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囊性为主成分的甲状腺鳞状细胞癌1例误诊分析

颜炜[1],叶晖[1],陈雲[2]
作者单位:[1]贵州医科大学附属医院甲状腺外科,贵州 贵阳550001;
[2]贵州康养职业大学,贵州 贵阳550081

摘要 目的 探讨囊性为主成分的甲状腺鳞状细胞癌(SCCT)误诊原因。**方法** 分析1例囊性为主成分的SCCT误诊过程,并对其结局随访,结合相关文献进行讨论。**结果** 男,67岁,发现甲状腺结节3年,颈部彩超发现甲状腺右叶囊实性包块,大小63 mm×49 mm×82 mm,因肿瘤较大且压迫气管,行右侧甲状腺腺叶切除术,术后病理报告为结节性甲状腺肿,伴囊性变及腺瘤样结构形成;遂按结节性甲状腺肿出院。术后1个月,病人颈部出现新生物,进行多项检查及多学科会诊后,取颈部新生物做病理活检,结果为原发性SCCT;第一次手术的诊断出现误诊;病人拒绝放疗并出院,随访结局为死亡,复发后生存期为2.5个月。**结论** 原发性甲状腺鳞状细胞癌(PSCCT)是一种极具侵袭性的肿瘤,预后较差,以囊性结节为首发病例的更少见,容易误诊,需结合病史、临床检查及免疫组化等诊断。
关键词 甲状腺肿瘤; 鳞状细胞癌; 原发性; 继发性; 诊断,免疫组化

Analysis of a case of misdiagnosis of cystic thyroid squamous cell carcinoma

YAN Wei[1],YE Hui[1],CHEN Yun[2]
Author Affiliations:[1]Department of Thyroid Surgery,Affiliated Hospital of Guizhou Medical University,Guiyang,Guizhou 550001,*China;[2]Guizhou Kangyang Vocational University,Guiyang,Guizhou* 550081,*China*

Abstract Objective To explore the outcome of the squamous cell carcinoma of the thyroid (SCCT) with cystic component. **Methods** The misdiagnosis process of a case of SCCT with cystic component was summarized and analyzed, and the outcome was followed up, and the relevant literature was discussed. **Results** A 67-year-old male patient complained of thyroid nodules 3 years ago. Color doppler ultrasound of the neck found a cystic solid mass in the right lobe of the thyroid gland, about 63 mm×49 mm×82 mm. Due to the large tumor and compression of the trachea, the patient underwent right thyroidectomy. The pathological results reported nodular goiter in the right lobe with cystic changes and adenomatous structure formation. The patient was discharged with nodular goiter. One month after surgery, the patient's neck neoplasm was found. After multiple examinations and multidisciplinary consultation, the neck neoplasm was taken for pathological biopsy, and the results showed that the neck neoplasm was primary thyroid squamous cell carcinoma. The patient's first surgery was misdiagnosed. The patient refused radiotherapy for personal reasons and was discharged. The patient was followed up and the outcome was death. The survival time after recurrence was 2.5 months. **Conclusions** Primary squamous cell carcinoma of the thyroid (PSCCT) is an aggressive tumor with poor prognosis, and cystic nodules as the first case is more rare and easy to be misdiagnosed. The diagnosis should be combined with medical history, clinical examination and immunohistochemistry.
Keywords Thyroid neoplasms; Squamous cell carcinoma; Primary; Secondary; Diagnosis, immunohistochemistry

甲状腺鳞状细胞癌(squamous cell carcinoma of the thyroid,SCCT)是一种罕见的甲状腺肿瘤,被认为是一种极具侵袭性的肿瘤,预后较差。报道1例囊性为主成分的SCCT误诊的过程,并随访其结局,总结误诊原因及经验。

