

累及下肢肌肉与椎体的慢性播散性念珠菌病 1例并文献复习

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摘 要

目的: 报道本院2024年12月收治累及下肢肌肉与椎体的慢性播散性念珠菌病1例患者。方法: 以“Chronic disseminated candidiasis”为关键词, 在PUBMED上搜索2016年1月~2026年3月间的18篇病例报告共20例患者, 总结其发病部位及治疗方案并复习文献。结果: 发病部位包括: 肝(12/20)、脾(9/20)、皮肤/肌肉(7/20)、肾(6/20)、中枢(4/20)、肺(3/20)、心脏(3/20)、眼(2/20)、骨骼(2/20)、淋巴结(2/20)、甲状腺(1/20)、十二指肠(1/20)、扁桃体(1/20)。1例患者死亡前尚未启动抗真菌治疗, 其余19例患者均接受抗真菌药物治疗, 10例单纯药物治疗, 其中2例病人死亡, 8例患者药物联合手术治疗, 其中1例病人死亡。结论: 慢性播散性念珠菌病的发病部位极少累及骨骼, 当累及骨骼时病情隐匿, 可能仅表现为发热及局部疼痛, 缺乏诊断的特异性, 早期的影像学检查对疾病的诊断具有指导意义。

关键词

慢性播散性念珠菌病, 急性髓系白血病, 抗真菌治疗

Chronic Disseminated Candidiasis Involving the Lower Limb Muscles and Vertebrae: A Case Report and Literature Review

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Abstract

Objective: To report a case of chronic disseminated candidiasis involving the lower limb muscles and vertebral bodies admitted to our hospital in December 2024. **Methods:** Using “Chronic disseminated candidiasis” as the key word, 18 case reports of 20 patients from January 2016 to March 2026 were retrieved from PUBMED. The sites of onset and treatment regimens were summarized and the literature was reviewed. **Results:** The sites of onset included: liver (13/20), spleen (9/20), skin/muscle (8/20), kidney (7/20), lung (3/20), brain (3/20), heart (3/20), eye (2/20), bone (2/20), lymph node (2/20), thyroid (1/20), duodenum (1/20), and tonsil (1/20). One patient died before antifungal treatment was initiated, and the remaining 19 patients all received antifungal drug treatment. Among them, 10 patients received drug treatment alone, with 2 deaths, and 8 patients received drug treatment combined with surgery, with 1 death. **Conclusion:** In chronic disseminated candidiasis, skeletal involvement is extremely rare. When the skeleton is affected, the disease presents in an insidious manner, which may only manifest as fever and local pain, lacking diagnostic specificity. Early imaging examinations are of guiding significance for the clinical diagnosis of this disease.

Keywords

Chronic Disseminated Candidiasis, Acute Myelogenous Leukemia, Antifungal Therapy

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1. 病例资料

患儿女，16岁，因“确诊急性髓系白血病复发1月余，回院化疗。”入院。既往史：10余年前曾于我院确诊AML(M2)，完成全部化疗计划，骨髓示完全缓解后出院。治疗经过：入院后行血常规、生化及腰椎穿刺，大致在正常范围内，住院2d给予IAH方案诱导化疗，14d患儿发热，体温超38℃，经验性给予美罗培南抗感染，完善降钙素原0.062，血常规+CRP：白细胞计数 $0.44 \times 10^9/L$ ，中性粒细胞计数 $0.10 \times 10^9/L$ ，C-反应蛋白32.39 mg/L。16d加用氟康唑初级预防真菌感染。20d患儿仍发热，热峰38.7℃，且中性粒细胞缺乏时间>10天，加用万古霉素抗感染，更换伏立康唑经验性治疗真菌感染，完善真菌G试验及曲霉GM试验均为阴性，送检血培养。22d细菌培养(外周血及PICC)结果：热带念珠菌，药敏示氟康唑耐药，启动目标治疗，根据药敏加用两性霉素B脂质体抗真菌感染，后续先后加用卡泊芬净、氟胞嘧啶等抗真菌药物治疗，并拔除PICC。行肺部HRCT、消化系统超声、心脏超声、颅脑MRI未见相关病灶。27d、33d、39d血培养阴性。39d患儿诉下肢疼痛、腰背痛，伴下肢肌肉压痛。完善下肢深静脉彩色多普勒超声检查：双侧小腿肌间探及多发低回声结节，右侧大者 $0.9 \times 0.6 \text{ cm}$ ，左侧大者 $0.9 \times 0.6 \text{ cm}$ ，形态尚规则，边界尚清，周边似见鼠尾征，CDFI：内未见明显血流信号。消化系统超声肝内及脾内多发低回声区。43d上腹CT动态增强扫描：肝脏、脾脏多发低密度影“见图1”；胸椎腰椎MRI示椎体内异常低密度信号，骨髓侵蚀样病变“见图2、图3”；行骨髓穿刺：骨髓中见 5.18×10^{-4} 的异常髓系原始细胞。为排除AML髓外浸润，行肝脏活检，穿刺部位：微灶状坏死物内见少量菌丝结构、未见肿瘤细胞“见图4”。送检NGS示热带念珠菌感染。因患儿基础状态差、脊椎病变部位较深，暂不行病变部位脊



