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胆囊腺肌症诊治的研究进展

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[摘要] 胆囊腺肌症(gallbladder adenomyomatosis, GBA)是一种后天获得的良性疾病,其病因及发病机制尚不明确。GBA术前诊断率不高,多于术后病理中发现。部分学者将GBA归为癌前病变。如果影像学检查发现本病,应根据临床表现和影像学分型决定治疗方案,腹腔镜胆囊切除术是治疗GBA的首选术式。随着对该病的深入研究及影像学技术的发展,GBA诊断与治疗水平有显著提高。

[关键词] 胆囊疾病; 胆囊腺肌症; 诊断; 影像; 治疗

Research progress in diagnosis and treatment of gallbladder adenomyomatosis

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Abstract Gallbladder adenomyomatosis (GBA) is an acquired benign disease, and its etiologies and pathogenesis are still unclear. GBA, mostly found in postoperative pathology, has been kept at a low level at preoperative diagnosis. Some scholars tend to classify GBA into precancerous lesions. The treatments of GBA should be determined according to clinical manifestation and imaging classification when it is found in imaging examination. Laparoscopic cholecystectomy is the first choice for the treatments of GBA. With the in-depth study of the disease and the development of imaging technology, there has been a significant improvement in diagnosis and treatment.

Keywords gallbladder diseases; gallbladder adenomyomatosis; diagnosis; imaging; treatment

胆囊腺肌症 (gallbladder adenomyomatosis, GBA)也可以称为胆囊壁憩室症、胆囊腺肌瘤症等,主要表现为无症状性胆囊肿块或胆囊壁增厚。其影像学主要分为弥漫型、节段型和局限型。GBA男女发病率大致相等,50岁以后发病率

呈上升趋势。迄今为止,1岁以内的儿童病例报道不足10例^[1]。胆囊切除术后病理中GBA的发现率为2%~9%^[2]。GBA的病理特征为胆囊腺体和肌层过度增生,合并黏膜层陷入肌层形成罗-阿氏窦(Rokitansky-Ashoff sinuse, RAS),随着胆汁的浓缩

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可形成晶体沉淀和钙化灶^[2-3]。GBA主要有4种病理类型:弥漫型、局限型、节段型和环状型。弥漫型GBA以整个胆囊壁弥漫性增厚为主要特征;局限型GBA是最常见的类型,通常以胆囊壁局灶性增厚为主要特征;节段型GBA的特点是病灶累及胆囊壁的大部分,通常是胆囊底和远端的1/3;环状型GBA的特征是胆囊壁呈环状增厚,其整体形态改变为沙漏形^[3]。据一些学者^[4]介绍,环形GBA应被看作是节段型GBA的一个子类型。

1 病因及发病机制

GBA的病因及发病机制尚不完全清楚,关于GBA的形成,主要有以下观点:1)与胆囊结石和慢性炎症有关。在慢性炎症的基础上,胆囊神经原性功能障碍,从而导致胆囊壁动力异常,囊内压力升高,胆汁排流受限,使黏膜陷入肌层从而形成憩室及特征性的RAS^[5]。2)与胰胆管汇合异常、胰液反流刺激有关。已有研究^[6]证明胆囊上皮细胞长期暴露于胰液而发生增生。笔者认为,GBA的形成不能一概而论,可能是以上多种因素共同作用的结果。

2 临床表现

GBA通常隐匿发生,无特异性临床表现。部分患者无临床症状;多数患者表现为右上腹隐痛、右肩部放射痛等;也有患者表现为非特异性消化功能紊乱:脂肪食物不耐受,胃肠胀气、恶心、呕吐;少数患者可有黄疸及Murphy征阳性体征,偶见不明原因发热。约50%的GBA合并结石,其中很少表现为右季肋部胆绞痛;无结石性GBA也会表现为右季肋部胆绞痛,这种症状往往持续数分钟到数小时不等,可自行消失。

3 影像学表现

3.1 常规超声

常规超声(ultrasound, US)是诊断GBA的显像模式之一,在大多数情况下,它能准确地识别和描述GBA。US的敏感度约为65%^[7],对于单纯的GBA,US诊断率更高。GBA的超声特点如下:1)局限型——胆囊壁局限性增厚,病变多位于胆囊底部,呈圆锥帽状增厚,病变可突向胆囊腔外。节段型——病变多位于胆囊体中部、底部或胆囊颈部与体部之间,可形成节段性增厚,增

