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左下肢非典型脂肪瘤样肿瘤1例报告及文献复习

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[摘 要] 非典型脂肪瘤样肿瘤（ALT）是一种起源于脂肪细胞组织且少见的软组织肉瘤。现报道1例下肢ALT患者的临床表现、影像学资料及病理检查资料，为该疾病的临床诊治提供参考。患者，男性，64岁，因左大腿肿物伴胀痛5年入院。查体于左大腿内侧触及皮下肿物，质软，活动性良好，压痛阳性。磁共振成像（MRI）平扫检查结果显示肿物边界清楚，包膜完整；T1WI图像呈高信号，其信号强度似皮下脂肪信号；T2加权成像（T2WI）-Ideal序列同相位图像呈高信号，水像显示肿块大部分呈低信号，其内可见多发高信号；T2WI脂肪抑制序列可见低信号肿块，内有多发斑片状高信号。患者入院3 d后行病损切除术。术中见肿物位于筋膜内、股四头内侧肌肉间，呈脂肪样，有完整包膜，与周围组织局部粘连较轻，肌肉部分有侵蚀，完整切除肿物及侵蚀肌肉。术后病理检查见灰黄色结节1枚，体积为16.0 cm×10.0 cm×4.0 cm，表面光滑，包膜完整，实质呈灰黄色，脂肪样，质软；另见灰黄色组织数块，总体积为5.0 cm×4.0 cm×1.2 cm，实质呈灰褐色，质地中等。显微镜下见病变组织主要由相对成熟的脂肪组织构成，可见细胞核增大、浓染，散在分布单核或多核的不典型间质细胞，纤维分隔区内存在数量不等的单泡状或多泡状脂肪母细胞。免疫组织化学染色显示细胞周期蛋白依赖性激酶4（CDK4）和鼠双微体2（MDM2）阳性，荧光原位杂交（FISH）基因检测显示肿瘤细胞内MDM2基因扩增。病理诊断为左下肢ALT。术后6个月随访，未见肿瘤复发。术前MRI检查可为ALT诊断提供有效依据，术后病理学检查可验证ALT诊断，有助于判定患者预后。

[关键词] 下肢；非典型脂肪瘤样肿瘤；脂肪细胞；预后；鼠双微体2

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Atypical lipomatous tumor of left lower limb: A case report and literature review

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ABSTRACT　Atypical lipomatous tumor (ALT) is a rare soft tissue sarcoma originating from adipocytic tissue. The clinical manifestations, imaging findings, and pathological examinations of one patient with ALT in the lower extremity were reported to provide reference for the clinical diagnosis and treatment of this disease. The patient was a 64-year-old male who was admitted due to a mass in the left thigh with swelling and pain for 5 years. The physical examination results showed a subcutaneous mass was palpable on the medial side of the left thigh, soft in texture, demonstrating good mobility and positive tenderness. The magnetic resonance imaging (MRI) non-contrast scan showed a well-defined lesion with an intact capsule. The lesion presented high signal intensity on T1-weighted image(T1WI), similar to subcutaneous fat signal; on T2-weighted image (T2WI)-Ideal in-phase images, the lesion showed high signal, while water images showed low signal, with multiple high-signal foci inside. On T2WI fat-suppression sequence, a low-signal mass was observed with multiple patchy high signals inside. Three days after admission, the patient underwent lesion resection. Intraoperatively, the tumor was located within the fascia, between the medial quadriceps muscles, presenting as lipomatous tissue with an intact capsule, mildly adherent to surrounding tissue, and with partial muscle invasion. The mass and invaded muscle were completely excised. The postoperative pathological examination results revealed a gray-yellow nodule measuring 16.0 cm×10.0 cm×4.0 cm, with a smooth surface and intact capsule. The cut surface was gray-yellow, fatty-like, and soft in texture. Additional gray-yellow tissue fragments were found, with a total volume of 5.0 cm×4.0 cm×1.2 cm, exhibiting a gray-brown cut surface with moderate texture. Under microscope, the lesion consisted mainly of relatively mature adipose tissue. Enlarged and hyperchromatic nuclei were observed, with scattered mononuclear or multinuclear atypical stromal cells. Fibrous septa contained variable numbers of univacuolated or multivacuolated lipoblasts. The immunohistochemistry results showed positivity for cyclin-dependent kinase 4 (CDK4) and murine double minute 2(MDM2). The fluorescence *in situ* hybridization (FISH) results demonstrated MDM2 gene amplification in tumor cells. The pathological diagnosis was ALT of the left lower extremity. At 6-month follow-up after operation, no tumor recurrence was observed. The preoperative MRI detection may provide effective evidence for the diagnosis of ALT, while postoperative pathological examination can confirm the diagnosis and help evaluate the prognosis of the patients.

