·综述·

皮肌炎诊断与治疗进展

张雅静 岳伟

【摘要】 皮肌炎的临床特征是皮肤改变和骨骼肌炎症反应，亦可累及其他器官。发病机制包括易感基因、环境应激源、免疫和非免疫诱发机制。临床主要表现为亚急性进行性近端肌无力、皮疹或二者兼有，以及肌外表现，如心脏异常、间质性肺病和恶性肿瘤。辅助检查包括肌炎自身抗体、肌酶谱、肌电图。针对皮肤损害，予以抑制光敏感药物和抗疟药；合并肌肉受累时系统性激素治疗是一线方案；免疫抑制剂常用于难治性皮肌炎或激素出现不良反应时的添加治疗；其他治疗方法还包括钙调磷酸酶抑制药、环磷酰胺、生物制剂、Janus激酶抑制剂等。

【关键词】 皮肌炎； 自身抗体； 肾上腺皮质激素类； 免疫抑制剂； 综述

Progress in diagnosis and treatment of dermatomyositis

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【Abstract】 Dermatomyositis (DM) is characterized by skin lesions, skeletal muscle inflammation, and involvement of other organs. The pathogenesis of DM includes susceptibility genes, environmental stressors, immune and non-immune inducing mechanisms. DM usually presents as subacute progressive proximal muscle weakness, skin rash, or both. Other common extramuscular findings include various heart abnormalities, interstitial lung disease (ILD), and malignant tumors. The auxiliary examination of DM includes the examination of myositis autoantibodies, myoenzymes and electromyography (EMG). Skin treatments for DM include photosensitivity inhibition drugs and antimalarial drugs. If the DM is associated with muscle involvement, systemic corticosteroids is the first line of treatment, and immunosuppressants are used for refractory diseases or as corticosteroids sparing agents in the event of side effects. Other treatments include oral calcineurin inhibitors, cyclophosphamide, biologic agents and Janus kinase (JAK) inhibitor.

【Key words】 Dermatomyositis; Autoantibodies; Adrenal cortex hormones; Immunosuppressive agents; Review

Conflicts of interest: none declared

特发性炎性肌病（IIM）是自身免疫介导的骨骼肌非化脓性疾病，以慢性进行性对称性肌无力为特征，伴有其他器官系统受累。临床表现多样，主要为近端肌无力、血清肌酸激酶（CK）水平升高、肌电图呈现活动性肌肉病改变，同时以间质性肺病（ILD）为代表的多系统损害、关节病变和肿瘤风险增加。关于特发性炎性肌病的分类尚未达成共识，目前主要包括皮肌炎（DM）、多发性肌炎（PM）、包涵体肌炎（IBM）、无肌病型皮肌炎（ADM）和免疫介导的坏死性肌病（IMNM）。

皮肌炎是一种有特征性皮肤改变的特发性炎性肌病[1]，其病因和发病机制尚未阐明，易感基因、环境应激源、免疫和非免疫诱发机制、干扰素途径信号转导异常[2]等均与皮肌炎的易感性和发病相关。临床通常表现为亚急性进行性近端肌无力、皮疹或二者兼有。特征性皮肤改变包括Gottron丘疹（掌关节和指间关节的紫丘疹），Heliotrope皮疹（亦称向阳性紫红斑，眼睑紫色皮疹）伴眶周水肿。其他常见肌外表现有心脏异常、间质性肺病和恶性肿

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瘤[3]。肌炎特异性自身抗体(MSAs)是目前颇受关注的生物学标志物,有助于进一步了解皮肌炎的发病机制并对诊断有提示意义。治疗方面,皮肌炎伴肌肉组织损害的患者首选激素,而免疫抑制剂常用于难治性皮肌炎或激素出现不良反应时的二线治疗,生物治疗成为新兴手段。本文综述皮肌炎诊断与治疗最新研究进展,以利于早期诊断、及时治疗,提高患者生活质量。

