抗MDA5抗体相关皮肌炎合并急进性肺间质病变的临床特点

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【摘要】 目的 回顾性分析抗黑色素瘤分化相关基因5(melanoma differentiation associated gene 5,MDA5)抗体相关皮肌炎合并急进性肺间质病变(rapidly progressive interstitial disease,RP-ILD)患者临床特点及预后不良因素。**方法** 回顾性分析2017年1月至2019年6月南京鼓楼医院风湿免疫科及呼吸科收住的67例抗MDA5抗体阳性的皮肌炎患者,收集患者的一般临床资料、实验室和影像学检查,按有无出现RP-ILD分组,并统计死亡情况,分析其预后不良因素。**结果** 67例患者中,26例出现RP-ILD,41例未出现RP-ILD,两组在临床无肌病皮肌炎(clinical amyopathic dermatomyositis,CADM)发生率、病初低氧血症发生率、早发ILD比例、淋巴细胞总数、$CD3^+CD4^+$T计数、IgM、ALP上差异有统计学意义。67例患者初诊时最常见的影像学分型是非特异性间质性肺炎(nonspecific interstitial pneumonia,NSIP)(46.3%),其次是NSIP+机化性肺炎(cryptogentic organizing pneumonia,COP)(17.9%)、COP(14.9%)和急性间质性肺炎(acute interstitial pneumonia,AIP)(9.0%),普通型间质性肺炎(usual interstitial pneumonia,UIP)最少见(3.0%)。影像学征象的单因素分析显示,RP-ILD组实变影、纵膈气肿更多见,两组在NSIP和AIP分型上差异有统计学意义。二元Logistic回归分析显示,病初合并低氧血症、$CD3^+CD4^+$T细胞计数下降是患者出现RP-ILD预后不良的因素。67例患者中29例(43.3%)死亡,均死于肺间质病变及感染。死亡风险的单因素分析显示,年龄、病初合并低氧血症、淋巴细胞总数、$CD3^+CD4^+$T细胞计数、$CD3^+CD8^+$T细胞计数、抗MDA5抗体滴度、影像分型为AIP共7种因素和死亡相关。排除年龄、MDA5抗体滴度等混杂因素后,病初合并低氧血症,$CD3^+CD4^+$T细胞计数和死亡风险相关。**结论** 抗MDA5抗体相关皮肌炎常合并RP-ILD,死亡率高,病初合并低氧血症、$CD3^+CD4^+$T细胞计数下降是患者出现RP-ILD及死亡的预后不良因素。

【关键词】 皮肌炎; 抗MDA5; 肺间质病变(ILD); 预后

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Clinical characteristics of anti-MDA5 antibody-positive dermatomyositis patients with rapidly progressive interstitial lung disease

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【Abstract】 Objective To retrospectively investigate the clinical characteristics and poor prognostic factors of patients with anti-melanoma differentiation associated gene 5 (MDA5) antibody-positive dermatomyositis with pulmonary interstitial disease. **Methods** The clinical data, laboratory and imaging examinations of 67 patients with anti-MDA5 antibody-positive dermatomyositis and interstitial lung disease

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(ILD) in Department of Rheumatology and Immunology and Department of Respiratory Medicine, Nanjing Drum Tower Hospital, from Jan.2017 to Jun.2019 were collected. These patients were grouped according to the presence or absence of rapidly progressive ILD (RP-ILD), and deaths were counted to analyze the poor prognostic factors. **Results** Of the 67 patients, 26 had RP-ILD and 41 had not, There were statistical differences in the incidence of clinical amyopathic dermatomyositis (CADM), the incidence of hypoxemia at the beginning of disease, the proportion of early-onset ILD, the total number of lymphocytes, $CD3^+CD4^+$ T counts, IgM, and ALP in the two groups. The most common imaging type at the time of initial diagnosis in 67 patients was nonspecific interstitial pneumonia (NSIP) (46.3%), followed by NSIP+cryptogentic organizing pneumonia (COP) (17.9%), COP (14.9%), acute interstitial pneumonia (AIP) (9.0%), and usual interstitial pneumonia (UIP) was the least common (3.0%). A single factor analysis showed that consolidation images, and pneumomediastinum were more common in the RP-ILD group, and there were statistical differences between the two groups in NSIP and AIP typing. Binary Logistic regression analysis showed that hypoxemia at the beginning of disease, decreased $CD3^+CD4^+$ T cell counts were poor prognostic factors for patients with RP-ILD. Of the 67 patients, 29 (43.3%) died, all of whom died of pulmonary interstitial disease and infection. By COX single factor regression analysis of death-related risk factors, age, early onset of hypoxemia, total lymphocyte counts, $CD3^+CD4^+$ T cell counts, $CD3^+CD8^+$ T cell counts, anti-MDA5 antibody titer, and the AIP image typing were related to the risk of death. After excluding confounding factors such as age and MDA5 antibody titer, hypoxemia at the beginning of the disease, $CD3^+CD4^+$ T cell is related to the risk of death. **Conclusion** Anti-MDA5 antibody-positive dermatomyositis is often associated with RP-ILD, and the death rate is high. Hypoxemia at the beginning of disease and decreased $CD3^+CD4^+$T cell counts are the adverse prognostic factors for RP-ILD and death.