KEYWORDS　Lower limb; Atypical lipomatous tumor; Adipocyte; Prognosis; Murine double minute 2

非典型脂肪瘤样肿瘤（atypical lipomatous tumor，ALT）是由脂肪细胞组织引起的软组织肉瘤[1]，当其发生于非肢体部位（如腹膜后、纵隔等）时被称为高分化脂肪肉瘤（well-differentiated liposarcoma，WDLPS）。位于四肢的ALT是一种少见的低级别软组织肿瘤，占全部软组织肉瘤的15%[2-4]。目前，关于下肢ALT的文献报道较少[5-6]。本文作者报道1例下肢ALT患者，结合其临床、影像和病理资料进行文献复习，为该病的诊疗提供临床依据。

1　临床资料

1.1　一般资料　患者，男性，64岁，因左大腿肿物伴胀痛5年，于2024年8月26日就诊于内蒙古自治区呼伦贝尔市人民医院，门诊以“左下肢脂肪瘤”收入骨科。患者自述于5年前出现左大腿近端内侧皮下肿物，体积逐年增大，一直未予特殊处理，近期胀痛加重伴左侧髋关节疼痛。既往史：入院1年前因下肢静脉曲张，形成左下肢静脉血栓，经溶栓后血栓伴部分再通。否认外伤史。患者入院后填写了医疗知情同意书。

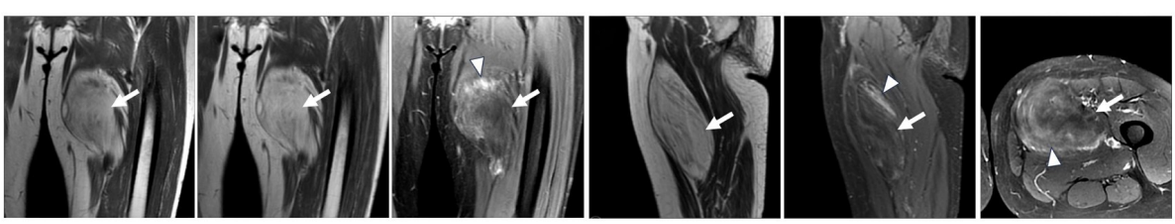
1.2　专科检查　生命体征平稳。左大腿内侧可触及1个皮下肿物，大小约为10.0 cm×15.0 cm×10.0 cm、质软，局部隆起于皮肤表面，活动性良好，有压痛，未见皮肤破溃；左下肢静脉曲张，肢体深浅感觉正常，四肢肌力正常，足趾活动良好，趾末梢血运良好。

1.3　辅助检查　彩色多普勒超声检查显示：左大腿肌间肿物，边界尚清，肿物内回声大致均匀，提示为脂肪瘤。采用3.0 T磁共振成像系统（美国GE SIGNA Pioneer MRI，美国通用电器公司）行MRI平扫图像检查。图像显示：左大腿内侧见1个

梭形肿块，边界清楚，包膜完整。冠状位T1加权成像（T1-weighted imaging，T1WI）图像显示：肿块呈高信号（图1A），其内大部分信号同皮下脂肪信号。冠状位和矢状位T2加权成像（T2-weighted imaging，T2WI）-Ideal序列inphase像示肿块呈高信号，水像示肿块大部分呈低信号（图1B～1E），其内可见多发高信号；横断位T2WI脂肪抑制序列示低信号肿块（图1F），内有多发斑片状高信号，提示诊断为脂肪肉瘤。结合临床表现、查体及辅助检查，入院诊断：左下肢脂肪肉瘤、左下肢静脉曲张。

1.4 治 疗 患者入院后3 d行左下肢肌肉病损切除术。取左大腿近端肿物外侧切口入路，长约13.0 cm，逐层切开。于筋膜下、股四头内侧肌肉间可见脂肪样肿物，包膜完整，呈类椭圆形，大小约为15 cm×10 cm×10 cm，质韧，呈实性结节感，与周围组织局部轻度黏连，肌肉有部分侵蚀。手术将肿物和侵蚀肌肉完整切除。