一、病因及发病机制

1.遗传易感性 皮肌炎易感基因包括人类白细胞抗原(*HLA*)基因[4]以及编码免疫球蛋白重链、细胞因子及其受体的多种基因,尤以*HLA*基因与皮肌炎易感性的关联性最强。研究显示,携带*HLA* DRB1*0301、DQA1*0501的白种人皮肌炎易感性增强,携带*HLA-b7*基因的亚裔人群易感性增强[5]。此外,特异性*HLA*等位基因与皮肌炎特异性自身抗体相关,如携带*HLA* DRB1*07或DQA*0201的患者多同时存在抗Mi-2抗体[5]。表观遗传学在皮肌炎的发病中也发挥重要作用[6-7],主要包括DNA甲基化、组蛋白修饰、微小RNA(miRNA)和长链非编码RNA(lncRNA)活性等。DNA甲基化受遗传DNA序列和环境因素的影响,是重要的表观遗传因子,通过改变基因内调控序列的转录染色质以调控基因表达;miRNA在皮肌炎细胞转化过程中以及lncRNA在皮肌炎肌肉损伤分子机制中发挥重要作用。

2.环境因素 病毒感染和紫外线照射[8]均为皮肌炎的诱发因素。病毒感染引起的免疫反应可以导致皮肌炎。幼年皮肌炎(JDM)最常见的感染是自限性病毒感染,如柯萨奇病毒(CV)、细小病毒B19、埃可病毒(ECHO)和流感病毒,偶见伯氏疏螺旋体感染的报道[9]。紫外线照射是重要的环境因素,地理与流行病学的相关数据显示,距离赤道越近、紫外线照射强度越大、皮肌炎发病率越高[10]。皮肌炎患者抗155/140 kD蛋白抗体与紫外线照射呈负相关[11]。过度暴露于紫外线可能抑制机体免疫系统和皮肤自然防御功能,从而诱发皮肌炎。

3.细胞免疫机制 $CD4^+$T细胞和巨噬细胞存在于皮肌炎患者肌束膜血管周围,但对T淋巴细胞在皮肌炎中的其他作用尚不十分清楚。尽管阻断或调节皮肌炎患者T淋巴细胞生成仅仅针对特定的T淋巴细胞亚群,但仍有望成为未来治疗选择[12]。皮肌炎患者血管周围可检出B淋巴细胞和浆细胞,研究显示,B淋巴细胞阻断治疗(如利妥昔单抗)有效,提示B淋巴细胞可能参与皮肌炎的发病[13]。此外,B淋巴细胞参与皮肌炎的发病还表现为特异性自身抗体的产生,抗MDA5抗体是最为特异性的肌炎特异性自身抗体,抗MJ/NXP-2、Mi-2以及转录中介因子1-γ(TIF1-γ)抗体分别是幼年皮肌炎、成人皮肌炎和肿瘤相关皮肌炎的特异性自身抗体[14]。

二、诊断

1.诊断标准 皮肌炎的诊断目前主要依据1975年Bohan和Peter[1]的诊断标准:(1)对称性近端肌无力,进展数周至数月,有或无吞咽困难和(或)膈肌无力。(2)血清肌酶谱升高,包括肌酸激酶、丙氨酸转氨酶(ALT)、天冬氨酸转氨酶(AST)、乳酸脱氢酶(LDH)。(3)肌电图异常,包括纤颤电位、正锐波、多相短小的运动单位电位(MUP)、插入性刺激、重复高频放电等。(4)肌肉组织活检异常,组织病理学表现为变性、再生、坏死和间质单核细胞浸润。(5)典型的皮肌炎皮疹(Heliotrope皮疹或Gottron丘疹)。(1)~(4)中任意3项+(5)诊断为确定的(definite)皮肌炎,(1)~(4)中任意2项+(5)即诊断为很可能的(probable)皮肌炎,(1)~(4)中任意1项+(5)则诊断为可能的(possible)皮肌炎。至1995年,Tanimoto等[15]对Bohan和Peter的诊断标准进一步修订,提出特异性皮肤改变包括Heliotrope皮疹、Gottron丘疹和四肢关节伸肌表面紫癜,其他表现包括近端肌无力、肌肉疼痛、非破坏性关节炎或关节痛、血清肌酸激酶或醛缩酶水平升高、全身炎症反应、肌电图呈现肌源性损害、抗Jo-1抗体阳性和组织病理学符合炎性肌肉病改变。同时具备3种特异性皮肤改变和4种其他表现的患者,即诊断为皮肌炎。

