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◇临床医学◇

肺纤毛黏液结节性乳头状肿瘤2例报告

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摘要: 目的 探讨2例肺纤毛黏液结节性乳头状肿瘤的诊治,提高对该疾病的认识,以减少误诊。**方法** 回顾性分析河北医科大学附属唐山市工人医院2017年11月收治的2例肺纤毛黏液结节性乳头状肿瘤的诊断治疗经过,参考相关文献,总结该类病人的临床特征和治疗经验。**结果** 本组2例病人均在完善术前检查及胸外、影像、麻醉科多学科讨论后,考虑肺部肿瘤可能,全麻下行胸腔镜肺叶楔形切除术。术后常规病理确诊为纤毛黏液结节性乳头状肿瘤。均术后恢复满意,随诊22个月无并发症及影像异常。**结论** 肺纤毛黏液结节性乳头状肿瘤是一种罕见的肺部肿瘤,早期无明显症状,手术效果良好。

关键词: 肺肿瘤; Ki-67抗原; 转录因子; 纤毛黏液结节性乳头状肿瘤; 黏液腺癌; 临床特征; 外科治疗

Ciliated muconodular papillary tumor of the pulmonary: report of two cases

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Abstract: Objective To investigate the diagnosis of ciliated muconodular papillary tumor of the pulmonary, and to improve the understanding of this disease, so as to reduce the rate of misdiagnosis. **Methods** The clinical data of 2 cases of ciliated muconodular papillary tumor of the pulmonary admitted to Tangshan Gongren Hospital Affiliated to Hebei Medical University in November 2017 were analyzed retrospectively, referencing to related literature and summing up the clinical features and treatment experience of these patients. **Results** After complete preoperative examination and multidisciplinary discussion in the departments of thoracic, radiography and anesthesiology, the possibility of lung tumor was considered in the 2 patients in this group, and thoracoscopic wedge resection was performed under general anesthesia. Routine pathology after surgery confirmed the diagnosis as ciliated mucinous nodular papil-

lary tumor. Both patients recovered satisfily after surgery, and there were no complications or imaging abnormalities after 22 months of follow-up. **Conclusion** Ciliated muconodular papillary tumor of the pulmonary is a rare lung tumor with no obvious early symptoms, and the result of the surgery is good.

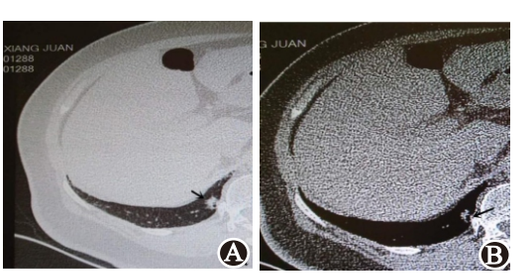
Key words: Lung neoplasms; Ki-67 antigen; Transcription factors; Ciliated muconodular papillary tumor; Mucinous adenocarcinoma; Clinical feature; Surgery

纤毛黏液结节性乳头状肿瘤(ciliated muconodular papillary tumors,CMPT)由 Ishikawa[1]于2002年首次报道,是位于外周的一种罕见的肺结节,以纤毛柱状细胞和杯状细胞为特征,目前尚未明确其临床表现。为提高临床工作者对该病的认识,本研究将河北医科大学附属唐山市工人医院收治的2例CMPT报告如下。

1 临床资料

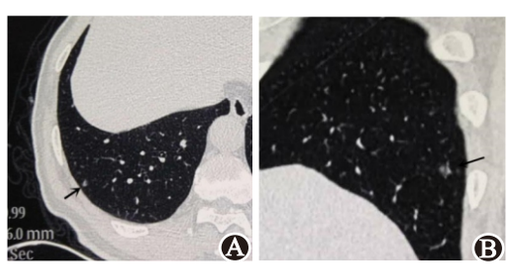
1.1 病例1 女,75岁,查体发现右肺下叶结节,于2017年11月3日入院。病人入院前15天常规体检行胸部CT检查提示右肺下叶结节,肿瘤性病变不除外。入院查体未见阳性体征。既往高血压病史30年,口服药物治疗,血压控制平稳,糖尿病病史10年,胰岛素控制血糖,效果好。无家族肿瘤遗传病史。全身骨扫描显示左侧骶髂关节骨代谢旺盛灶,建议结合局部CT或磁共振成像(MRI)影像资料定期复查;左侧膝关节骨代谢旺盛灶,考虑退行性变所致。胸部CT:右肺下叶后基底段软组织结节,直径约11.2 mm,考虑周围型腺癌可能(图1)。心电图、B超、头颅CT、超声心动图、肺功能、血常规、尿常规、肝功能、肾功能、肿瘤标志物未见明显异常。入院第7天顺利行右肺下叶楔形切除术。术中冰冻病理:右肺下叶涎腺腺瘤,考虑来源支气管腺体,待常规明确诊断。术后常规病理:右肺下叶CMPT,紧邻脏层胸膜,周围肺组织见多灶肺泡上皮不典型增生(AAH),直径0.1~0.2 cm;肺切缘净;送检淋巴结3枚,其中1枚淋巴结钙化明显,伴骨化。免疫组织化学检测:calponin(-),CK5/6(肌上皮+),细胞增殖抗原Ki-67(3%+),p63(肌上皮+),甲状腺转录因子(thyroid transcription factor-1,TTF-1)(+)(图2)。

