胆囊神经内分泌肿瘤的 CT 与 MRI 影像学表现

黄泽弟[1]，王东烨[2]，罗晏吉[3]，何佳秀[4]，刘　雪[4]，沈　君[2]
(1. 深圳市宝安区中心医院放射科，广东 深圳 518102；2. 中山大学孙逸仙纪念医院放射科，广东 广州 510120；
3. 中山大学附属第一医院医学影像学部，广东 广州 510080；4. 林芝市人民医院放射科，西藏 林芝 860114)

摘　要：【目的】总结胆囊神经内分泌肿瘤的 CT 与 MRI 影像学表现特征。【方法】回顾性分析 2010 年 1 月至 2018 年 5 月经手术病理证实的 10 例胆囊神经内分泌肿瘤的 CT 与 MRI 检查资料，其中 6 例仅行胆囊 CT 检查，3 例仅行 MRI 检查，1 例同时行 CT 与 MRI 检查。观察胆囊肿瘤的大小、形态、强化方式，是否合并肝转移、胆管与肝周转移、淋巴结转移、胆囊结石等情况。【结果】10 例胆囊神经内分泌肿瘤，肿块 T_1 最大径为 39~120 mm，表现为广基底附着于胆囊壁，并突向胆囊腔内；其中 7 例 CT 表现为软组织密度不规则肿块；4 例 MRI 上，肿瘤在 T_1 加权成像为均匀等信号，T_2 加权成像为不均匀高信号，弥散加权成像上弥散受限。10 例胆囊肿瘤增强后呈中度不均匀持续性强化。10 例中，8 例伴有肝转移，其中肝 4、5 段转移 7 例，其它肝段多发转移 1 例；6 例侵犯胆管，3 例侵犯肝门部脂肪；7 例伴有肝门或腹膜后淋巴结转移；1 例合并胆囊结石。【结论】胆囊神经内分泌肿瘤 CT 及 MRI 表现有一定特征性，多表现为胆囊部位的大肿块，易侵犯邻近的肝实质，沿胆囊颈、胆囊管蔓延，伴肝门、腹膜后淋巴结转移，并肝门部脂肪侵犯。

关键词：胆囊肿瘤；神经内分泌肿瘤；体层摄影术；X 线计算机；磁共振成像
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CT and MRI Imaging Findings of Gallbladder Neuroendocrine Tumor

HUANG Ze-di[1], WANG Dong-ye[2], LUO Yan-ji[3], HE Jia-xiu[4], LIU Xue[4], SHEN Jun[2]
(1. Department of Radiology, Baoan Central Hospital of Shenzhen, Shenzhen 518102, China; 2. Department of Radiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510120, China; 3. Department of Radiology, the First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China; 4. Department of Radiology, Linzhi People's Hospital, Linzhi 860114, China)
Correspondence to: SHEN Jun; E-mail: shenjun@mail.sysu.edu.cn

Abstract: 【Objective】To summarize the CT and MRI imaging features of gallbladder neuroendocrine tumor. 【Methods】CT and MRI data of 10 patients with gallbladder neuroendocrine tumors proven by surgical pathology between January 2010 and May 2018 were retrospectively analyzed. Among them, 6 patients underwent CT examination, 3 underwent MRI examination, and 1 patient underwent both CT and MRI examinations. The size, morphologic features and contrast enhancement pattern of gallbladder tumors, and the presence of liver metastasis, bile duct and perihepatic metastasis, lymph node metastasis, and the presence of gallbladder stone were assessed. 【Results】Among these 10 cases of gallbladder neuroendocrine tumor, the largest dimension of tumors ranged from 39 mm to 120 mm. The tumors manifested as a mass protruding into the lumen with a broad base adhering to the wall of the gallbladder. In 7 patients who had undergone CT examination, the tumors manifested as an irregular mass with soft tissue density on CT. In 4 patients who had undergone MRI, the tumors showed homogeneous iso-intense signal on T_1-weightedimaging, heterogenous hyper-intense signal on T_2-weighted imaging, and limited diffusion on diffusion-weighted imaging. All tumors in 10 patients showed

