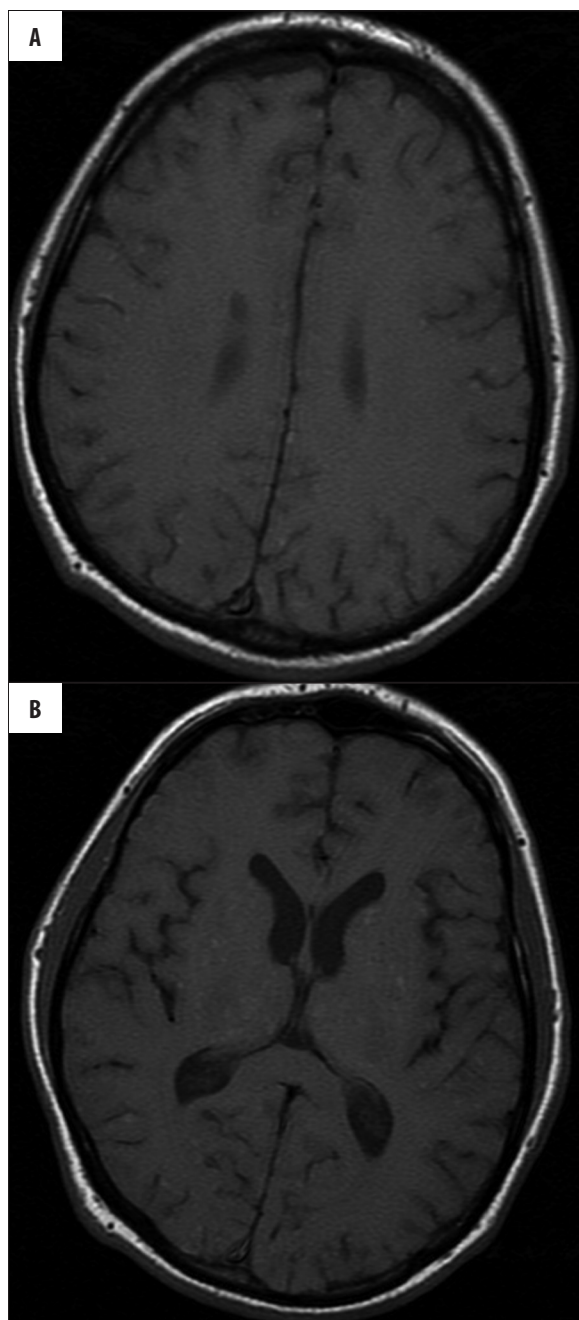


Figure 1A–C. Brain MRI. SE/T1-weighted images. Countless, tiny, weakly hyperintense foci disseminated in the meninges, supratentorial compartment and cerebellum.

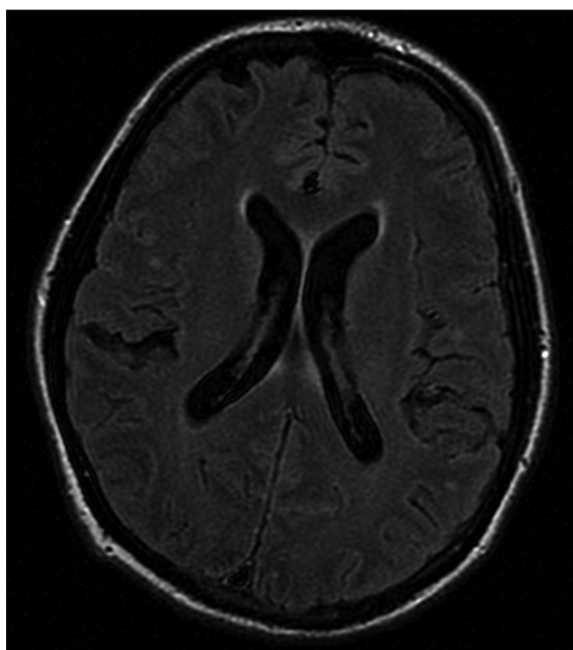


Figure 2. FLAIR image. Only four foci are detectable in this slice as hyperintense lesions.

disease with origin in the lungs (papillary adenocarcinoma). Numerous nodules were disseminated in both lungs and associated with suppurative pneumonia and edema. Numerous metastatic lesions were found in mediastinal lymph nodes, suprarenal glands, spleen, both cerebral and cerebellar hemispheres (Figure 4) and the meninges.