2.临床表现 皮肌炎通常表现为亚急性进行性近端肌无力、皮疹或二者兼有。如果患者在6个月或更长时间内皮肤表现符合皮肌炎改变,但是血清肌酶谱正常且无肌无力,则为无肌病型皮肌炎(ADM)[16-18]。肌肉病变常为无痛性,肌酸激酶、丙氨酸转氨酶和天冬氨酸转氨酶水平升高或正常[19]。皮肌炎的皮肤表现是变化的[20],特征性表现为临床确诊意义的皮肤表现、高度特征性皮肤表现、特征性皮肤表现、幼年皮肌炎常见皮肤表现和罕见皮肤表现5种类型[21]。(1)临床确诊意义的皮肤表现为Gottron丘疹[22-23]。(2)高度特征性皮肤表现包括Heliotrope皮疹伴眶周水肿。(3)特征性皮肤表现包括肘关节、指节、膝盖和踝伸肌表面红斑皮疹,面

部、颈部和胸部红斑皮疹，称为“V型征”，或颈部和肩部背面红斑皮疹，称为“披肩征”；以及手掌水平裂缝的角化过度（技工手）、甲周毛细血管扩张、面颊皮疹，这些皮损呈光敏感性，通常伴有瘙痒[21]。(4)皮肤钙质沉着多见于幼年皮肌炎[21]。(5)罕见皮肤表现包括无瘢痕性脱发、红皮病、囊泡性大疱病、白细胞破屑性血管炎和网状青斑[21]。其他常见肌外表现还包括心脏异常、间质性肺病和恶性肿瘤。心脏异常表现为心律失常、充血性心力衰竭、心肌炎、心包炎、心绞痛和继发性纤维化[21]。症状性心脏受累在急性皮肌炎患者中并不常见，但高达50%的皮肌炎患者检出无症状性心脏受累[21]。慢性皮肌炎患者常发生心力衰竭，是应用激素致长期高血压所致[21]。但心脏受累与皮肌炎严重程度无关，可发生于疾病各阶段[24]。间质性肺病的病因尚不明确，其特征性病理改变是肺部炎性细胞浸润和间质纤维化，此类患者临床症状较严重，预后较差，应定期行肺功能检查[25-27]。有研究显示，抗MDA5抗体与快速进展性间质性肺病有关，且此种抗体仅在皮肌炎和无肌病型皮肌炎中检测到[28]。此外，皮肌炎还与卵巢癌、肺癌、胰腺癌、胃癌和结肠癌等恶性肿瘤密切相关[29]。约15%的成年皮肌炎特别是年龄>40岁的患者，存在恶性肿瘤或者进展为恶性肿瘤[29]。幼年皮肌炎患儿罹患白血病和淋巴瘤的风险增加16倍[30]。高龄、皮肤溃疡、复发性疾病或抗155/140 kD蛋白抗体阳性的特发性炎性肌病患者潜在恶性肿瘤风险较高[29]。吞咽困难、发声困难和误吸提示咽部和食管横纹肌受累，患者预后不良[31]。

3.病理改变　皮肤病理改变无明显特异性，肌肉病理改变主要是血管周围或束间隔及其周围炎症反应，而非肌束内，浸润的炎性细胞以B淋巴细胞和$CD4^+$T细胞为主；肌肉组织毛细血管密度降低但剩余毛细血管管腔明显扩张；肌纤维损伤或坏死，通常涉及部分肌束或束周而致束周萎缩，是皮肌炎的特征性病理改变（图1）。肌肉组织活检显示束周萎缩，即使未见明显的炎症反应也可以诊断皮肌炎。染色方法主要有HE染色、免疫组化染色、四氮唑还原酶（NADH）染色、细胞色素氧化酶（COX）染色、改良Gomori三色（MGT）染色，高碘酸-雪夫（PAS）染色等。

