[DOI]10.12016/j.issn.2096-1456.2019.12.007

·防治实践·

下颌骨外周原始神经外胚层瘤病例报道及文献复习

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【摘要】　目的　探讨下颌骨外周原始神经外胚层瘤(peripheral primitive neuroectodermal tumor, pPNET)的临床、影像学及病理特征，并进行相关文献复习提高对下颌骨pPNET的认识和诊治水平。**方法**　对新疆医科大学第一附属医院诊治的1例下颌骨pPNET患者的临床及影像学特点、病理检查、治疗和预后进行观察，结合文献复习进行分析。**结果**　该患者临床表现为下颌骨渐大性肿物，质地偏硬，边界不清，累及牙松动，伴下唇麻木；CT、MRI均表现为溶骨性及侵袭性的生长方式手术行下颌骨肿物切除及下颌骨部分截断性切除钛板重建术，术后病理切片HE染色镜下表现为小圆细胞肿瘤，免疫组化显示Vimentin及Fli-1表达为阳性，病理诊断为外周原始神经外胚层瘤。患者术后未行放化疗，随访9月后因肿瘤复发死亡。经相关文献复习，pPNET是一组罕见的高度恶性的小圆细胞肿瘤，多发生于儿童和青少年，恶性程度很高，病程短、转移快，主要的转移途径为血性转移，绝大多数患者在2年内死亡，3年生存率仅30%，5年生存率不超过10%。影像学上一般无特异性，故容易被误诊，最终的肿瘤类型依靠病理诊断。目前的治疗方法以手术完整切除为主，结合术后放化疗，但必要时，对于不同的患者给予个体化治疗很关键。**结论**　pPNET恶性程度高、易复发转移、预后差，早期确诊及治疗极为重要。

【关键词】　外周原始神经外胚层肿瘤；　Ewing′s肉瘤；　下颌骨；　溶骨性破坏；　小圆细胞肿瘤；　Vimentin蛋白；　Fli-1蛋白；　手术切除；　肿瘤复发；　预后
【中图分类号】　R78；R739.8　**【文献标志码】**　A　**【文章编号】**　2096-1456(2019)12-0784-04　开放科学(资源服务)标识码(OSID)
【引用著录格式】　卜海力齐古丽·麦麦提图尔荪，帕提姑丽·吾斯曼，阿地力·莫明.下颌骨外周原始神经外胚层瘤病例报道及文献复习[J]. 口腔疾病防治, 2019, 27(12): 784-787.

Peripheral primitive neuroectodermal tumor of the mandible: a case report and literature review

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【Abstract】　Objective　To explore the clinical, imaging and pathological characteristics of mandibular peripheral primitive neuroectodermal tumors, and to review relevant literature to improve the understanding and diagnosis of pPNET in mandible. **Methods**　The clinical and imaging features, pathological examination, treatment and prognosis of a case of mandibular pPNET diagnosed and treated at the First Affiliated Hospital of Xinjiang Medical University were observed, and analyzed a literature review. **Results**　The patient′s clinical manifestations were an enlarged mass of the mandible, hard texture, unclear borders, involving loose teeth, and numbness of the lower lip; CT and MRI showed osteolytic and aggressive growth patterns. The mandibular tumor was resected and the mandibular partial truncated resection was performed on the titanium plate. Postoperative pathological sections showed small round cell tumors under HE staining and Vimentin and Fli-1 were positive, and the pathological diagnosis was pPNET. The patient did not undergo chemoradiotherapy after surgery and died of tumor recurrence after 9 months of follow-up. A review of the relevant literature revealed that pPNETs are a group of small round cell tumors, which are more common in children and adolescents. pPNETs have a high degree of malignancy, a short course of disease and fast metastasis. The main route of metastasis is through the blood circulation. Most patients die within 2 years, the 3-year survival rate is only 30%, and the 5-year survival rate is less than 10%. Imaging is generally nonspecific; therefore, pPNETs are easily mis-

