Current Advances in Diagnosis of Hepatic Metastases from Neuroendocrine Carcinomas

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Neuroendocrine carcinomas (NEC) arising in various locations constitute a morphologically heterogenous group of lesions. They originate from the dispersed or diffuse neuroendocrine cell system. Hepatic metastases are common in NEC, especially in patients with gastro entero pancreatic disease as the portal vein drains directly into the liver [1]. Liver metastases are found at presentation in 44-85% of patients with midgut tumors and are the most common imaging finding [2,3]. However, liver metastases can be present in patients with NEC involving other sites (for instance head and neck areas). The presence of metastases is an important prognostic factor for survival [4-7]. The accurate identification of suspected malignant hepatic mass(es) is mandatory and imaging modalities are fundamental [1].

The histology of the primary tumor seems to correlate clearly with the risk of distant metastases. Some tumors such as verrucous carcinomas, basal cell carcinomas, low-grade salivary gland cancers, rarely metastasize and extensive screening seems an unnecessary use of resources. In NEC, given the frequent presence of metastatic disease especially into the liver, the use of different radiological methods for patient's staging is very important. Laboratory biochemical investigations as Alanine Aminotransferase (ALT), Lactic Dehydrogenase (LDH), Aspartate Aminotransferase (AST), γ-Glutamyl-transferase (γ-GT) are not sensitive and extremely non-specific; therefore, they are not used for staging or follow-up after treatment.

Neuroendocrine tumors commonly present as an over expression of the somatostatin-receptor-subtype 2 (SSR2) [1,8,9]. The somatostatin analog DOTA(0)-Phe(1)-Tyr(3)-octreotide (DOTATOC) specifically binds to SSR2 while it only shows a low unspecific uptake in normal liver; moreover, positron emission tomography (PET) appears to be a reliable method for parenchimal hepatic evaluation [1,10]. 68Ga-labeled DOTATOC as a PET-tracer has shown both high sensitivity and specificity for neuroendocrine neoplasms detection and staging [11-14].

However, PET provides only limited anatomical information and today is commonly performed in combination with computed tomography (CT) using hybrid imaging systems to correlate anatomical and functional information [1,15,16]. In-111 pentetreoide was also found to be significantly superior to conventional imaging investigations [17]. 68Ga-DOTATOC-PET is generally considered to be superior to In-111 pentetreoide scintigraphy and single-photon emission CT (SPECT), suggesting that multiphase 68Ga-DOTATOC-PET/CT can be expected to yield promising results also in the detection of hepatic metastases (11). Neuroendocrine hepatic metastases may be difficult to identify on CT, as they may be isointense to the liver on portal venous phase. A combination of pre-contrast, hepatic arterial-dominant phase and portal venous phase imaging will improve the sensitivity of detection, as in some cases a lesion may only be seen on one of the phases [17,18].

While CT is useful for metastatic location, magnetic resonance imaging (MRI) can provide more detailed anatomical information. Bader et al. [19] found that on MRI 75% of neuroendocrine liver metastases appeared as low signal intensity on T1- and high signal intensity on T2-weighted images, with 94% of metastases being hypervascular on hepatic arterial phase post-gadolinium images and 15% of hepatic metastases being seen only on the immediate post-gadolinium images [19]. A consolidated view indicates that there is a need for combined molecular (DOTATOC-PET) and anatomic (MRI or CT) imaging. But it still remains unclear which modality, using dedicated hepatic examination protocols, provides the best morphologic presentation of the hepatic tumor burden. The results of a recent study suggest that 68Ga-DOTATOC-PET-MRI fusion using a hepatocyte-specific MRI contrast agent detects significantly more neuroendocrine liver metastases - the small ones (<1 cm), in particular - than contrast enhanced multiphase 68Ga-DOTATOC-PET-CT [13]. The higher sensitivity for small liver metastases is mainly attributable to the excellent spatial resolution and soft-tissue contrast of MRI compared to PET and CT [13].

References