4.肌炎自身抗体　肌炎自身抗体分为肌炎相关自身抗体（MAAs）和肌炎特异性自身抗体两个亚群（表1）。(1)肌炎相关自身抗体：诊断特异性较低，亦常见于其他结缔组织病（CTDs），但仍是重要的诊断指标。①抗PMScl抗体，是最常见的肌炎相关自身抗体，可见于各种结缔组织病[32]，主要见于多发性肌炎共病硬皮病（Scl），并增加间质性肺病、关节炎、技工手和雷诺现象的风险。②抗U1-核小核糖核蛋白（U1-snRNP）抗体，仅存在于3%～8%的成年和青少年皮肌炎或多发性肌炎患者，但在肌炎共病其他疾病患者中比例较高（25%～40%），常见于肌炎共病结缔组织病的患者。研究显示，抗U1-snRNP抗体对激素治疗反应良好[16]。③抗Ku抗体，见于肌炎共病系统性红斑狼疮（SLE）、硬皮病以及混合或未分化结缔组织病患者，阳性率为9%～19%[33]。抗Ku抗体阳性的肌炎患者予以大剂量激素（甲泼尼龙250～1000 mg/d静脉滴注），尽管治疗反应良好，但间质性肺病呈现出严重的激素耐药[34]。④抗干燥综合征A型和B型抗体（SSA和SSB），在特发性炎性肌病患者中亦较常见，SSA可见于9%～19%的成年皮肌炎或多发性肌炎患者、6%的幼年皮肌炎患儿和14%～25%的肌炎重叠患者，SSB可见于2%～7%的多发性肌炎和4%～12%的皮肌炎患者[33]。(2)肌炎特异性自身抗体：目前已在约50%的皮肌炎和多发性肌炎患者中检出肌炎特异性自身抗体。研究显示，每一种肌炎特异性自身抗体均与一种临床表型相关，是重要的生物学标志物[31,35-36]，有助于诊断和指导治疗[37-38]。①抗氨基酰tRNA合成酶自身抗体（ASAs），迄今已报道8种抗氨基酰tRNA合成酶自身抗体，分别为抗Jo-1、pPL12、PL7、EJ、OJ、KS、Zo和Ha抗体，尤以抗Jo-1抗体最为常见，可见于9%～24%的成年特发性炎性肌病患者[39]。抗氨基酰tRNA合成酶自身抗体阳性的患者诊断为抗合成酶综合征（ASS），临床主要表现为间质性肺病、雷诺综合征、技工手[40]、无糜烂性骨关节炎、发热等，有时伴皮疹，此类患者对激素有良好的治疗效果，且预后良好[41]。②抗Mi-2抗体，是皮肌炎的特异性标志物[33]，可见于11%～59%的成年皮肌炎患者[42-43]和4%～10%的幼年皮肌炎患者[43]。抗Mi-2抗体与一系列特征性皮肤改变相关，如Gottron丘疹、日光红疹、“V型征”、“披肩征”、角质层过度生长等[42]。抗Mi-2抗体阳性的皮肌炎患者对免疫抑制治疗反应良好，预后较好[44]。③抗小泛素样修饰物激活酶（SAE）抗体，与皮肤改变和皮肌炎表型相关，而与肿瘤或者间质性肺病无关联性[45]。抗SAE抗体阳性还可能提示皮肌炎患者存在吞咽困难[46-47]。④抗