【收稿日期】2019-01-03；　【修回日期】2019-06-05
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diagnosed. The final tumor type is determined by pathological HE staining and immunohistochemical characteristics. Current treatment methods are mainly complete surgical resection combined with postoperative radiotherapy and chemotherapy, but it is critical to provide individualized treatment to patients when necessary. **Conclusion**　pPNETs have a high degree of malignancy, easy recurrence and poor prognosis, so early diagnosis and treatment are extremely important.
【Key words】 peripheral primitive neuroectodermal tumor; Ewing's sarcoma; mandible; osteolytic destruction; small round cell tumor; Vimentin protein; Fli-1 protein diagnosis; surgical resection; tumor recurrence; prognosis
J Prev Treat Stomatol Dis, 2019, 27(12): 784-787.

外周原始神经外胚层瘤（peripheral primitive neuroectodermal tumor，pPNET），又称为尤文氏肉瘤（Ewing's肉瘤），是发生于软组织和骨组织的小圆细胞恶性肿瘤。该病可发生于各个年龄段，但多发生于儿童和青少年，主要发生于四肢长骨、脊旁区、胸壁、盆腔体和肾脏等脏器，具有侵袭性强、恶性程度高，易发生转移等特点[1-3]，常可转移至其他部位骨骼和肺、肝、脑等脏器[4-5]，故预后很差。国内外很少有报道关于下颌骨的pPNET。本文报道1例下颌骨的pPNET的临床、影像学及病理特征，并进行相关文献复习。

1　病例资料

1.1　一般资料

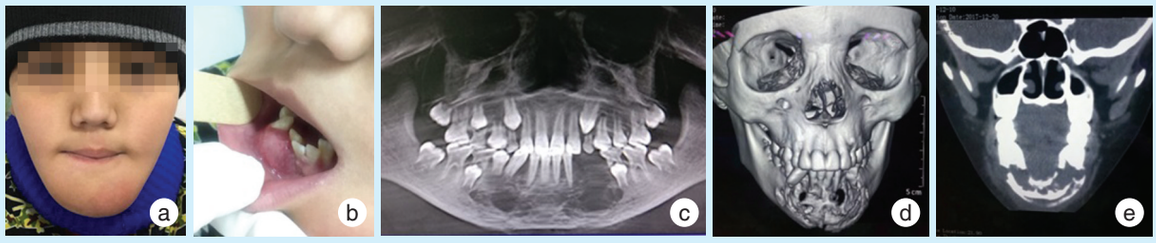
患者，男，10岁，因左侧下颌骨一渐大性肿物就诊于当地医院，诊断为"左侧下颌骨成釉细胞瘤"，并行手术治疗。术后10 d发现右侧下颌骨一肿物，偶有瘙痒感，患儿自述颏部麻木不适，无局部皮肤及黏膜溃烂出血，遂1月后转诊新疆医科大学第一附属医院。

1.2　临床检查

颏部可触及大小约4 cm × 3 cm的肿物，质地偏硬，活动度差，边界不清，无明显压痛，局部皮肤无红肿、糜烂、破溃；口内：42～45颊侧前庭沟局部隆起，可触及4 cm × 3 cm大小肿物，质地硬，边界不清，无活动，43倾斜至舌侧，局部黏膜发红，无糜烂出血，无波动感，无明显异常渗出物，对侧前庭沟可触及相似病损，32～42颊侧前庭沟处及33～35牙槽嵴处可见线性瘢痕，无明显异常渗出，下颌前牙松动（图1a～b）。

1.3　辅助检查及诊断

曲面断层片及CBCT结果提示：下颌骨前牙区颌骨内多发囊状骨质破坏区合并软组织密度肿块（图1c～e）。胸部X线片、血常规及血生化未见明显异常，身体其余骨骼未见异常，考虑多房型成釉细胞瘤。