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作者简介：黄泽弟，副主任技师，研究方向：消化系统疾病，E-mail：hzd_666@163.com；沈君，通信作者，教授，研究方向：影像诊断学与分子影像学，E-mail：shenjun@mail.sysu.edu.cn

moderate, heterogeneous and persistent enhancement. Eight patients had liver metastasis, among whom 7 had metastases in liver segments 4 and 5, and 1 had multiple metastases in other liver segments. Six patients had bile duct invasion and 3 had hilar fat invasion. Seven patients had lymph node metastasis. One patient had gallstone.【Conclusion】Gallbladder neuroendocrine tumor has certain characteristic CT and MRI findings, such as a large mass in gallbladder, which tends to invade adjacent liver parenchyma, and extend along gallbladder neck and gallbladder ducts, accompanied with hepatic portal and retroperitoneal lymph node metastasis, and hilar fat invasion.

Key words: gallbladder tumor; neuroendocrine tumor; tomography; X-ray computer; magnetic resonance imaging

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神经内分泌肿瘤(neuroendocrine tumor, NET)是指来源于神经内分泌细胞的一种恶性肿瘤,占全身恶性肿瘤不足1%,以胃肠道及呼吸道多见[1-2]。胆囊NET临床罕见,仅占所有NET的0.5%,占全部胆囊肿瘤的2.1%[3]。但是胆囊NET的缺乏特异性的临床表现,其恶性程度高、进展迅速,多数胆囊NET预后差,往往在确诊时已出现淋巴结和肝脏转移[4]。CT与MRI是目前腹部病变诊断及术前评估的常用影像学检查手段,然而目前有关胆囊NET的CT[5-7],尤其是MRI表现报道不多。笔者回顾性分析10例经手术病理证实的胆囊神经NET的CT与MRI表现,旨在提高对于该病的认识,帮助提高术前影像学诊断准确率。

1 材料与方法

1.1 临床资料

回顾性分析2010年1月至2018年5月中山大学附属第一医院、中山大学孙逸仙纪念医院,经手术病理证实且有完整术前CT、MRI影像资料的10例胆囊神经内分泌肿瘤患者资料。本研究经以上医院医学伦理委员会同意,因属回顾性研究免除签署病人知情同意书。10例患者(女4男6);年龄42~74岁,平均年龄57.2岁。7例患者表现为腹痛、腹部饱胀不适感;4例纳差、恶心、呕吐;2例黄疸;2例腹部触及肿块。6例患者行胆囊CT平扫与增强扫描,3例患者行MRI检查,包括MRI平扫及增强扫描、弥散加权成像(diffusion-weighted imaging, DWI)以及MR胰胆管造影(magnetic resonance cholangiopancreatography, MRCP)检查。其中1例同时行CT和MRI检查。

1.2 MRI检查

MRI检查使用Philips Achieva 3.0 T或Siemens Magnetom Trio 3.0 T超导型磁共振机扫描仪,采用体部表面线圈,常规使用呼吸门控技术。扫描范围包括肝脏、胆囊及胰腺。首先进行平扫:扫描序列包括横断位T_2加权成像(T_2-weighted imaging, T_2WI),扫描参数为重复时间(repetition time, TR):1 700~2 000 ms,回波时间(echo time, TE):80~85 ms,层厚:4.5~5 mm,层间距:1 mm,视野(field of view, FOV):350~395 × 317~330 mm,信号平均次数(number of signal averaged, NSA):2次;横断位T_1加权成像(T_1-weighted imaging, T_1WI),扫描参数为TR:325~500 ms,TE:40~50 ms,层厚2 mm,层间距0 mm,FOV:350~375 × 304~328 mm,NSA:1次;冠状位T_1WI成像,TR:3.0~3.1 ms,TE:1.45~2.2 ms,层厚3 mm,层间距0 mm,FOV:350 × 398 mm,NSA:2次;DWI:b = 0、800 s/mm^2。MRCP:采用流动补偿和脂肪抑制重T_2WI,TR:4 576~5 100 ms,TE:73~74 ms,FOV:350~375× 304~328 mm,NSA:1次。平扫完成后经肘静脉注射对比剂钆喷替酸(马根维显,德国拜耳先灵公司),剂量为0.1 mL/kg,注射后,行T_1WI横断位与冠状位增强扫描,增强扫描各参数与平扫相同。