【Key words】 dermatomyositis; anti-MDA5; interstitial lung disease (ILD); prognosis

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皮肌炎是一类主要累及横纹肌,同时伴有皮肤损害的自身免疫性疾病,常并发肺间质病变。近年来陆续发现皮肌炎患者体内存在肌炎特异性抗体(myositis-specific autoantibodie,MSA),与皮肌炎独特的临床表型相关,有助于疾病诊断、分型、评估病情和判断预后[1],其中抗黑色素瘤分化相关基因5(melanoma differentiation associated gene 5,MDA5)抗体与肺间质病变尤其是急进性肺间质病变(rapidly progressive interstitial lung disease, RP-ILD)高度相关[2]。抗MDA5抗体相关皮肌炎患者常在发病初期就出现RP-ILD,激素和常规免疫抑制剂治疗效果不佳,死亡率高。有研究发现[3],病初铁蛋白增高、白蛋白降低、肺泡动脉氧分压差增大是抗MDA5抗体阳性患者预后不良的预测因素,但国内相关报道少见。本研究通过对抗MDA5抗体阳性的皮肌炎患者进行分析,总结其临床特征及预后不良因素。

资料和方法

研究对象 回顾性分析2017年1月至2019年6月南京鼓楼医院风湿免疫科及呼吸科收住的67例抗MDA5抗体阳性的皮肌炎患者,上述患者均满足1975年提出的皮肌炎分类标准Bohan和Peter[4]。临床无肌病皮肌炎(clinical amyopathic dermatomyositis,CADM)包括无肌病皮肌炎和低肌病皮肌炎。所有患者按有无出现RP-ILD分组。RP-ILD被定义为肺间质病变(interstitial lung disease, ILD)发病3个月内出现急进性呼吸衰竭,劳力性气促加重,并伴有下列任意一项:(1)肺部高分辨CT(high resolution computed tomography,HRCT)表现进展;(2)动脉血气血氧分压下降>1.33 kPa[5]。所有患者均行HRCT检查,层厚1 mm,由2名5年以上年资的影像科医师对图像进行分析:根据Fleischner协会诊断标准[6]评估病变形态特征,并根据2013年美国胸科

协会更新的特发性间质性肺炎的声明[7]评价ILD类型，包括普通型间质性肺炎（usual interstitial pneumonia，UIP）、非特异性间质性肺炎（nonspecific interstitial pneumonia，NSIP）、机化性肺炎（cryptogenic organizing pneumonia，COP）、NSIP-COP和急性间质性肺炎（acute interstitial pneumonia，AIP）。

方法　收集患者的一般资料（性别、年龄）、病史（病程、全身症状、肺部症状）、体征（治疗初血氧饱和度、皮疹、肌力）、实验室检查（谷丙转氨酶ALT、谷草转氨酶AST、乳酸脱氢酶LDH、谷胺酰转肽酶GGT、碱性磷酸酶ALP、白蛋白ALB、免疫球蛋白IgA/G/M、铁蛋白、补体C3、C4、血沉、C反应蛋白、肌酸激酶CK、淋巴细胞计数、抗MDA5抗体、抗RO52抗体）、影像学检查及治疗方案，电话随访生存情况（是否死亡及死亡时间），观察时间18个月）。抗MDA5抗体由欧盟公司抗肌炎抗体谱IgG检测试剂盒检测。