Discussion

Miliary metastatic process in the brain is very rare and therefore rarely described. The neuroradiological methods used to show it are not of equal value: it may be not detected on computed tomography (CT) and also hard to visualize on MRI but after gadolinium-based contrast medium injection it shows contrast enhancement and is

conclusively demonstrated [1,2]. We found only two cases in the literature resembling ours. One was a case of lung adenocarcinoma with miliary metastases in the brain on autopsy and normal brain MRI, before and after gadolinium administration [3]. That case was similar to ours in terms of the lack of contrast enhancement. The lesions in our case however, although hardly, were visible on MRI, mainly on T1-weighted images before contrast medium

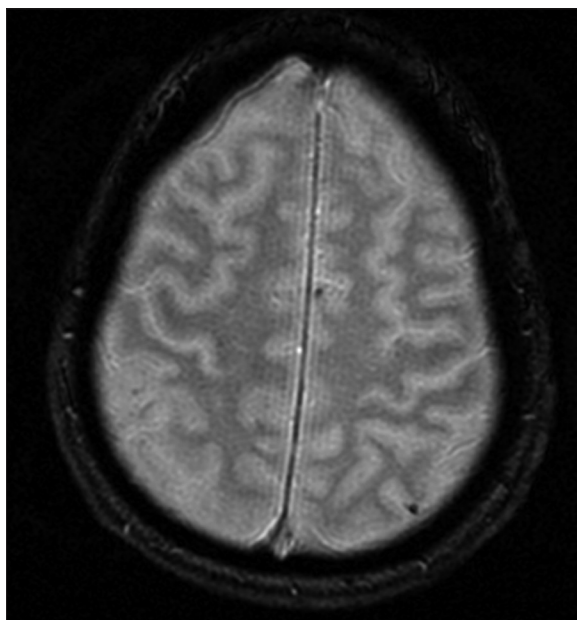


Figure 3. GRE/T2*-weighted image. Only two hypointense foci are seen in this slice.

administration – as hyperintense foci. In the second case the miliary metastases were not visible on T1-weighted images before or after contrast administration but they were detected on T2-weighted images [4]. That case was also similar to ours in terms of the lack of contrast enhancement of the lesions.

There are not many causes of hyperintense signal on T1-weighted images of the brain. Fat, hemoglobin breakdown products (methemoglobin), iron, copper, manganese and melanin belong to them [5–7]. Calcifications may be paradoxically hyperintense on T1-weighted images as well as neurofibromatosis (type 1) bright objects located in the globi pallidi. In our patient, CT of the head was normal and calcifications were considered as improbable. Disseminated, miliary character of the lesions suggested metastatic process although the lesions were extremely small and did not have any surrounding oedema or mass effect. Melanoma was taken into account as the most probable diagnosis because melanin deposits are spontaneously hyperintense on T1-weighted images. Lung cancer was a surprising diagnosis because metastases of this neoplasm (and of most of the neoplasms) are usually hyperintense on T2-weighted images and hypointense on T1-weighted

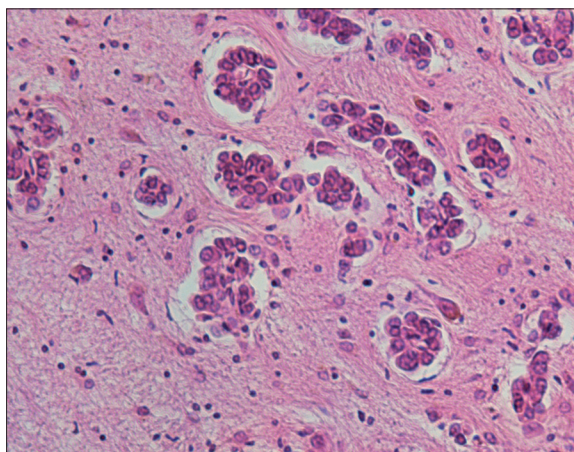


Figure 4. Pathologic specimen of the brain showing the metastases. H&E stain $\times 200$.

images, with strong contrast enhancement, also in case of miliary spread [1].

Papillary adenocarcinoma of the lung, micropapillary in particular, is a very aggressive subtype of adenocarcinoma and always poorly differentiated (G3). Frequently at the time of diagnosis the disease is already at an advanced stage, with poor prognosis. Micropapillary adenocarcinoma invades adjacent structures locally and forms distant metastases, especially to the lymph nodes.

Morphology of this tumor is very specific and according to the new classification of the lung tumors from the year 2011, evidence of about 5% of micropapillary subtype of adenocarcinoma within the tumor volume in the assessed slides is very important for the prognosis and clinical course of the disease. Cuboidal and columnar cells building papillary and micropapillary structures are seen in the microscope. In the papillary variant, the fibrovascular core predominates in the papillary structures of the tumor. In the micropapillary subtype those structures are frequently without that fibrovascular core and form clusters of neoplastic cells in the alveolar spaces [8–10].

As shown in this case report, adenocarcinoma of the lung may produce miliary spread with very uncommon MR appearance. In addition to a short list of T1-hyperintense brain lesions, miliary spread of lung adenocarcinoma should be taken into account.

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