1.3 CT检查

CT检查使用Siemens Somatom Sensation 64或Toshiba Aquilion 64螺旋CT机。扫描参数为管电流200~350 mAs,管电压120 kV,层厚1 mm,层间隔0.75 mm,螺距1.2,准直宽度64 × 0.6 mm,0.33~0.5 s/360°,矩阵512 × 512。增强扫描:经肘静脉团注射非离子型碘对比剂碘帕醇(典比乐,上海博莱科信谊公司,含碘300 mg/mL),剂量1.5~2.0 mL/kg,注射流率3.0~4.0 mL/s。在腹主动脉第1腰椎

水平设置触发阈值（100 HU），采用自动追踪技术达阈值后启动动脉期增强扫描，对比剂注射后55~65 s进行门静脉期扫描，对比剂注射后120 s进行平衡期扫描。

1.4　图像分析

由2名从事腹部影像诊断的放射科副主任医师共同阅片，参考文献报道的胆囊癌影像诊断标准[8]对胆囊肿瘤的大小、形态、强化方式、肝转移、胆管及肝脏周边转移、淋巴结转移、胆囊结石等影像表现进行分析，意见不一致时经讨论达成一致意见。

1.5　病理检查

10例患者均进行了手术切除，病理标本进行HE染色，以及干细胞、磷脂酰肌醇蛋白聚糖-3、P53、神经特异性烯醇化酶、突触素、嗜铬素A、CD56、Ki67、细胞角蛋白、甲胎蛋白、细胞角蛋白7、细胞角蛋白19、细胞角蛋白8/18、尾侧型同源转录因子2等免疫组化染色检测。NET病理诊断标准参照中国胃肠胰神经内分泌肿瘤专家共识（2016年版）[9]。肿瘤病理类型按照文献报道分为：小细胞型胆囊神经内分泌癌、大细胞型胆囊神经内分泌癌及混合性腺神经内分泌癌[10]。混合性腺神经内分泌癌是指同时具有腺管形成的典型腺癌和神经内分泌肿瘤形态特点的上皮性肿瘤，每种成分至少各占肿瘤的30%。根据肿瘤核分裂数和Ki-67指数分为3级：分级1（G1）指低级别，核分裂象数1/10高倍视野或Ki-67指数≤2%；分级2（G2）指中级别，核分裂象数2~20/10高倍视野或Ki-67指数3%~20%；分级3（G3）指高级别，核分裂象数>20/10高倍视野或Ki-67指数>20%。

2　结　果

10例胆囊神经内分泌肿瘤的CT与MRI表现见表1。10例胆囊神经内分泌肿瘤，1例为大细胞性，4例为小细胞性，5例为混合性腺神经内分泌肿瘤；1例为G1，5例为G2，4例为G3。10例均表现为不规则形肿块，多数肿块较大，呈广基底附着于胆囊壁，并突向胆囊腔内。7例进行CT检查，其胆囊肿块表现为软组织密度（图1A），增强后中度不均匀持续性强化（图1B~E）。4例进行MRI检查，其胆囊肿块表现为T_1WI均匀等信号（图2B），T_2WI不均匀稍高信号（图2A），DWI弥散受限（图2C），增强后呈中度不均匀持续性强化（图2D，E）。10例中，8例肝转移，其中肝4、5段转移7例（图1 A~F；图2C，E），其它肝段多发转移1例；6例胆管受侵，3例侵犯肝门部脂肪（图1A~D）；7例伴有肝门或腹膜后淋巴结转移（图1F）；1例合并胆囊结石。