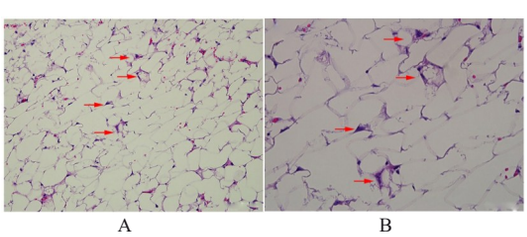
1.5 术后病理检查 术后组织标本送至内蒙古自治区呼伦贝尔市人民医院病理科行常规病理检查，并送至吉林大学中日联谊医院病理科进行免疫组织化学染色和基因检测。术后常规病理检查结果显示：灰黄色结节样肿物1枚，表面光滑，包膜完整，体积为16.0 cm×10.0 cm×4.0 cm，切开见实质内呈灰黄色，脂肪样，质软；另见数块灰黄色组织，总体积为5.0 cm×4.0 cm×1.2 cm，切开见实质内呈灰褐色，质地中等。显微镜下见病变组织主要由相对成熟的脂肪组织构成，可见多少不一、较厚且不规则的纤维分隔或纤维带；脂肪细胞大小不等，局灶可见核的异型性或浓染核；肿瘤内可见散在细胞核增大、浓染，单核或多核的不典型间质细胞；纤维分隔区内存在数量不等的单泡状或多泡状脂肪母细胞（图2）。免疫组织化学：细胞周期蛋白依赖性激酶4（cyclin-dependent kinase 4，CDK4）（＋）（图3A），鼠双微体2（murine double minute 2，MDM2）（＋）（图3B）。MDM2荧光原位杂交（fluorescence *in situ* hybridization，FISH）基因检测：肿瘤细胞内MDM2基因扩增（图4）。术后病理诊断：左下肢ALT。术后6个月随访，患者病灶消失，未见肿瘤复发。



A：Coronal plane T1WI image；B：Coronal plane T2-weighted IDEAL sequence in-phase image；C：Coronal plane T2WI-Ideal sequence water image；D：Sagittal plane T2WI-Ideal sequence in-phase image；E：Sagittal plane T2WI-Ideal sequence water image；F：Axial T2WI fat-suppressed sequence image. Arrow showed phyma position.

图1 左下肢ALT患者术前MRI影像学表现

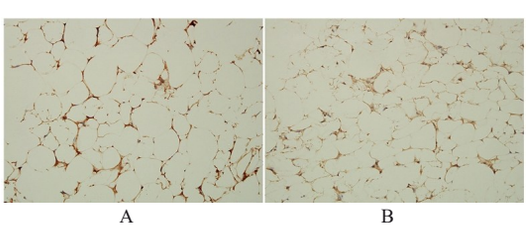
Fig. 1 MRI images of patient with ALT in left lower limb before operation



A：×200；B：×400.

图2 HE染色检测左下肢ALT患者术后肿瘤组织病理形态表现

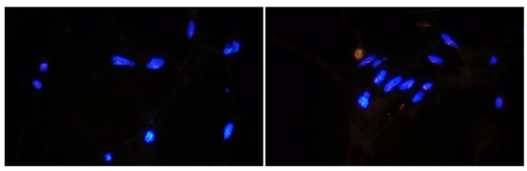
Fig. 2 Pathomorphology of tumor tissue of patient with ALT in left lower limb after operation detected by HE staining



A：CDK4；B：MDM2.

图3 左下肢ALT患者术后肿瘤组织中CDK2和MDM2表达情况（免疫组织化学，×200）

Fig. 3 Expressions of CDK2 and MDM2 in tumor tissue of patient with ALT in left lower limb after operation (Immunohistochemistry, ×200)



A　B

A：Outside of tumor；B：Center of tumor.

图4　左下肢ALT患者术后肿瘤组织中MDM2表达情况(荧光原位杂交，×1 000)

Fig. 4　Expression of MDM2 in tumor tissue of patient with ALT in left lower limb after operation (Fluorescence *in situ* hybridization，×1 000)

2　讨　论

近年来，脂肪肉瘤（liposarcoma，LPS）包括四肢脂肪肉瘤相关研究得到了广泛关注[7-11]。世界卫生组织（World Health Organization，WHO）根据LPS的恶性程度将其分为4种亚型：非典型脂肪瘤样肿瘤或高分化脂肪肉瘤（typical lipomatous tumor/well-differentiated liposarcoma，ALT/WDLPS）、去分化脂肪肉瘤（dedifferentiated liposarcoma，DDLPS）、黏液样脂肪肉瘤（myxoid liposarcoma，MLPS）和多形性脂肪肉瘤（pleomorphic liposarcoma，PLPS）[1]。由于ALT/WDLPS与成熟良性脂肪瘤组织和正常脂肪组织在组织学上非常相似[12]，因此ALT的确切诊断困难。