统计学处理　应用SPSS 18.0统计软件进行数据统计分析，符合正态分布的计量资料用$\bar{x}\pm s$表示，采用t检验进行分析；定性资料采用率或构成比表示，采用χ^2检验分析；多项分类资料采用二元Logistic逐步回归分析；死亡风险因素采用COX回归分析。$P<0.05$为差异有统计学意义。

结　　果

一般情况　67例患者中，女性48例，男性19例，男女比例为1∶2.5。平均年龄51.3（21～86）岁。从起病到诊断的平均时间3.0（1～24）个月。43例（64.2%）以皮疹乏力等症状首诊于风湿科，24例（35.8%）以发热咳嗽气喘等症状首诊于呼吸科。50例（74.6%）被诊断为CADM。所有患者均合并间质性肺炎，其中26例（38.8%）出现RP-ILD，按是否出现RP-ILD分组，两组在CADM发生率上差异有统计学意义（$P<0.05$），在性别、年龄、病程方面，两组差异无统计学意义（表1）。将皮肌炎和ILD发病间隔短于1个月定义为同时发病，67例患者中35例以皮肌炎症状起病，25例以皮肌炎和ILD同时起病，仅有7例以ILD症状起病。将ILD症状早于或同时于皮肌炎起病的定义为早发ILD，两组中早发ILD更易出现RP-ILD（表1）。

临床症状和体征分析　67例患者中，半数以上有乏力感，40%～50%病初有发热、关节痛，31%有肌肉酸痛症状，26%查体有肌力减退（肌力＜5级）。少数出现咽痛声嘶、饮水呛咳或吞咽困难（12%）。大部分患者有典型皮肌炎皮疹，其中Gottron征最多见（78%），其次为向阳疹（63%）、V字征（43%）、技工手（42%）和皮肤或指端溃疡（15%）。病初低氧血症（SPO_2＜90%）占31%。对临床症状和体征进行单因素分析发现，RP-ILD组的病初低氧血症发生率更高（$P<0.05$），而在关节痛、发热、肌力减退、咽痛声嘶、吞咽困难、特征性皮疹方面，两组差异无统计学意义（表1）。

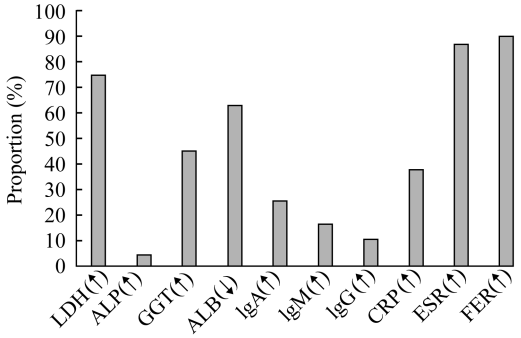
表1　RP-ILD组和非RP-ILD组临床特征比较

Tab 1　Comparison of clinical characteristics between RP-ILD group and non-RP-ILD group　[n（%）]

Clinical characteristics	RP-ILD（n=26）	Non RP-ILD（n=41）	χ^2	P
CADM	25（96.15）	25（60.98）	10.40	**0.001**
Early ILD	17（65.38）	15（36.59）	5.29	**0.021**
Hypoxemia	17（65.4）	4（9.8）	22.88	**＜0.001**

CADM：Clinical amyopathic dermatomyositis；RP-ILD：Rapidly progressive interstitial lung disease.

实验室检查分析　大部分患者有铁蛋白、血沉升高，60%～80%出现LDH升高、淋巴细胞总数降低、白蛋白降低。半数患者有肝功能异常，主要表现为ALT、AST或GGT升高，ALP升高较少。30%～40%患者出现肌酸激酶（CK）和CRP升高，少数有免疫球蛋白增高（图1）。67例患者中合并



LDH：Lactate dehydrogenase；ALP：Alkaline phosphatase；GGT：Gamma glutamyl transpeptidase；ALB：Albumin；CRP：C-reactive protein；ESR：Erythrocyte sedimentation rate；FER：Ferritin.