3　讨　论

胆囊NET为胆囊罕见肿瘤，多见于中老年女性，发病年龄38~81岁，平均年龄64岁[11]。多数胆囊NET患者临床无特异性表现，可表现为腹部饱胀感、上腹痛、纳差、消瘦、黄疸等非特异性症状。部分患者在体检时才发现胆囊占位，有的患者临床表现类似于胆囊结石、胆囊炎、胆囊息肉、胆囊癌等。胆囊NET具有特异的副肿瘤综合征表现的不足1%[12]。胆囊NET的组织起源至今仍存在争议，胆囊颈部黏液腺体有散在的神经内分泌细胞，肿瘤可能来源于这些细胞。目前胆囊神经内分泌肿瘤确诊主要依靠病理及免疫组化检查，常用的免疫组化指标主要有特异性烯醇化酶、嗜铬素A、突触素等。

目前有关胆囊NET的影像学表现报道较少。朱世华等[7]曾报道1例胆囊NET的CT表现为胆囊内不规则肿块，增强后肿瘤轻度强化，内有低密度液化坏死区。本组10例胆囊NET，多数表现为胆囊部位的较大不规则肿块，其CT密度为软组织密度，MRI上表现T_1WI均匀等信号，T_2WI不均匀稍高信号，DWI弥散受限。CT及MRI的信号特征以及DWI表现与胆囊其他常见肿瘤十分相似，并不特异。胃肠道、胰腺神经内分泌肿瘤CT与MRI常具有“增强扫描的动脉期明显强化”的特征性表现[13-14]。然而，本组10例胆囊NET，与胃肠道、胰腺神经内分泌肿瘤典型表现不同，均未观察到动脉期明显强化的征象，而表现为中度不均匀持续性强化。

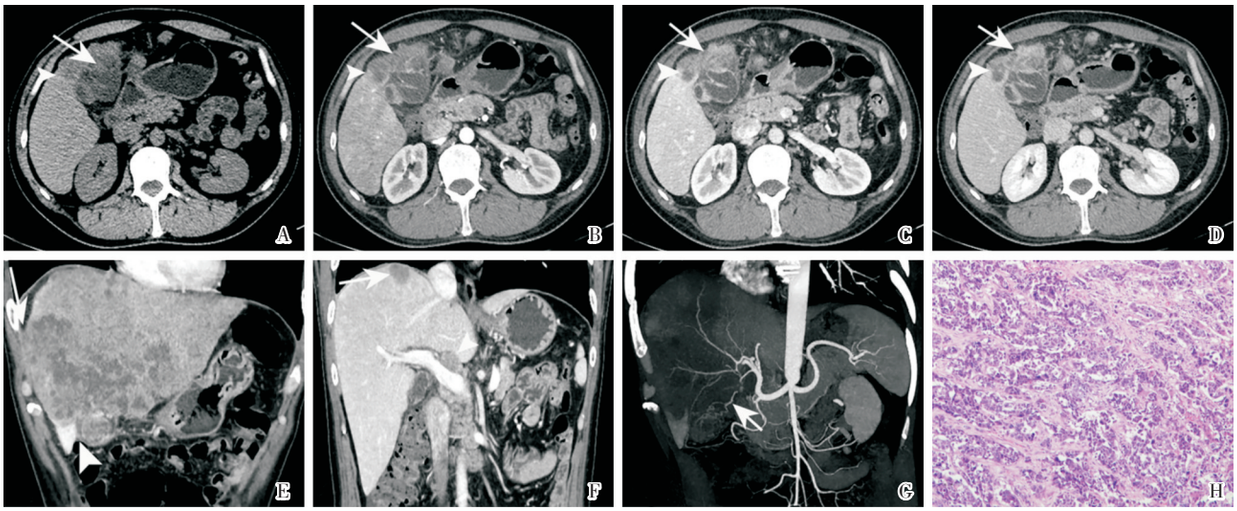
本组10例胆囊NET，大多数侵犯邻近的肝实质，沿胆囊颈、胆囊管侵犯，伴肝门、腹膜后淋巴结转移及侵犯肝门部脂肪。胆囊NET发展快，可能由于胆囊部位的空间较小且周围管道结构较多，肿瘤易引起胆囊管阻塞，并沿胆囊颈、胆囊管侵犯，肿瘤发现时常占据整个胆囊。本组10例NET