1 资料与方法

1.1 一般资料 男,67岁,3年前发现甲状腺右叶结节,未予治疗;后于贵州医科大学附属医院复查,颈部彩超发现甲状腺右叶囊实性包块,大小约63 mm×49 mm×82 mm,包膜完整,边界清晰,形态欠规则,囊性部分透声差,可见颈部多枚淋巴结,门结构清晰,未见明显异常淋巴结(图1,2);喉镜检查未见异常,双侧声带运动良好;胸部正侧位片显示心、肺、隔未见异常(图3);颈部二期增强CT显示甲状腺右叶囊实性肿块,肿块压迫气管,气管左偏(图4);电解质、甲状旁腺激素(PTH)未见异常。建议病人手术。

1.2 治疗经过 病人接受手术,术中肉眼见囊实性

包块占据整个甲状腺右叶,包块呈暗红色,大小约7 cm×6 cm,囊壁厚0.2~1.2 cm,囊壁布满乳头。进行了右侧甲状腺腺叶切除术,在切除前,使用注射器抽出50 mL咖啡色黏稠液体,其中有部分液体渗出术区,但肿块包膜无破溃,肿块及右叶甲状腺腺叶完整切除,缝合前使用无菌蒸馏水及生理盐水对术区进行冲洗。术中冰冻病理回报甲状腺右侧腺叶及囊实性包块考虑结节性甲状腺肿,伴囊性变及腺瘤样结构。术后的常规病理及免疫组化检查见结节性甲状腺肿改变,伴囊性变及腺瘤样结构形成,部分区域细胞生长活跃,免疫组化CK(+),CK19(+),HBME-1(少数+),CD56(部分+),TPO(+),Calretinin(-),Calectin-3(部分+),Ki-67(约3%+),结合HE形态及免疫组化结果,认为甲状腺右侧腺叶及囊实性包块考虑为结节性甲状腺肿改变,伴囊性变及腺瘤样结构形成;病人遂按结节性甲状腺肿出院。术后1个月,病人因颈部切口处肿物就诊,视诊见病人颈部切口瘢痕处左侧皮肤见一个约2 cm×2 cm×2 cm包块,表面有破溃,质地硬,无压痛,渗出少量血性液体,颈部切口瘢痕处右侧皮肤见一个约1 cm×1 cm×1 cm包块,无破溃,质地硬,无压痛(图5)。考虑病人原因不明的颈部新生物,也不排除病人切口感染可能性,为查明原因,病人再次入院,查白细胞19.84×10^9/L,中性粒细胞0.84,但体温、脉搏正常;取分泌物培养后,感染科会诊考虑为组织坏死,颈部和胸部CT平扫发现病人颈部的新生物与原甲状腺右叶术区相连续,为一个实性的肿物(图6);肺部新发多发结节,考虑为转移瘤(图7)。颈部新生物活检病理(图8)及免疫组化(图9):镜下见大量异型细胞,CK(+),Vim(-),P40(+),P63(+),TTF-1(-),TG(-),TPO(-),HBME-1(-),Calectin-3(-),Calretinin(-),CD56(-),CD68(-),CD34(-),CD31(-),HMB45(-),S100(-),sox10(-),Melan-A(-),P53(突变型+),Ki-67(约40%+),结合HE形态及免疫组化结果(图4,5),考虑颈部新生物为鳞状细胞癌,病人首次手术的诊断存在误诊。肺部多发结节,考虑为其他部位转移至肺部,不考虑原发性的肺部鳞癌。结合病人病史,考虑病人为原发性的SCCT。

