Well-Differentiated Neuroendocrine Carcinoma Mimicking an Echinococcus Cyst of the Liver in CT – MRI Findings with Hepatocyte Specific Contrast Material

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Abstract

Gastroenteropancreatic neuroendocrine tumors and their metastases have an inconsistent appearance with only a small percentage of lesions appearing as cystic masses in computed tomography (CT) and magnetic resonance imaging (MRI) and can therefore be mistaken as benign or infectious lesions, leading to a false diagnosis with delayed and inadequate treatment. We report a patient with upper abdominal pain lasting for several months, caused by a huge cystic neuroendocrine carcinoma of the liver which was mistakenly interpreted as an echinococcus cyst and present the findings in the initial CT and the subsequently performed MRI under application of hepatocyte specific contrast material, which led to distinct differential diagnoses and therefore had a capacious impact on the therapeutic strategy.

Key words

Neuroendocrine carcinoma – liver tumor – echinococcus cyst – CT – MRI – Gd-EOB-DTPA.

Case report

A 53-year-old female patient without prior abdominal operations presented with several months history of unspecific pain in the upper right quadrant of the abdomen and gastric reflux disease. Hematology laboratory data were within the normal range. Contrast enhanced computed tomography (CT) from an external institution showed a hypodense mass in the right liver lobe with a thick capsule around liquid content and trabecular septations. The imaging findings were evaluated to be most likely an echinococcus cyst of the right liver lobe (Fig. 1). Additionally, there were smaller cystic lesions in both liver lobes which had been interpreted as simple cysts. The patient was referred to our center for surgical therapy.

At our center, for further preoperative evaluation, magnetic resonance imaging (MRI) of the liver was performed with unenhanced T1- and T2-weighted images with and without fat suppression and contrast enhanced sequences using 7ml Gd-EOB-DTPA (Primovist®, Bayer Schering Pharma, Berlin, Germany) with early dynamic acquisition and delayed imaging in the hepatobiliary phase after 20 minutes (1.5T; Gyroscan ACS-NT; Philips, Best, The Netherlands).

On MRI, the lesion in the right liver lobe, measuring 6.5x6.0cm, showed a thick capsule and trabecular septa. On T1-weighted transverse gradient echo sequences the wall and septa appeared hypointense, while the liquid content showed hypo-, iso-, and hyperintense partitions (Fig. 2A), whereas on T2-weighted transverse turbo spin echo sequences it was hyperintense and several fluid-fluid-levels were detectable within the lesion (Fig. 2B). Dynamic imaging demonstrated the hypervascularity of the wall and septations of the lesion with intensive enhancement in the arterial and portal venous phase, while the cyst content remained hypointense (Fig. 2C). On the late T1-weighted images, 20 minutes after contrast media injection, no contrast media
uptake of the mass was present (Fig. 2D). Based on these findings, a cystic hypervascularized tumor was preferred as differential diagnosis in the MRI. The other cystic lesions appeared as benign liver cysts without dynamic or delayed enhancement.

To avoid distribution of tumor cells by a percutaneous puncture of the cystic mass and as no primary tumor was detected, a right hemihepatectomy (segments V-VIII) was performed. The specimen revealed an invasive cystic neoplasm of epithelial origin, containing hemorrhages of different ages (Fig. 3). A small number of mitoses were found and there was an expression of CK7 and CK18, chromogranine, synaptophysin, CK20 and CA19-9. The surrounding liver parenchyma showed lymphoid infiltrations (Fig. 4). These findings resulted in the diagnosis of a well-differentiated neuroendocrine carcinoma (NEC), probably of gastroenteropancreatic origin. However, similar to the preoperative workup, a subsequently performed whole-body Ga-68-DOTATOC-PET/CT did not reveal any candidate lesion as a possible primary tumor. Some of the small cysts were contained in the resected specimen and were proven to be benign liver cysts with the cysts in the remaining liver having a similar appearance in intraoperative ultrasound. In the follow-up (13 months) no enlargement of the remaining cysts has been observed so far.

**Discussion**

Gastroenteropancreatic neuroendocrine tumors (GEP-NET) represent approximately 2% of all gastrointestinal tumors [1, 2]. The major categories of NET defined by the WHO are: 1) well-differentiated tumors (benign or low-grade malignancy); 2) well-differentiated carcinomas (low-grade malignancy); 3) poorly differentiated endocrine carcinomas (high-grade malignancy), and some subordinate categories [3-5]. The main localization of metastasis is the liver. Often, as in the present case, no primary cancer is found, even though it can be assumed to be of gastrointestinal or pancreatic origin.