生以狭窄处为主,胆囊的囊腔变窄,呈“葫芦状”,严重者胆囊腔可闭合。弥漫型——较少见,胆囊壁呈弥漫性增厚,黏膜层和浆膜层连续完整,内壁凹凸不平。2)增厚的胆囊壁内可以见到小囊状的低回声或无回声,或者胆囊壁上附着强回声,后伴彗星尾征。一项报道^[8-9]称:高频超声探头(2.5~7 MHz)对GBA与胆囊癌的鉴别诊断特别敏感,其灵敏度相当于MRI。此外,凸阵探头与线阵探头联合应用,可能提高对GBA的检出率^[10]。

3.2 超声内镜

超声内镜(endoscopic ultrasound, EUS)是一种侵入性成像模式,能够准确评估胆囊壁。在评估胆囊壁厚度方面,比US有更高的准确性。尤其对于肥胖患者,EUS可以更好地显示胆囊^[2]。已有研究^[3]证明:使用EUS可以观察到胆囊癌中的微小空间,因此在GBA与胆囊癌的鉴别诊断方面,EUS比US敏感性更高^[11]。然而,考虑到EUS的侵入性、低耐受性和高成本,临床上一概不将其作为常规检查。

3.3 超声造影

超声造影(contrast-enhanced ultrasound, CEUS)已成为快捷、准确、可靠的影像检查方法,可以更清晰地显示胆囊壁的完整性并判断其内部回声是否均匀一致,诊断效能明显优于US^[12]。GBA在CEUS声像图的动脉相和静脉相均呈现出不均匀增强,内部可见散在性细小无增强区域,有时伴随彗星尾征,即为RAS^[13]。CEUS在鉴别诊断胆囊良恶性病变方面具有一定的应用价值,尤其在判断胆囊癌浸润周围肝组织以及肝内是否转移方面优势明显^[14]。有学者^[15]指出:US与CEUS结合,可以提高局限型GBA的检出率。Tang等^[16]也证实:CEUS可以通过增加RAS的可视化程度而提高节段型GBA的检出率。CEUS的不足之处主要表现为慢性炎症导致的胆囊局限性增厚,易误诊为GBA;急性炎症导致的胆囊局限性增厚,易误诊为胆囊癌^[17]。

3.4 CT检查

CT对总体疾病的诊断率在61.75%~75%,但是对GBA的诊断率只有38%~43%^[18]。GBA在CT上典型的表现是囊壁增厚和壁内钙化。CT有助于鉴别胆囊底部的局灶型腺肌症和局灶性慢性胆囊炎^[18],借助多层螺旋CT有助于发现RAS,从而诊

断GBA^[19]。此外,根据不同的病理分型,GBA在CT上表现不同,弥漫型——胆囊壁增厚欠均匀,囊腔内面轮廓不整,壁内见多个RAS,部分与囊腔相通。局限型——胆囊底部呈帽状增厚,多向外凸出,囊腔内面较光整。节段型——胆囊壁节段性增厚,胆囊缩窄变形,远端囊腔内可伴有小结石。增强CT主要表现为胆囊壁节段性增厚,壁内多发小憩室样突出,胆囊腔呈节段性狭窄。如GBA发生在胆囊颈部,则胆囊呈葫芦状或哑铃状变形;如在胆囊底部则部分胆囊壁增厚,壁内有小憩室样突出,底部中心常可见脐样凹陷^[20]。过去认为与MRI相比,CT检查并不能很好地鉴别GBA和胆囊癌。最近Yang等^[21]研究显示:在局限型或弥漫型GBA与胆囊癌鉴别诊断方面,增强CT显示的“棉球征”比MRI显示的“珍珠项链征”有更高的敏感性和特异性。