2 结果

确诊病人为原发性的SCCT后,建议病人进行放疗,但病人及家属因为经济及个人的原因拒绝治疗,随访病人,病人在出院后2.5个月死亡。

3 讨论

3.1 SCCT的概述 SCCT是一种罕见的甲状腺肿瘤,在2017年发布的WHO内分泌肿瘤分类中,SCCT是甲状腺癌的一个独立分类[1]。SCCT可由原发性或继发性肿瘤引起,原发性甲状腺鳞状细胞癌(primary squamous cell carcinoma of the thyroid,PSCCT)占甲状腺恶性肿瘤的0.3%[2],而继发性甲状腺鳞状细胞癌(secondary squamous cell carcinoma of the thyroid,SSCCT)的发病率高出PSCCT 10倍,常由呼吸消化道产生的鳞状细胞癌(squamous cell carcinoma,SCC)引起[3]。PSCCT被认为是一种极具侵袭性的肿瘤,预后较差,生存期通常短于1年[4]。值得注意的是,PSCCT被定义为仅具有鳞状分化的癌,也有报道其可能是由甲状腺乳头状癌转变而来[5];但甲状腺乳头状癌合并鳞状细胞癌是甲状腺乳头状癌的一种变体,这种甲状腺乳头状癌的预后与一般的乳头状癌相比预后更差,而具有鳞状分化的未分化癌被称为甲状腺未分化癌[1,6]。PSCCT发病常见于老年女性,在临床表现上,PSCCT类似于未分化或者间变性的甲状腺癌的临床表现,主要表现为快速生长的颈部前方肿物,累及一侧或双侧甲状腺,产生压迫症状,包括呼吸困难,吞咽困难等[7]。

3.2 误诊原因分析及经验 本例诊断存在误诊,原因主要有:(1)首次手术后的免疫组化标志的多肽或蛋白过少,没有PSCCT免疫组化检测相关标志物如P63、P40、Pax8、TG、TTF-1、P53等,在术后1个月的活检病理中,才加入了这些免疫组化标志,帮助了我们确诊PSCCT。其中P63阳性和P40阳性是鳞状细胞分化的敏感标志,也是PSCCT免疫组化辅助诊断最主要的标志物。而P40在识别PSCCT方面比P63更具特异性[8]。Pax8也是PSCCT的重要生物标志物,PSCCT常表现为Pax8阳性,而SSCCT多数表现为Pax8阴性,可用Pax8鉴别甲状腺鳞癌是否为原发性鳞癌[9-10]。此外PSCCT还常有CK5/6阳性和P53的过表达,但部分PSCCT也会有阴性或不表达;而CEA、降钙素、CD5、TG和TTF-1也常为阴性[11-13],但少部分PSCCT也为阳性[14]。总而言之,对于甲状腺鳞癌的诊断,应加入P63、P40、Pax8、TG、TTF-1、P53、CEA、降钙素等免疫组化标志检测去辅助诊断。(2)PSCCT病人其发病率低且缺乏典型的影像学表现,早期难以诊断[15],多数PSCCT常表现为孤立的、明显的实性低回声甲状腺肿块,边缘不规则,与正常甲状腺的边界不清晰[16],文献报道PSCCT呈囊性低回声肿块边缘光滑的病例中,只发现1例[17]。而本例病人,就是以囊性为主成分的结节,难以让人将囊性包块联想到PSCCT。

本例病人在确诊后拒绝进行治疗,最终生存期只有2.5个月,已报道的文献里,PSCCT病人大多数生存时间都在1年以内,预后极差[3-4,14,18-19]。文献报

道根治性手术切除是治疗PSCCT的理想方法，然而，由于局部进展，完全切除的病例很少[20]。

本例中，病人肿瘤侵袭性很强，存在误诊，且拒绝治疗，没有完整手术切除及术后放疗治疗，这是病人生存期只有2.5个月的主要原因。其次，病人第一次手术时为了减少肿瘤囊性成分，便于切除，使用注射器抽出部分囊液，有部分囊液渗出进入术区，虽然缝合颈部切口前对术区进行了冲洗，但也有可能因此造成了术区肿瘤的扩散，因此对于怀疑囊性成分为主的甲状腺恶性肿瘤，应该避免这样的操作。

综上所述，PSCCT是一种极具侵袭性的肿瘤，预后较差，以囊性结节为首发病例的更少见。本例的误诊是给予我们一个教训。当我们遇到快速生长的囊性甲状腺结节时，我们对其的诊断需要小心谨慎，需结合病史、临床检查去诊断，如果细胞学形态鉴别存在困难，建议加做不同亚型甲状腺癌敏感标志物的免疫组化标志，对于甲状腺鳞癌的诊断，应加入P63、P40、Pax8、TG、TTF-1、P53、CEA、降钙素等免疫组化标志检测去辅助诊断；其次，囊性成分为主的甲状腺恶性肿瘤手术时，应该时刻注意手术术中无瘤的操作原则。

（本文图1~9见封三）

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