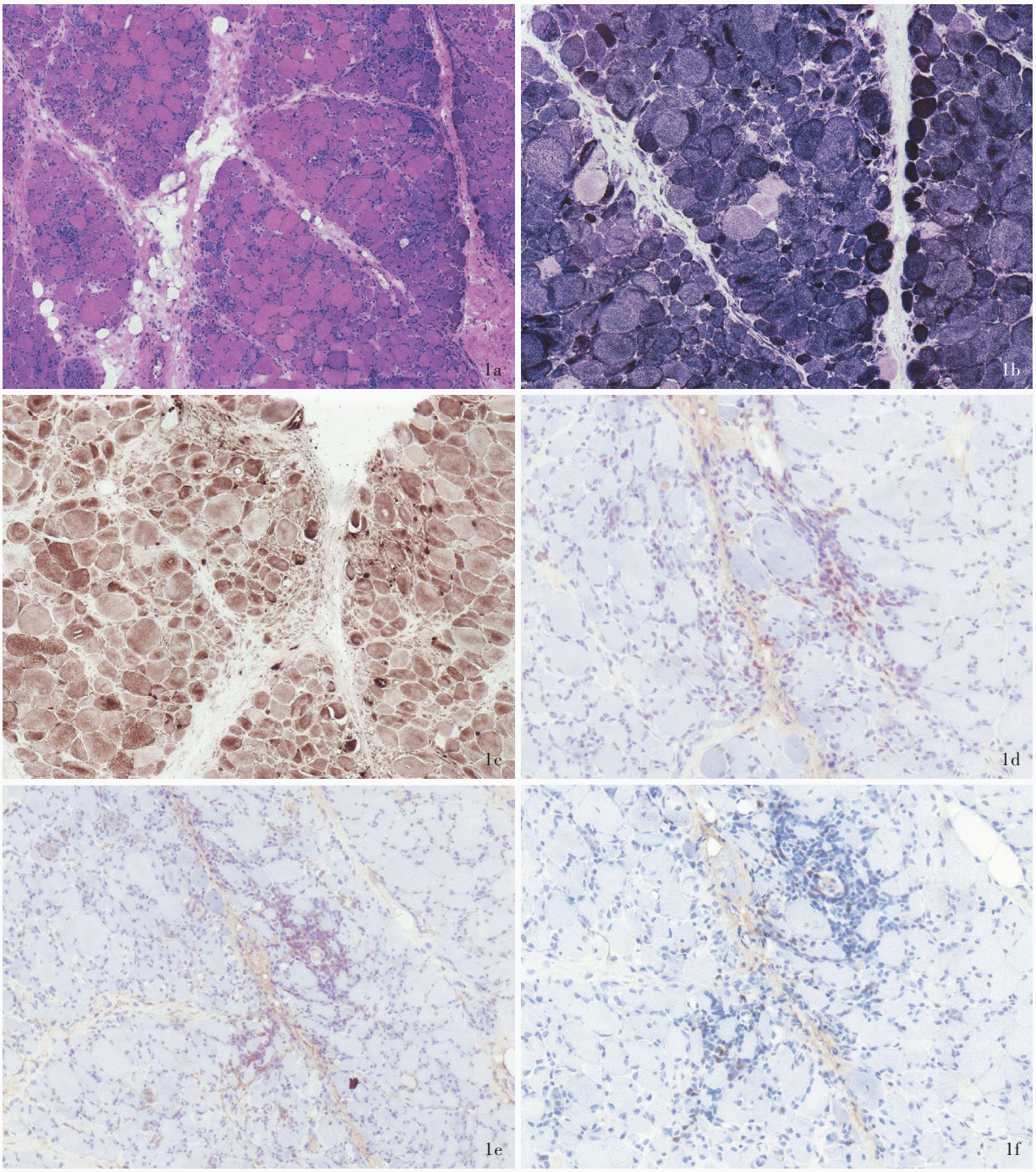

图1　皮肌炎肌肉组织病理学检查所见　×40　1a　肌纤维萎缩、坏死，淋巴细胞浸润，束周纤维萎缩，核内移　HE染色　1b　肌纤维萎缩、坏死　NADH染色　1c　肌纤维萎缩、坏死　COX染色　1d　胞膜CD3呈阳性　免疫组化染色（EnVision二步法）　1e　胞膜CD4呈阳性　免疫组化染色（EnVision二步法）　1f　胞膜CD8呈阳性　免疫组化染色（EnVision二步法）

Figure 1　Muscle histopathology of dermatomyositis　×40　Muscle fiber atrophy and necrosis, lymphocyte infiltration, perifascicular fiber atrophy and nuclear migration (Panel 1a). HE staining　Atrophy and necrosis of muscle fibers (Panel 1b). NADH staining　Atrophy and necrosis of muscle fibers (Panel 1c). COX staining　Cell membrane CD3 (Panel 1d), CD4 (Panel 1e) and CD8 (Panel 1f) were positive. Immunohistochemical staining (EnVision)

TIF1抗体，与成人肿瘤相关肌炎显著相关[48]，亦可见于幼年皮肌炎患儿但与肿瘤无关联性[49]。有研究显示，抗TIF1抗体阳性的成年和青少年皮肌炎患者发生严重皮肤改变的风险增加[49-50]。流行病学调查显示，白种人群抗TIF1抗体阳性比例高于亚洲人群[51-52]。⑤抗信号识别颗粒（SRP）抗体，是特发性

表1 肌炎自身抗体的分类
Table 1. Classification of myositis autoantibodies

分类	抗体
肌炎相关自身抗体	抗PMScl抗体
	抗U1-snRNP抗体
	抗Ku抗体
	SSA和SSB
肌炎特异性自身抗体	ASAs
	抗Mi-2抗体
	抗SAE抗体
	抗TIF1抗体
	抗SRP抗体
	抗MDA5抗体
	抗NXP-2抗体
	抗HMGCR抗体