表1 10例胆囊神经内分泌肿瘤的CT与MRI影像学表现特征

Table 1 Main CT and MRI imaging features of 10 patients with gallbladder neuroendocrine tumor

No.	Sex	Age /years	CT/ MRI	Size /mm	Morphologic features	CT density or MRI signal intensity	Adjacent tissue invasion	Liver metastasis	Lymph node metastasis	Pathological diagnosis
1	Female	69	CT	90×40×40	Irregular mass and a broad base adhering to the wall of the gallbladder	Soft tissue density	Absent	Liver segments 4 and 5 metastases	Absent	Small cell neuroendocrine carcinoma (G3)
			MRI			Homogeneous iso-intense signal on T_1WI, heterogenous hyper-intense signal on T_2WI and limited diffusion on DWI				
2	Male	74	MRI	85×40×25	Extensive thickening of gallbladder wall	Homogeneous iso-intense signal on T_1WI, heterogenous hyper-intense signal on T_2WI and limited diffusion on DWI	Bile duct invasion and hilar fat invasion	Absent	Absent	Mixed adenoneuroendocrinoma (G2) with bundle invasion
3	Male	42	MRI	120×45×40	Irregualr mass in the wall of the gallbladder	Homogeneous iso-intense signal on T_1WI, heterogenous hyper-intense signal on T_2WI and limited diffusion on DWI	Absent	Liver segments 4 and 5 metastases	Present	Mixed adenoneuroendocrinoma (G2)
4	Male	44	CT	80×50×38	Irregular mass in the wall of the gallbladder	Soft tissue density	Bile duct invasion and hilar fat invasion	Multiple hepatic and peritoneal metastases , Peritoneal metastasis	Absent	Large cell neuroendocrinoma (G1)
5	Female	55	CT	90×50×30	Irregular mass in the gallbladder duct	Soft tissue density	Bile duct invasion and hilar fat invasion	Liver segments 4 and 5 metastases and peritoneal metastasis	Present	Mixed adenoid neuroendocrinoma (G2)
6	Male	50	CT	110×50×50	Irregular mass in the wall of the gallbladder	Soft tissue density	Bile duct invasion	Liver segments 4 and 5 metastases	Present	Small cell neuroendocrine carcinoma (G3)
7	Male	62	CT	120×92×93	Irregular mass in the wall of the gallbladder	Soft tissue density	Bile duct invasion	Liver segments 4 and 5 metastases	Present	Small cell neuroendocrine carcinoma (G3)
8	Male	65	CT	120×90×90	Irregular mass in the wall of the gallbladder	Soft tissue density	Absent	Absent	Present	Mixed adenoneuroendocrinoma (G2)
9	Female	56	CT	39×18×15	Irregular mass in the wall of the gallbladder	Soft tissue density	Absent	Liver segments 4 and 5 metastases	Present	Small cell neuroendocrine carcinoma (G3)
10	Female	55	MRI	120×90×90	Extensive mass in the wall of the gallbladder	Homogeneous iso-intense signal on T_1WI, heterogenous hyper-intense signal on T_2WI and limited diffusion on DWI	Bile duct invasion	Liver segments 4 and 5 metastases	Present	Mixed adenoneuroendocrinoma (G2)

T_1WI: T_1-weighted imaging; T_2WI: T_2-weighted imaging; DWI: diffusion-weighted imaging.



