Calcified Liver Metastases from a Neuroendocrine Tumor of the Lung (Atypical Carcinoid) – A Case Report

Introduction
Pulmonary neuroendocrine tumors (NETs) are rare tumors with an incidence rate of 0.2–2/100,000 population/year in Western countries (M. E. Caplin et al. Ann Oncol 2015; 26:1604–20). They account for 1–2% of all neoplasms of the lung and constitute one-fourth to one-third of all NETs. Atypical carcinoids are far less common than typical carcinoids and predominantly occur in male smokers aged 50–70 years. Most pulmonary NETs are asymptomatic due to their peripheral location. Surgical resection is the treatment of choice. Medical management should take hormone-related symptoms into account.

To the best of our knowledge, this is the first report of a pulmonary NET with unusual calcified liver metastases. Diagnostic workup of the patient included ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound-guided biopsy of the liver lesions.

Case Description
A 75-year-old woman with visual impairment of the right eye was admitted to the Department of Ophthalmology of our hospital. She had a history of type II diabetes mellitus, partial strumectomy and arterial hypertension. The clinical examination and complete blood count were normal. Her medications included levothyroxine, trimeprazine, hydrochlorothiazide, and pantoprazole. Optical coherence tomography revealed a choroidal lesion in the right eye.

Pathology
No melanin production was demonstrated in the biopsy tissue. Histology revealed liver metastases from an NET (G2 according to WHO), most likely from a primary in the lung (atypical carcinoid). The differential diagnosis included choroidal and gastrointestinal NET. However, the pattern of metastatic spread made these primary tumor sites unlikely.

Discussion
To the best of our knowledge, this is the first report of a pulmonary NET with unusual calcified liver metastases. A PubMed database search (search terms: calcified metastases, pulmonary NET, calcified liver metastases, hepatic calcifications) revealed no case of pulmonary NET with calcified liver metastases. Our search revealed only a single case of a patient with pancreatic NET and calcified liver metastases (T. Kawamoto et al. Clin J Gastroenterol 2014;7:460–4).

The sonographic appearance of the liver lesions did not allow definitive characterization as benign or malignant. Their appearance was consistent with hepatic metastases, calcified adenomas, and hepatic tuberculosis. Further workup with CT and MRI allowed definitive classification of the lesions as calcified metastases. The ultrasound-guided liver biopsy was crucial for identifying the primary tumor. Otherwise multiple calcified liver metastases would primarily suggest metastatic spread from a mucin-producing primary tumor, for example in the colon, breast, stomach, or ovaries (C. Stoupis et al. Radiographics 1998;18:675–85).

We did not perform contrast-enhanced ultrasound (CEUS) in our patient because of the multiplicity of liver lesions and acoustic shadowing due to calcification of the lesions. It is known from previous studies that the detection and characterization of hepatic lesions, e.g., metastases from colorectal cancer, can be significantly improved by CEUS compared to non-enhanced ultrasound (V. Cantisani et al. Ultraschall Med 2010;31:500–5, M. D’Onofrio et al. Radiol Med 2008;113:76–86).

In the case presented here, imaging findings and liver biopsy ruled out the initially suspected choroidal melanoma, leading instead to the diagnosis of a pulmonary NET with metastatic spread to the liver.
choroid and lymph nodes. Workup was initiated based on this diagnosis.

However, the cause of calcification of liver and lymph node metastases in our patient remains unclear. At the time of diagnosis, no hypercalcemia was apparent (Ca\(^{2+}\) = 2.4 mmol/l, n = 2.2–2.5 mmol/l). Therefore, metabolic causes or a paraneoplastic syndrome with calcification seems unlikely. We hypothesize that rapid growth of the metastases led to necrosis with subsequent dystrophic calcification.

Conflict of Interest

The authors declare that they have no conflict of interest.

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