U1-snRNP, U1-small nuclear ribonucleoprotein, U1-核小核糖核蛋白; SSA, A type Sjögren syndrome antibody, 抗干燥综合征A型抗体; SSB, B type Sjögren syndrome antibody, 抗干燥综合征B型抗体; ASAs, anti-aminoacyl-tRNA synthetase autoantibody, 抗氨基酰tRNA合成酶自身抗体; SAE, small ubiquitin-like modifier activating enzyme, 小泛素样修饰物激活酶; TIF1, transcriptional intermediary factor 1, 转录中介因子1; SRP, signal recognition particle, 信号识别颗粒; HMGCR, 3-hydroxyl-3-methylglutaryl coenzyme A reductase, 3-羟基-3-甲基戊二酰辅酶A还原酶

炎性肌病的特异性抗体。抗SRP阳性的特发性肌炎患者病理学特征可见大量肌纤维坏死和再生，炎症反应少见；临床表现为严重的坏死性肌病，快速进行性肌无力，且对标准治疗反应较差[53]。⑥抗MDA5抗体，见于20%～30%的亚裔皮肌炎患者，临床表现为无肌病型皮肌炎[14]和快速进展性间质性肺病[54-55]。抗MDA5抗体阳性的皮肌炎患者具有特异性皮肤表现，被认为是皮肤血管病变[25,56]。⑦抗NXP-2抗体，多见于约25%的青少年或成年皮肌炎患者，而多发性肌炎少见[57]。在男性成年皮肌炎患者中，抗NXP-2抗体与肿瘤显著相关。抗NXP-2抗体阳性的皮肌炎患者临床表现为严重复发性肌肉疼痛、近端和远端肌无力，以及严重吞咽困难[58]。⑧抗3-羟基-3-甲基戊二酰辅酶A还原酶（HMGCR）抗体，是免疫介导的坏死性肌病的特异性标志物，并非完全由他汀类调脂药所致。抗HMGCR抗体阳性的皮肌炎患者临床表型与其他特发性炎性肌病类型相似，即近端肌无力、血清肌酸激酶水平显著升高、肌电图呈现肌肉病特征、对免疫抑制治疗有反应。肌纤维坏死和变性是特征性病理改变，偶伴特异性炎性细胞浸润。

5.其他　近年来，MRI逐渐用于皮肌炎和多发性肌炎的诊断以及与其他肌肉病的鉴别诊断[59]；亦可用于评估幼年皮肌炎患儿，以避免肌电图或有创性肌肉组织活检术。MRI用于定位肌肉组织活检部位和监测治疗反应，超声也可用于区分正常与病变肌肉组织，正常肌肉组织的超声表现为肌纤维被肌内膜包裹，聚集成束状，被肌束膜包裹，病变肌肉组织的肌纤维类似强回声，纤维脂肪层肿胀，伴渗出液。因此，对于有MRI检查禁忌证的患者，超声不失为一种选择。对于疑似特发性炎性肌病的患者，应进行血清肌酶谱测定、神经传导检测和针刺肌电图检查。多发性肌炎和绝大多数皮肌炎患者血清肌酸激酶水平升高，但肌酸激酶正常并不能排除诊断。不同患者之间无法通过肌酶谱比较病情，但同一例患者可通过肌酶谱的变化判断病情进展。神经传导检测可评估其他原因导致的肌无力，如重症肌无力（MG）或Lambert-Eaton肌无力综合征（LEMS）。皮肌炎的肌电图表现为特征性“三联征”，即纤颤电位和正锐波、波幅降低和时限缩短、插入性刺激和异常高频放电。针刺肌电图有助于排除神经源性损害。

三、治疗

治疗原则方面应遵循个体化方案，需综合考虑患者年龄、皮肌炎亚型、病情严重程度以及共病情况。皮肌炎伴皮肤损害的患者建议联合应用抗疟药和系统性激素治疗。光敏性预防与治疗对皮肤改变具有重要意义[60]，口服抗疟药不仅可以预防光照射引起的皮肌炎，而且具有抗炎症反应特性[61]，可以联合应用激素。一线抗疟药为羟氯喹，剂量为200 mg/次（1～3次/d）。针对非难治性皮肌炎的皮肤改变，局部应用激素是皮肤炎症反应以及典型烧灼感和瘙痒的一线治疗，每日皮损区涂抹一次[62]；针对难治性皮肌炎的皮肤改变，静脉注射免疫球蛋白（IVIg）2 g/（kg·次）、1次/月的疗效已经随机对照试验证实[63]。