Figure 1. CT of liver and spleen

图 1. 肝脏、脾脏 CT



Figure 2. MRI of the lumbar spine

图 2. 腰椎 MRI

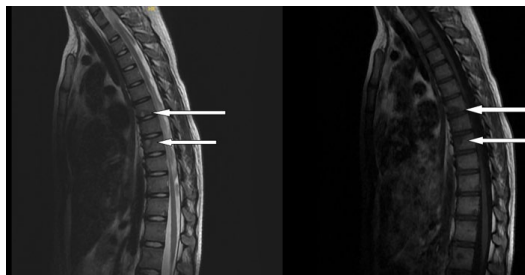


Figure 3. MRI of the thoracic spine

图 3. 胸椎 MRI

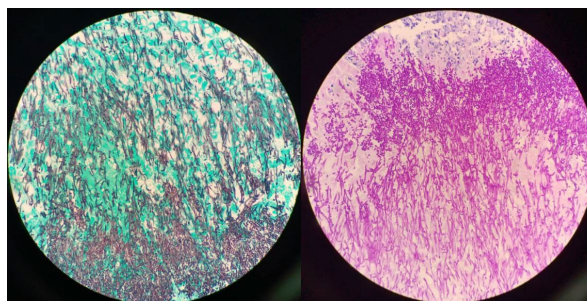


Figure 4. Pathology of liver biopsy site-few fungal hyphae identified within micro-foci of necrosis

图 4. 肝脏穿刺部位病理微灶状坏死物内见少量菌丝结构

柱穿刺活检。57 d 体表肿物超声：下肢肌间未见异常结节。70 d 患儿体温正常 3 天，一般状态可，血常规条件允许，为防止原发病复发，给予小剂量化疗(维奈克拉 + 阿糖胞苷 + 高三尖杉酯碱)3 天，体温升高，热峰大于 39℃，考虑感染未控制，遂停止。121 d 患儿间断发热，热峰较前下降(<38℃)，无其他不适，复查白血病微小残留灶检测：未见异常髓系原始细胞；全身骨显象胸腰椎显像剂未见明显显像剂异常浓聚或稀疏区；肝脾 CT 病灶较前缩小。准予出院，出院后继续口服伏康唑抗真菌。在本次住院过程中患儿共抗真菌药物治疗 3 月余，期间患儿因抗真菌药物副作用出现顽固性低钾 2 次、白蛋白低 1 次、谷丙转氨酶长期升高，给予口服及静脉补钾、输注白蛋白、口服及静脉保肝药物对症治疗，其中两性霉素 B 脂质体因顽固性低钾停用两性霉素 B 脂质体 2 次，血钾恢复正常范围后复用。

2. 讨论

侵袭性真菌病(invasive fungal disease, IFD)：指真菌侵入人体，在组织、器官或血液中生长、繁殖，并导致炎症反应及组织损伤的感染性疾病。近期俄罗斯的一项纳入 34 篇文献的 meta 分析[1]表示，血液肿瘤患儿化疗合并 IFD 的发生率为 5.22%；其中念珠菌感染占比为 48.6%，为侵袭性真菌病的主要病原体，其次为曲霉菌感染(38.0%)。侵袭性念珠菌病(invasive candidiasis, IC)是由念珠菌属真菌侵入血液或深部组织引起的系统性感染。血液恶性疾病化疗患者中男性、真菌感染既往史、未缓解疾病接受诱导或再诱导化疗、中心静脉置管、粒细胞缺乏持续超过 10 d、低蛋白血症为 IC 的危险因素[2] [3]。血液恶性肿瘤患者合并侵袭性念珠菌病的预后差，Melike Sezgin Evim 等人[4]认为急性白血病患者合并 IFD 相关死亡率可达 18%。长期中性粒细胞减少[5]、初始药物的选择(使用氟康唑抗真菌治疗死亡率高于棘白菌素类)、合并脓毒血症[6]为影响 IC 预后的独立危险因素。慢性播散性念珠菌病(chronic disseminated candidiasis, CDC)是一种特殊的侵袭性念珠菌病，主要指念珠菌侵入血循环，并在血液中生长繁殖后，进一步播散至 2 个或 2 个以上不相邻器官，引起相应器官慢性感染[7]。一项涵盖 49 例患者的研究表示[8]，恶性血液肿瘤患者中发生 CDC 的患者以 AML 患者多见(42.9%)，病变部位主要累及肝脏(89.7%)，脾脏病变(69.3%)，肾脏病变(18.3%)。