A 44-year old male with a large cell neuroendocrine tumor of gallbladder. Unenhanced CT image (A) shows an irregular mass in the gallbladder with soft tissue density (arrow) and fat invasion around the liver and the gallbladder fossa, and a metastatic nodule in liver segment 5 (arrowhead). Arterial phase (B), portal venous phase (C) and equilibrium phase (D) contrast-enhanced images show the gallbladder mass (arrows) with moderate, heterogeneous, persistent enhancement, and the metastatic nodule of liver segment 5 (arrowhead) with rim enhancement. Coronal portal venous phase images (E, F) show the gallbladder mass with perihepatic (arrow) and gallbladder fossa fat invasion (arrowhead), and multiple metastatic nodules in liver segments 4, 5 and 8 (arrow) and hilar lymph node metastasis (arrowhead). Maximum intensity projection of arterial phase contrast-enhanced image (G) shows that the gallbladder mass is supplied by the gallbladder artery (arrow). Micrograph of HE staining (magnification× 100, H) shows that tumor cells are densely distributed and have a small size, few cytoplasm and dark nuclei.

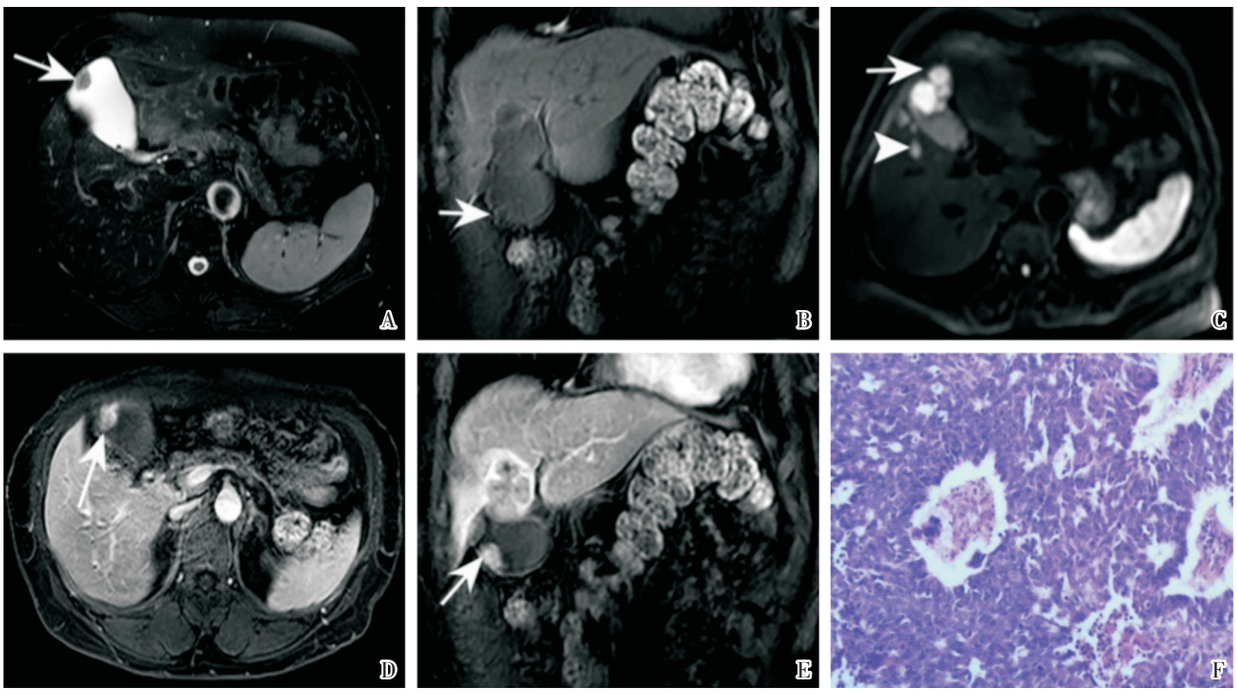
图1　胆囊神经内分泌肿瘤的CT表现

Fig.1　CT findings of a gallbladder neuroendocrine tumor

中，肝转移8例，其中肝4、5段转移7例，其原因可能是胆囊NET沿胆囊和肝脏之间的网状组织内的静脉，汇入门静脉，而转移到肝实质；同时由于胆囊体与肝相接面缺乏浆膜层，胆囊纤维肌层菲薄，胆囊NET癌细胞可沿静脉途径迅速向肝右叶转移。既往报道NET具有沿淋巴管转移的特点[5]。本组病例中7例淋巴结转移。胆囊-肝接触面有少量淋巴管与肝淋巴管相连，胆总管淋巴引流到沿线淋巴结、肝门附近淋巴结、胰腺周围淋巴结，最终进入腹腔动脉组淋巴结。胆囊周围丰富的淋巴管网及其回流特点，可能导致胆囊NET易出现肝门淋巴结及腹膜后淋巴结转移。此外，本组病例有肝门部脂肪侵犯3例，提示胆囊NET也较易侵犯邻近脂肪组织。曾焕忠等[15]报道，胆管癌可合并胆道结石，且合并胆道结石的胆管癌在CT与MRI上更多表现为肿块性和息肉型，而不伴结石的多表现为浸润型。本组病例中仅有1例胆囊ENT合并有胆囊结石，提示胆囊NET合并结石较少见。