皮肌炎合并肌肉受累时，系统性激素治疗是一线方案[60,64-65]。成年皮肌炎患者最常应用泼尼松，初始剂量为1 mg/（kg·d），最大剂量为80 mg/d；幼年皮肌炎患儿的推荐初始剂量为2 mg/（kg·d）[66]，治疗4～8周后根据症状改善和肌酶谱降低程度逐渐减量（每周减量10 mg），并根据病情随时调整剂量。出现严重肌肉病变或脏器受累时，予以甲泼尼龙250～1000 mg/d连续静脉滴注3天后改为口服泼尼松1 mg/（kg·d）[67]。系统性激素治疗6～12个月，并

通过临床症状和血清肌酸激酶水平监测治疗反应。

免疫抑制剂常作为难治性皮肌炎或出现药物不良反应(如激素诱导的肌肉病便长期存在)时激素的添加治疗。甲氨蝶呤(MTX)是临床最常应用的免疫抑制剂,剂量为15 mg/(m^2·次)、1次/周皮下注射或口服,一般不超过30 mg,应定期监测血常规、肝肾功能;同时建议补充叶酸10 mg/次(3次/d);妊娠期女性禁用。硫嘌呤类药硫唑嘌呤(AZA)也是临床常用的免疫抑制剂,是伴间质性肺病的皮肌炎患者的首选药物,初始剂量25~50 mg/d,可增至150 mg/d[1.50 mg/(kg·d)],常见不良反应为胃肠道耐受不良以及急性或慢性白血病、溶血性贫血等。吗替麦考酚酯(MMF)亦可用于皮肌炎的免疫治疗,其适应证与硫唑嘌呤相似,也可用于幼年皮肌炎患儿,但与硫唑嘌呤相比,致畸性是其主要缺点,而硫唑嘌呤用于妊娠期女性是安全的,剂量为750~1500 mg/(m^2·次)、2次/d或3 g/d,应注意监测血常规和肾功能[66]。

幼年皮肌炎患儿可发生钙质沉着,导致潜在的严重功能损害。早期积极予大剂量[30 mg/(kg·d)]甲泼尼龙静脉滴注可减少后遗症,如钙质沉着[68]。在某些特定的情况下,轻度钙质沉着可能随着时间的推移而自行消退[68],此时物理治疗可以预防挛缩和残疾。钙调磷酸酶抑制药是有效的,但受限于其毒性作用,较少用于皮肌炎,主要用于治疗成年难治性或伴间质性肺病的严重肌炎,且主要适用于成人[66,69-71]。环磷酰胺仅用于多种结缔组织病重叠、激素耐药或伴严重的间质性肺病或难治性肌肉病的三线治疗,剂量为300~800 mg/(m^2·月)静脉滴注,至少6个月,但该药具有潜在的严重不良反应,尤其可增加感染和恶性肿瘤风险[66]。

生物制剂是新兴治疗方法[13,66]。利妥昔单抗是针对B淋巴细胞CD20的单克隆抗体,静脉滴注利妥昔单抗375 mg/(m^2·次)、1次/周耐受性良好,对皮肌炎的皮肤外表现特别是皮肌炎相关间质性肺病和难治性肌炎有效[72-73]。肿瘤坏死因子-α(TNF-α)抑制剂治疗皮肌炎出现完全不同的结果:英夫利昔单抗和阿达利马单抗的疗效较差[13];仅一项随机对照试验显示,依那西普作为激素的添加治疗在皮肌炎中具有显著疗效,甚至某些患者可停用激素[74],而其他研究并未显示出依那西普有效[13]。阿仑单抗是一种针对CD52的人源单克隆抗体,仅见个案报道,但是疗效不尽一致[13,66,75]。阿巴西普是一种阻断T淋巴细胞协同刺激信号的药物,已成功用于成人和儿童难治性特发性炎性肌病[13]。干扰素-α和β(IFN-α和IFN-β)介导的先天性免疫通路在皮肌炎的发病过程中发挥重要作用[13]。而白细胞介素-1(IL-1)抑制剂阿那白滞素治疗难治性多发性肌炎、皮肌炎和包涵体肌炎尚存争议[13,66]。自体干细胞移植显示出较好的疗效[13]。此外,肌肉受累患者进行适度的康复治疗也是很有必要的[76]。