ALT/WDLPS主要由非典型基质细胞、成熟脂肪细胞和少量脂肪母细胞组成。依据WHO分类，ALT/WDLPS进一步被分为脂肪细胞、硬化和炎症等3种亚型[13]。脂肪细胞亚型由大小不一的脂肪细胞小叶组成，伴核异型性、深染和损伤过深的基质细胞，这些基质细胞多存在于厚度可变的纤维隔膜内，通常数量较少[4, 14-15]。发生在肢体的肿瘤称为ALT。本例患者术后病理检查显示大量分化良好的脂肪细胞，纤维分隔区内存在数量不等的单泡状或多泡状脂肪母细胞，符合ALT的病例特征，证实病灶为ALT。

尽管LPS各亚型具有不同的分子遗传学特征，其诊断仍需结合组织学与分子检测技术。对LPS亚型特异性分子和细胞遗传学改变的深入理解有助于开发新的LPS靶向疗法[14]。目前已知与WDLPS发生存在关联的基因包括*CDK4*（12q14.1），*TSPAN31*（12q14.1），高迁移率族蛋白A 2（high-mobility group AT-hook 2，*HMGA2*）（12q14.3），*MDM2*（12q15），羧肽酶M（carboxypeptidase M，*CPM*）（12q15）和*YEATS4*（12q15）等[15-17]。DDLPS中还常见*MAP3K12*，T盒转录因子5（T-box transcription factor 5，*TBX5*），*CDK2*，GLI同源盒转录因子1（GLI family zinc finger 1，*GLI1*）和ALX同源盒基因1（ALX homeobox 1，*ALX1*）等基因扩增[18-19]。其中，*MDM2*扩增是LPS的关键致癌机制之一，基于FISH基因检测分析已成为LPS的重要诊断标志[20-21]。该患者术后病理检查结果显示：*CDK4*和*MDM2*基因免疫组织化学染色结果为阳性，且*MDM2* FISH基因检测显示肿瘤细胞内*MDM2*基因扩增，以上结果进一步证实患者病灶的性质为ALT/WDLPS。

影像学检查如CT和MRI也是LPS诊断的重要依据。朱刚等[22]研究回顾性分析了43例四肢脂肪肉瘤患者情况显示：患者CT特征为病灶呈不规则低密度阴影，增强后病变部位分隔明显增强；MRI特征为T1短信号、T2长信号和短时间反转恢复序列成像等信号；分化良好型脂肪肉瘤以脂肪信号为主，增强后轻度强化。ZHANG等[23]研究显示：通过比较14例DDLPS患者和16例ALT/WDLPS患者的MRI结果，发现两者病灶内非脂肪区域比例、MRI信号不均匀程度和肿瘤边缘的清晰程度均存在明显差异，MRI可为区分这2种亚型提供诊断依据。SHIM等[24]研究显示：MRI增强扫描可较好地区分脂肪瘤和DDLPS，其敏感度为80%，特异度近95%，准确度近92%。KAWAGUCHI等[25]研究显示：T1W1的病灶最大直径、非脂肪区域占比和脂肪抑制T2W1上实性高信号区域是区分浅表脂肪瘤和ALT/WDLPS的重要影像特征。该患者的MRI平扫检查包括T1WI图像、T2WI-Ideal序列inphase像和水像及T2WI脂肪抑制序列检查，结果提示该患者病灶性质为LPS，为病灶切除边缘处理提供了影像学依据。

ALT虽为低级别软组织肿瘤，但仍具有局部复发可能[2-4]。研究[3]表明：接受了显微镜下病灶及病灶阳性边缘切除手术的原发性肢体ALT患者，术后局部复发率可达到13%。另有临床研究[26]显示：接受边缘切除的ALT患者术后复发率为11.9%。本例患者术后6个月随访证实预后良好，未见肿瘤复发。

综上所述，术前MRI平扫和增强扫描检查可为WDLPS诊断提供有效依据，并有助于确定手术

切除病灶边界。术后病理学检查可作为确诊ALT和评估患者预后的关键手段。

利益冲突声明：

所有作者声明不存在利益冲突。

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