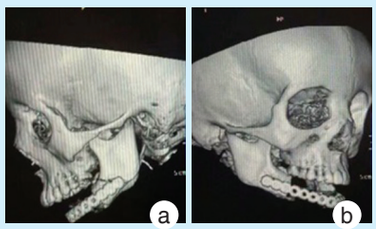
a：颏部肿物隆起；b：右侧前牙区隆形团块，表面牙齿松动及歪斜；c：曲面断层片显示颏部可见多囊性溶骨性病变，下颌支未见病损波及；d：下颌骨三位重建片，下颌骨颏部不规则的溶骨性破坏；e：下颌骨CT冠状面，下颌骨前牙区颌骨内可见多发大小不等的囊状骨质破坏区，局部颌骨内外侧骨皮质不连续，合并软组织肿胀及软组织密度肿块

图1　患者下颌骨肿物

Figure 1　Patient's mandibular mass

2　结　果

本院给予患者"双侧下颌骨巨大肿物切除术"，双侧下颌骨病变刮除并拔出病变区患牙，术中送快速冰冻检查。检查结果提示：恶性肿瘤，肿瘤已累及切缘，故行肿瘤摘除术及双侧下颌骨部分截断性切除术，用2.4系列重建板塑形颏部外形（图2）。术后常规病理检查结果提示：外周原始神经外胚层瘤（pPNET）（图3）。免疫组织化学染色



a:左侧;b:右侧

图2　术后下颌骨前部缺损钛板重建

Figure 2　Postoperative reconstruction of anterior mandible defect with titanium plate

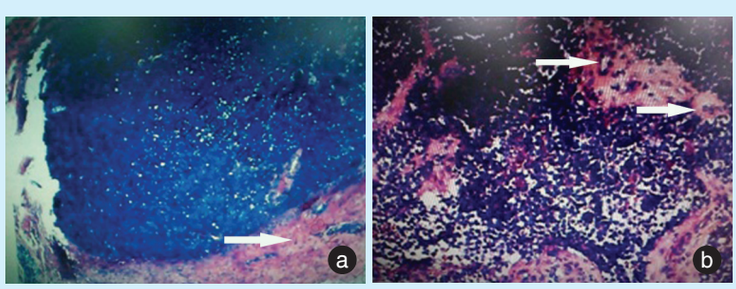
示:Vimentin及Fli-1阳性,CD99、CK、Des、MyoD1、Myogenin、Syn、CgA、STAT6、EMA、CD3、CD20、Ki-67(+60%)、S-100、CD56呈阴性。

术后患者家属因经济及个人原因拒绝放化疗,并要求出院。术后3个月复查,肿瘤复发,上界至左侧下眼睑,下界至颈部(图4),因拒绝就诊未给予任何治疗。术后9个月后患者死亡。

3　讨　论

3.1　病因

近年来研究表明,骨组织尤文氏肉瘤和外周



HE染色,a:弥漫性的核浓染的小圆细胞(箭头所示);b:Homer-Wright菊形团及核浓染的小圆细胞(箭头所示)

图3　术后病理检查

Figure 3　Microscopic observation of postoperative pathology

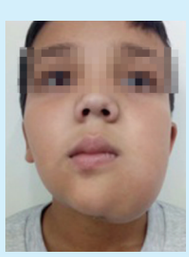


图4　患者术后3个月肿瘤复发

Figure 4　Tumor recurred after surgery 3 months

性原始神经外胚层肿瘤都属于同一谱系的肿瘤家族,外周性PNET与骨组织尤文氏肉瘤有许多相似之处,两者都具有相同的同源染色体的移位,故将其称为骨外尤文氏肉瘤[6]。细胞遗传学研究发现:Ewing's肉瘤具有11号和22号染色体的相互易位t(11、22)或21号和22号染色体相互易位t(21、22),导致EWS基因与FLI-1基因或ERG基因重排形成EWS-FLI1融合基因而发病[7-8]。