INF-Ⅰ和INF-Ⅱ相关信号转导通路在皮肌炎的发病机制中发挥关键作用。胞质内信号转导是通过受体相关Janus激酶(JAK)实现的,因此JAK抑制剂是一种有潜力的治疗药物。JAK抑制剂用于幼年皮肌炎或抗MDA5阳性皮肌炎的间质性肺炎和纵隔气肿的病例报道陆续见诸文献[77-78]。

综上所述,皮肌炎的病因和发病机制、诊断与治疗尚有不明确之处。临床准确识别病因、临床特征和特异性皮肤改变是早期诊断、及时治疗的基础。皮肌炎潜在免疫机制研究的进展,使其临床亚型与特定生物学标志物相关联,从而为探寻新的治疗方法提供依据。治疗初期同时应用激素和免疫抑制剂是有益的,生物制剂是有前景的治疗方法之一,目前新的治疗方法主要集中于细胞因子IL-1β、IL-2、IL-6、IL-17、IL-18、TNF-α等,进一步验证皮肌炎的生物治疗和多靶点治疗的有效性以及研发新的治疗靶点是十分重要的。

利益冲突 无

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·小词典·

中英文对照名词词汇（四）

树突状细胞 dendritic cells(DC)
水通道蛋白4 aquaporin 4(AQP4)
随机对照试验 randomized controlled trial(RCT)
髓鞘少突胶质细胞糖蛋白 myelin oligodendrocyte glycoprotein(MOG)
糖化血红蛋白 glycosylated hemoglobin(HbA1c)
特发性高颅压 idiopathic intracranial hypertension(IIH)
特发性炎性肌病 idiopathic inflammatory myopathies(IIM)
调节阀开放压力 opening pressure(OP)
统一帕金森病评价量表 Unified Parkinson's Disease Rating Scale(UPDRS)
微创钻颅术 twist drill craniotomy(TDC)
微管相关蛋白-2 microtubule-associated protein-2(MAP-2)
微小RNA microRNA(miRNA)
无肌病型皮肌炎 amyopathic dermatomyositis(ADM)
B细胞淋巴瘤/白血病-2 B-cell lymphoma/leukemia-2(Bcl-2)
B细胞淋巴瘤-2促细胞凋亡 B-cell lymphoma 2 interacting mediator of cell death(Bim)
纤维蛋白降解产物 fibrin degradation product(FDP)
纤维蛋白原 fibrinogen(FIB)
小泛素样修饰物激活酶 small ubiquitin-like modifier activating enzyme(SAE)
小脑后下动脉 posterior inferior cerebellar artery(PICA)
信号识别颗粒 signal recognition particle(SRP)
旋转血栓弹力图 rotational thromboelastometry(ROTEM)
血管周围间隙 perivascular spaces(PVS)［Virchow-Robin间隙 Virchow-Robin spaces(VRS)］
血栓弹力图 thrombelastograph(TEG)
血小板计数 platelet count(PLT)
血小板/淋巴细胞比值 platelet to lymphocyte ratio(PLR)
延髓内侧梗死 medial medullary infarction(MMI)
硬膜外血贴术 epidural blood patch(EBP)
硬膜外血肿 epidural hematoma(EDH)
硬膜下血肿 subdural hematoma(SDH)
运动单位电位 motor unit potential(MUP)
运动认知风险综合征 motoric cognitive risk syndrome(MCR)
增强子结合蛋白同源蛋白 enhancer binding protein homologous protein(CHOP)
正常灌注压突破现象 normal perfusion pressure breakthrough(NPPB)
直接血栓抽吸技术 a direct aspiration fist-pass technique(ADAPT)
中性粒细胞/淋巴细胞比值 neutrophil to lymphocyte ratio(NLR)
肿瘤坏死因子-α tumor necrosis factor-α(TNF-α)
转录中介因子1-γ transcriptional intermediary factor 1-γ(TIF1-γ)
椎动脉 vertebral artery(VA)
自发性低颅压综合征 spontaneous intracranial hypotension(SIH)
自发性小脑出血 spontaneous cerebellar hemorrhage(SCH)
总胆固醇 total cholesterol(TC)
左旋多巴等效剂量 levodopa equivalent dose(LED)