Cystic appearance of NEC metastases is rare. The low incidence of NEC and the unusual, large solitary cystic lesion in the liver made this differential diagnosis quite unlikely, which initially resulted in the interpretation as an echinococcal cyst, based on the monophasic contrast enhanced CT. On CT, hydatid cysts appear as homogeneous hypodense formations with a thick wall and trabecular septations [6, 7]. These findings were present in our patient. However, the solid components of the lesion appeared to show a mild contrast enhancement on the monophasic venous phase CT, which led us to further examination with MRI of the liver, which in our center is routinely performed under application of Gd-EOB-DTPA, a hepatocyte specific contrast agent. On MRI, hydatid cysts evidenced a hypointense content on T1-weighted images while on T2-weighted images the cystic content appeared hyperintense. Wall and septations are hypointense on T1- and T2-weighted images.

After application of a contrast agent, echinococcal cysts may show a subtle circular enhancement due to a pseudocapsule and inflammatory reactions around the lesion [6, 7]. However, the septations and the wall itself do usually not show contrast material uptake or even hypervascularization.
Neuroendocrine tumor mimicking hydatid cyst

with early intense contrast enhancement. Using the MRI findings, a hydatid cyst is not very likely, particularly because of the intense hypervascularization of solid lesion components, which was sufficiently demonstrated by the Gd-EOB-DTPA. This hepatocyte specific contrast agent is known to be almost equal to extracellular MRI contrast agents regarding the T1-positivity in the early dynamic phases due to the high T1-relaxivity, even though the applied dose is lower [8]. This hyperarterialization is unusual for biliary cysts, biliary cystadenomas, and intraductal papillary mucinous tumors (IPMT), even though biliary cystadenomas, dedifferentiated IPMT, and, more characteristically, biliary cystadenocarcinomas can show these findings; so these are the top differential diagnoses of this lesion [9]. Metastases from ovarian cancer or mucinous adenocarcinoma from the gastrointestinal tract were rather unlikely differential diagnoses as no primary cancer or peritoneal carcinomatosis was identified on abdominal CT and hypervascularization is not a typical feature of these entities.

The delayed hepatospecific phase of the Gd-EOB-DTPA, which is internalized by hepatocytes and then excreted with the bile, ruled out differentiated hepatocellular origin of the solid components as well as an open communication of the cysts with the biliary system by absence of delayed contrast accumulation [8]. Hepatocellular carcinomas or cholangiocellular carcinomas do not usually show cystic transformation. Similarly, large cystic mucinous metastases from colorectal cancer and melanoma are possible but rare [10]. Fluid-fluid levels could be present in infectious abscesses; however, no leukocytosis or fever was present.

Altogether, the findings resulted in a cystic hemorrhagic hypervascularized tumor of the liver, with cystadenocarcinoma and cystic NET metastasis as the differential diagnoses in favor. A primary tumor could not be found on preoperative examinations and the cystic morphology of the tumor prevented us from taking a needle biopsy with the risk of tumor spilling, thus leading us to the surgical approach. In view of the original hypothesis of a hydatid cyst, the MRI findings had a capacious impact on the management even regarding the surgical technique, as an oncological radical hemihepatectomy was performed instead of enucleation of the cyst. The other cystic lesions appeared to be benign which was confirmed by surgical exploration, intraoperative ultrasound and follow-up.

While the smooth septa and large cysts in the macroscopic aspect of the resected lesion correlate well with the misleading hydatid cyst like appearance on cross-sectional imaging, the above mentioned histological results and the immune phenotype of the lesion proved the malignant status and were indicative for a GEP-NET [2, 4, 5]. According to the histological results, the presented lesion was classified as a well-differentiated (low-grade) neuroendocrine carcinoma without hormonal activity.

**Conclusion**

GEP-NET are rare neoplasms of the gastrointestinal tract often metastasizing into the liver. In most cases, the liver is infiltrated before the disease is diagnosed, demonstrating that the diagnosis of GEP-NET remains a challenge for clinicians. The presented case is an example illustrating the variability of NET appearance in imaging, which in some cases may lead to a false diagnosis and to wrong treatment. Therefore, careful analysis and interpretation of imaging findings is necessary. MRI of the liver, with a dedicated hepatocyte specific contrast agent, aids in the differential diagnosis of such lesions.

**Conflicts of interest**

None to declare.

**References**

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