3.2　诊断

pPNET很少原发于颌骨,如有颌骨发现此肿瘤,大部分都来自于其他部位骨骼肿瘤的远处转移[9]。在下颌骨中,下颌支是主要的发生部位,只有几个病例报道下颌体及颏部的pPNET[10]。发生于颌面部的pPNET生长迅速,根据发病部位不同可出现局部疼痛、麻木、张口受限、累及牙齿松动等症状[11]。颌骨pPNET的影像学表现与颌骨骨髓炎、成釉细胞瘤及颌骨囊肿有些相似,影像学上,可见不规则的溶骨性破坏且边缘模糊,可有皮质破坏或扩张。因pPNET的临床表现及影像学检查缺乏特异性,故早期均难以鉴别及确诊,需要组织病理学及免疫组织化学才能确诊。在病理学检查上,镜下pPNET由形态单一、幼稚的小细胞组成,瘤细胞是圆形或椭圆形、核轮廓清晰但细胞边缘模糊、核浓染,细胞间质少,易见核分裂现象,常可见到Homer-Wright菊形团[12]。在免疫组化上,通常用Zhang等[13]标准诊断pPNET,即免疫组化染色有2种或2种以上神经标记物表达阳性。Ewing肉瘤免疫组化恒定表达的往往是CD99和FLI-1,而且CD99的阳性率比其他神经标志物高[12-13],但是此病例跟其他病例不同的是CD99呈阴性,故属特例。值得一提的是,通过FISH方法检测PNET特异性的染色体移位而形成的融合基因,敏感性为92.3%、特异度为100%[14],故EWS/FLI-1融合基因及其特异性染色体移位是诊断的依据。为明确诊断,需将临床、影像学、病理3者综合分析[15]。

3.3　鉴别诊断

pPNET需要跟颌面部小细胞恶性肿瘤相鉴别，鉴别诊断：①小细胞骨肉瘤：CD99呈阴性，血清AKP升高，而pPNET血清AKP无明显变化，CD99呈阳性；②神经母细胞瘤：两者都来源于神经上皮，所以容易混淆，神经母细胞瘤患者的年龄比pPNET更早，一般发生在2岁以下儿童，但不表达CD99和Vimentin，此病例中Vimentin呈阳性；③横纹肌肉瘤：其也有幼稚的小圆细胞，但是表达Des、MyoD1、Myogenin阳性，所以排除了横纹肌肉瘤；④母细胞性淋巴瘤：患者年龄较大，且肿瘤细胞表达TdT，CK呈阳性；⑤小细胞恶性黑色素瘤：肿瘤细胞表达HMB45、Melan-A等黑素色细胞标记。大多数情况下，HE染色及免疫组化可以对pPNET作出明确诊断。

3.4　治疗及预后

pPNET恶性程度很高，病程短、转移快，主要的转移途径为血性转移，据文献报道，绝大多数患者在2年内死亡，3年生存率仅30%，5年生存率不超过10%[2-3,8]。随着医学的发展，局限性尤文氏肉瘤治疗后5年生存率逐渐提高。pPNET的治疗虽然有了很多新的进展，但尚无统一的治疗方案，目前主张手术完整切除联合放、化疗的综合性治疗方案，手术完整切除是最重要的预后因素[8]。目前临床上常用的化疗方案为CAV（环磷酰胺、阿霉素、长春新碱）与IE（依托泊苷、异环磷酰胺）交替使用，至少12周期[16]。放疗也是一种治疗手段，有些患者对化疗不耐受，此时给予患者手术治疗+放疗，pPNET患者为了改善预后要接受手术治疗辅助化疗或放疗，但不能将化疗及放疗联合，联合治疗会增加并发症出现的风险[17]。发生于口腔颌面部的肿瘤常影响患者的语言及咀嚼功能，而且直接影响到患者的美观，对患者的心理生理产生较大的影响，下颌骨外周原始神经外胚层瘤作为高度恶性肿瘤，对患者的正常功能、美观、健康影响大，预后更差，故为了提高患者生存率及生命质量，早期确诊及治疗极为重要。

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(编辑　罗燕鸿，曾曙光)