以“Chronic disseminated candidiasis”为关键词，PUBMED 上搜索 2016 年 1 月~2026 年 3 月间的病例报告，共 18 篇[9]-[26]，涉及 20 例患者。综合上述 20 例患者分析，男性患者有 9 例，女性患者有 11 例，包含 2~68 岁的患者，中位年龄为 47.5 岁，累及发病部位包括：肝(12/20) [10] [11] [14]-[16] [18] [20] [21] [23] [24] [26]、脾：(9/20) [9]-[11] [14] [15] [17] [21] [23]、皮肤/肌肉(7/20) [11] [13] [14] [16] [21] [22] [25]、肾(6/20) [9]-[11] [14] [15] [17]、中枢(4/20) [14] [22] [23] [26]、肺(3/20) [9] [13] [20]、心脏(3/20) [9] [11] [14]、眼(2/20) [13] [19]、骨骼(2/20) [21] [26]、淋巴结(2/20) [21] [26]、甲状腺(1/20) [12]、十二指肠(1/20) [20]、扁桃体(1/20) [21]。1 例[20]患者死亡前尚未启动抗真菌治疗，其余 19 例患者均接受抗真菌药物治疗，10 例单纯药物治疗，其中 2 例病人死亡，8 例患者药物联合手术治疗，其中 1 例病人死亡。7 例[11] [13] [14] [16] [21] [22] [25]累及皮肤或肌肉的患者中，绝大多数以皮肤肌肉表现(如皮下结节、皮下脓肿、肌痛等)为 CDC 的除发热外的首表现，多数可直接活检得到病原，这提示我们皮肤/肌肉相关的临床表现可能是相对早期且特异的临床表现。2 例[21] [26]累及骨骼的患者均为多部位真菌感染(大于 3 部位)，存在发热及局部疼痛，均采取抗真菌药物联合手术治疗，即病初给予棘白菌素类抗生素，辅以手术切除脾或清创(骨骼)，并给予长期氟康唑(>6 月)维持治疗，后续复查二者病灶均较前缩小。

回顾病例，此患儿为复发的 AML 患者，既往诊断真菌性肺炎，化疗后中性粒细胞缺乏 13 天并长期使用广谱抗生素，留置中心静脉导管，为 IFD 的高危人群。本例患者在治疗过程中仅表现发热、下肢痛、腰背痛，经腹部 CT 及肝脏穿刺病理活检，诊断慢性播散性念珠菌病。患儿胸腰椎 MRI 可见椎体上终板轮廓模糊、不完整，呈现出明显的局限性虫蚀样溶骨性破坏，椎旁见蔓延的肉芽肿或脓肿，椎体形态相

对保留, 虽然有破坏, 但该椎体整体高度并未出现大面积压缩, 同时缺乏弥漫性骨髓替代征象, 更倾向于真菌感染而非白血病浸润, 考虑真菌侵袭椎体。结合下肢静脉超声最终诊断慢性播散性念珠菌病, 累及下肢肌肉、肝、脾及椎体。根据《血液病/恶性肿瘤患者侵袭性真菌病的诊断标准与治疗原则(第六次修订版)》指南推荐[3], 给予抗真菌的初级预防、经验性抗真菌治疗及目标治疗, 即给予氟康唑进行初级预防; 当在广谱抗生素的覆盖下患儿仍粒缺伴发热持续 6 天时, 给予伏立康唑经验性抗真菌治疗; 明确病原后, 给予两性霉素 B 脂质体、卡泊芬净等药物进行目标治疗。血培养念珠菌阳性的患者, 在治疗阶段拔除 PICC 会显著提高患者的生存率[27], 因此我们在该患儿血培养热带念珠菌(+)后便将其拔除。由于本例患儿基础条件差, 申请腰椎处穿刺活检及手术被拒, 暂放弃手术。王东江等学者[28]认为近年来热带念珠菌对氟康唑等三唑类药物天然耐药率显著升高, 对华东地区的念珠菌进行耐药性分析显示热带念珠菌对氟康唑、伏立康唑、泊沙康唑、伊曲康唑的耐药率分别为 29.55%、26.24%、76.60%、21.99%, 对棘白菌素类药物耐药率为 2.36%。推荐棘白菌素类为播散性念珠菌病的首选用药。有研究[8]表示接受单药治疗和联合治疗的患者之间在 1 个月的生存率、3 个月的缓解率以及总生存率方面无显著差异。但江信宏等人[29]认为两性霉素 B 脂质体联合卡泊芬净或泊沙康唑治疗 CDC 的有效率, 高于卡泊芬净或两性霉素 B 脂质体单药治疗。最终, 我们制定了以两性霉素 B 脂质体为主, 联合卡泊芬净、氟胞嘧啶等抗菌药物的治疗方案。

局限性: 本例病人累及椎体的播散性念珠菌病仅通过临床表现及影像学临床诊断, 没有取得病理学诊断, 仍不能除外原发病浸润骨髓的可能。未能行穿刺取得病, 治疗欠精准, 但通过后续抗真菌治疗, 患儿腰背痛减轻, 体温下降, 也更倾向于真菌感染可能。

目前慢性播散性念珠菌病的确诊依赖于临床表现、影像学及微生物学, 其临床表现缺乏特异性, 但常以“不明原因持续性发热”为起点, 在发热基础上, 若出现局部疼痛、肝脾肿大或特征性的皮肤结节/皮疹, 应强烈考虑本病可能。对于特定高危患者, 即使无症状, 也需通过影像学 and 真菌标志物进行监测, 及早启动目标治疗是治疗成功的关键。

声 明

所有作者声明无利益冲突, 已获取家属知情同意。

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