胆囊NET别诊断：①胆囊腺癌：胆囊恶性肿瘤中，以腺癌多见，常表现为局限或环形肿块，边界不清，黏膜破损，而胆囊NET更多表现为胆囊弥漫肿块型。胆囊腺癌常可见高特异性的“脐样”征[16]，而胆囊NET未见此征象，笔者认为“脐样”征可作为鉴别点。胆囊腺癌肝转移较神经内分泌肿瘤迟，且肝转移瘤常较小。而胆囊NET淋巴结转移更快，常见肝门及腹膜后淋巴结转移，预后较胆囊腺癌更差[10]。②胆囊转移癌：十分少见，已报道的大多数病例是恶性黑色素瘤、肾细胞癌或乳腺癌等转移至胆囊。③胆囊腺肌增生症：表现为局灶性或弥漫性胆囊壁增厚，MRI的T2WI可显示Rokitansky-Aschoff窦，是胆囊腺肌增生症较为特异性征象，可用于两者的鉴别。④胆囊息肉：附于胆囊黏膜、带蒂突起，形态较为规则，增强后轻度强化，不难与恶性肿瘤鉴别。

综上所述，胆囊NET的CT与MRI影像学表现有一定特征性，多表现为胆囊不规则较大肿块，易侵犯邻近的肝实质，沿胆囊颈、胆囊管蔓延，伴有肝门、腹膜后淋巴结转移及侵犯肝门部脂肪。临床上遇到胆囊肿块较大，且周围器官明显侵犯及伴有肝门淋巴结转移时，应考虑到本病的可能性。



A 69-year old female with a small cell neuroendocrine tumor of gallbladder. Fat-suppressed T_2-weighted image (A) shows the nodule tumor in the gallbladder nodule with slightly hyper-intense signal (arrow). T_1-weighted image (B) shows the gallbladder tumor with iso-intense signal (arrow). Diffusion-weighted image (C) shows limited diffusion of the gallbladder lesion (arrow) and the metastatic nodules (arrowhead) in liver segments 4 and 5. Transverse (D) and coronal portal venous phase contrast-enhanced MR images (E) show moderate, heterogeneous, persistent enhancement of the gallbladder mass (arrows), and rim enhancement of the metastatic lesion in liver segment 4. Micrograph of HE staining (magnification ×100, F) shows that tumor cells are densely distributed and have a small size, few cytoplasm and dark nuclei.

图2 胆囊神经内分泌肿瘤的MRI表现

Fig.2 MRI findings of gallbladder neuroendocrine tumor

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