1.2 病例2 男,68岁,查体发现右肺下叶结节,于2017年11月6日入院。病人入院前1周常规体检行胸部CT检查发现右肺下叶结节,直径约7.7 mm,肿瘤性病变不除外(图3)。入院体格检查未见阳性体征。既往高血压病史10年,口服药物治疗,血压控制平稳。无家族肿瘤遗传病史。全身骨扫描、心电图、B超、头颅CT、超声心动图、肺功能、血常规、尿常规、肝功能、肾功能、肿瘤标志物未见明显异常。入院第7天行右肺下叶楔形切除术,手术过程顺利。术中冰冻病理:考虑为腺癌,直径0.4 cm,待常规。术后病理:右肺下叶CMPT,直径约0.4 cm,肿瘤旁见原位腺癌,镜下最大径0.2 cm;肺切缘净;送检淋巴结10枚:(四组)0/5,(七组)0/5。免疫组织化学染色:Ki-67(5%+),平滑肌肌动蛋白(SMA)(-),TTF-1(+)。



注:箭头所示为病灶。

图1 病例1胸部CT所见肺部结节:A为肺窗;B为纵隔窗



注:箭头所示为病灶。

图3 病例2胸部CT所见肺部结节:A为肺窗;B为肺窗三维重建

2 结果

2例病人术后均恢复满意,随访22个月,均无明显不适。

3 讨论

Kamata等[2]对10例CMPT做了分子检测,发现8/10CMPT中存在高频鼠类肉瘤滤过性毒菌致癌同源体B1(BRAF)或成纤维生长因子受体(FGFR)基因突变,4例存在BRAF(V600E)突变、1例BRAF(G606R)突变及3例表皮生长因子受体(EGFR)的第19号外显子缺失突变,EGFR的缺失均为E7746-T51/S752V亚型。Liu等[3]报道了4例来自西方的肺CMPT病例,显示肿瘤有BRAF V600E和间变性淋巴瘤激酶基因(AKT)1 E17K突变,Jin等[4]及Taguchi等[5]各报道了1例肺CMPT病例,显示肿瘤有ALK基因重排。Kataoka等[6]报道4例CMPT中有三种突变分别为BRAF(V600E),EGFR(del E746-T751/S752V),以及EGFR(E709G)和鼠类肉瘤病毒癌基因(KRAS)(G12V)。这些基因改变支持CMPT是一种肿瘤性病变,而非反应性或化生性病变。

CMPT通常起病隐匿,临床表现无特异性,有报

道统计以往病例报告,病人一般无临床症状,多在健康体检时发现,仅3例因咳嗽、胸部不适或感冒症状就诊发现。本病好发于中老年人,也有报道发生于青年,多为日本人或其他东亚人群,这可能与种族易感性或基因差别有关[7-8]。

CMPT确诊需要病理学检查。有报道分析了10例CMPT的临床病理特征[9]。病变由纤毛柱状细胞、黏液细胞及基底细胞组成,5例以腺样结构为主,5例以乳头样结构为主,肺泡弹性框架结构缺失或破坏,3种细胞成分所占比例在不同病例各有不同,肿瘤细胞无异型,未见核分裂象及坏死。3种细胞均弱表达TTF-1,而不表达HNF-4α,基底细胞p40强阳性表达,纤毛细胞局灶表达MUC5AC,黏液细胞不表达MUC5AC,最近一篇报道指出在一些肿瘤中黏液细胞表达MUC5AC和MUC6。CMPT的特征性标志物是CEA,TTF-1和CK7,而CK20是阴性的[10]。本研究中2例病人均为中老年病人,无特异性症状,体检时发现,不能排除恶性,怀疑为肺部肿瘤,术后经病理学检查确诊为CMPT。此外,CMPT还需与黏液腺癌、胶样腺癌、黏液表皮样癌、细支气管鳞状上皮化生、乳头状瘤相鉴别[7,11-12]。CMPT罕见,且与其他肿瘤病理形态改变有相似之处,易病理误诊,尤其是术中快速冰冻诊断时。本研究报道2例病人,术中冰冻分别为涎腺腺瘤和腺癌,但最终常规病理回报为CMPT。本病的诊断需要依据病理形态、免疫组化等进行正确诊断。

CMPT被认为是一种良性病变,目前治疗以手术为主,术后随访2~120个月(平均42个月)。所有病变均未见局灶复发或远处转移[12-14]。组织学上纤毛细胞的出现,缺乏坏死和核分裂象,一致的基底细胞增生均提示良性。但也有一些与低度恶性肿瘤相关的组织学特征,如肿瘤无包膜,破坏肺泡正常结构,存在跳跃式病灶,有微乳头结构,形成黏液湖,间质纤维组织增生,提示其可能具有恶性潜能。

有研究认为CMPT可能是黏液腺癌的癌前病变[15]。目前国内外报道CMPT病例,除1例病人伴发黏液腺癌[16],其余均诊断为CMPT。本研究中2例病人术后常规病理分别伴有不典型腺瘤样增生和原位腺癌,这可能与CMPT的恶性潜能有关,因此进一步提高对CMPT的认识有比较重要的意义。本病较罕见,同种病例的积累仍然十分必要。

(本文图2见插图3-6)

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