3.5 MRI/MRCP 检查

由于近年来技术的发展以及它的高组织密度分辨率、多参数、多方位成像等优势,MRI/MRCP在诊断胆囊疾病方面越来越受到重视^[22]。在T2WI,STIR序列中,尤其是STIR序列,RAS表现为增厚的胆囊壁及壁内点状或小囊状高信号,此为典型的MRI表现。MRCP显示的增厚的胆囊壁内出现多个小圆形高信号称为“珍珠项链征”,是GBA的特征性表现,它能够精确定位RAS的位置。此外,MRI/MRCP能够很好地对胆囊壁厚度、胆囊壁是否光整、显示RAS窦、胆囊壁是否出现钙化现象、肝胆交界是否清晰以及浆膜层是否存在强化等影像学表现进行评价,上述影像学征象可作为鉴别诊断GBA与胆囊癌的重要参考指标^[23]。有研究^[24]显示:MRCP对的肿瘤的鉴别诊断帮助很大,灵敏度大于80%。此外,Tomizawa等^[25]证实:弥散加权成像有助于区分GBA和胆囊癌,并提高胆囊癌诊断率。

早期胆囊癌合并GBA时影像学诊断困难,临床医生应对此加以警惕^[26]。GBA与早期的壁厚型胆囊癌在影像学上具有相似性,两者之间的鉴别诊断是临床上的一个挑战^[27]。笔者认为:实际情况中,若一种影像学方法不能明确诊断GBA,则应联合几种影像学检查,尽量做到明确诊断,才能决定下一步治疗方案。

4 GBA 的治疗

关于GBA的治疗,国外学者^[28]最近提出以

下观点:1)对于胆囊切除术后病理中偶然发现的GBA,不需要后续治疗。2)疑似但全面的影像学检查还不能确诊GBA时,为排除胆囊癌,建议行胆囊切除术。若因GBA导致胆囊壁增厚,则无需后续治疗;若因胆囊癌,则应尽快行专科治疗。当怀疑胆囊癌时,不建议行腹腔镜手术。3)有症状的GBA,无论合并胆囊结石,都是胆囊切除术的指征^[29],因以往报道的病例均通过手术缓解了症状。然而,必须先排除其他病因引起的腹痛,GBA最好通过MRCP来确定诊断。在没有禁忌证的情况下,腹腔镜胆囊切除术应作为首选。病理结果确定为GBA后,无需后续治疗。4)对于无症状的局限型GBA,通过类比息肉>10 mm有癌变倾向,有学者^[30]建议胆囊病变>10 mm作为胆囊切除术的手术指征。然而并没有文献证明局限型GBA>10 mm有癌变倾向。因此,对于无症状的局限型GBA,不建议行胆囊切除术。无症状的局限型GBA合并结石也不建议行手术治疗,因为无症状的胆囊结石并不是手术指征。5)无症状的节段型或弥漫型GBA,可以手术,由于老年节段型GBA患者的癌变率较高,以及弥漫型GBA有时难以与胆囊癌相鉴别,因此弥漫型GBA和节段型GBA可以考虑手术治疗^[30];与胰胆管汇合异常相关的无症状的GBA,即使没有原发性胆管囊状扩张,也必须预防性行胆囊切除术,因为这是已知的胆囊癌的危险因素。该手术指征与GBA类型无关。7)儿童GBA。儿童GBA发病率极低,所有报道的病例均为有症状的儿童患者,在行胆囊切除术后,症状均完全消失。因此,对于这种罕见的有症状的GBA病例,提倡行腹腔镜胆囊切除术。

5 结语

随着影像学技术的发展,GBA的诊断率逐渐提高。但由于影像设备及技术等差异,漏诊、误诊的病例时有发生。目前,尚缺乏GBA与胆囊癌之间的分子生物学关联,但两者常同时存在,可能具有相同的促炎症领域^[28]。对于这种共存现象,临床医生应加以警惕。

随着对胆囊功能的进一步认识,胆囊除具有存储、浓缩、排出胆汁和调节胆道压力的作用,还具有复杂的化学、免疫、酸碱及肠道菌群的调节能力^[31]。胆囊切除术后会出现十二指肠液的胃反流及胃液食管反流、消化不良性腹泻等各种不良并发症。因此,对于GBA是否手术治疗,应该结合影像学诊断、临床表现决定治疗方案,严格

把握手术指征, 避免不要的手术切除。

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