图1　67例患者的实验室检查结果

Fig 1　Laboratory examination results of 67 patients

RO52抗体阳性47例(70%)。单因素分析显示,RP-ILD组和非RP-ILD组的淋巴细胞总数、$CD3^+CD4^+$T计数都偏低,淋巴细胞总数、$CD3^+CD4^+$T和发生RP-ILD呈负相关,IgM和ALP在两组患者中差异有统计学意义,但均值均在正常范围之内,有无临床意义需进一步观察(表2、图2)。两组在ALT、AST、LDH、GGT、白蛋白、IgA、IgG、铁蛋白、肌酸激酶、补体、血沉、CRP、$CD3^+CD8^+$T、B淋巴细胞、NK淋巴细胞、MDA5抗体、RO52抗体方面,差异均无统计学意义。

表2 RP-ILD组和非RP-ILD组实验室检查比较

Tab 2 Comparison of laboratory tests between RP-ILD group and non-RP-ILD group ($\bar{x}\pm s$)

Laboratory tests	RP-ILD (n=26)	Non-RP-ILD (n=41)	t	P
Total lymphocytes (10^9/L)	0.73±0.32	0.98±0.34	−2.95	0.004
$CD3^+CD4^+$T (10^9/L)	0.28±0.13	0.42±0.18	−3.55	0.001
ALP (IU/L)	89.35±40.62	70.22±26.04	2.05	0.045
IgM (g/L)	1.89±1.06	1.38±0.52	2.23	0.030

ALP: Alkaline phosphatase.

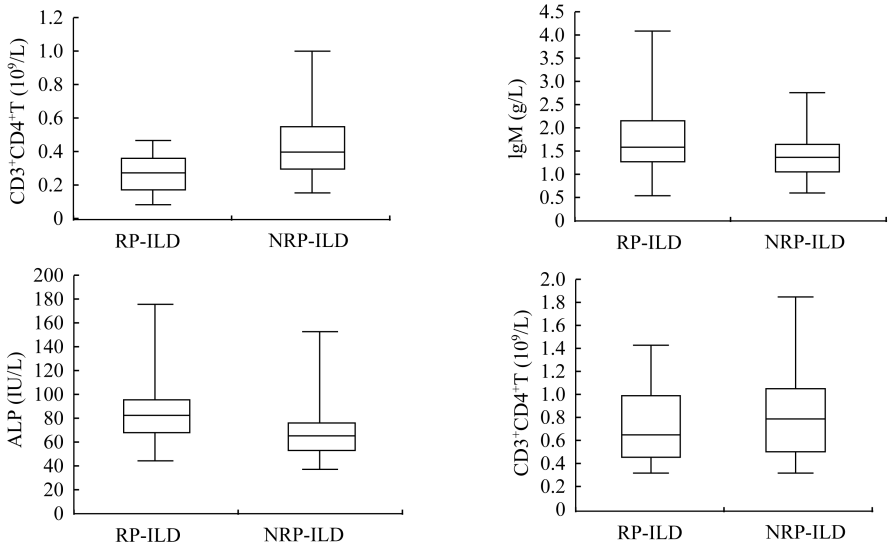
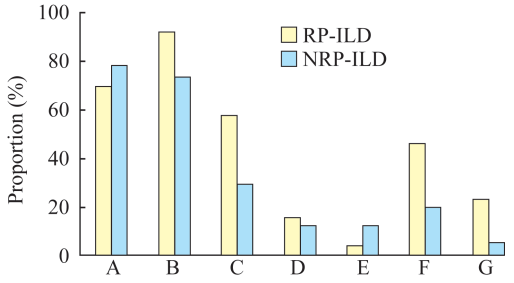


图2 RP-ILD组和非RP-ILD组的$CD3^+CD4^+$T计数、IgM、ALP和淋巴细胞总数

Fig 2 $CD3^+CD4^+$T counts, IgM, ALP, total lymphocyte counts in RP-ILD group and non-RP-ILD group

影像学检查分析 67例患者初次诊断ILD时影像学表现中,磨玻璃影最多见(80%),其次是网线状影(75%)、实变影(40%)、牵拉性支气管扩张(27%)、结节影(13%)、蜂窝影(9%),病程中有8例出现纵膈气肿(12%)。影像学征象的单因素分析显示,两组在实变影(58%和29%,P=0.021)、纵膈气肿(23%和5%,P=0.048)上的差异有统计学意义(图3)。因患者缺乏肺活检病理,仅根据临床和影像学检查排除6例不确定分型的,最常见的影像学分型是NSIP(46%),其次是NSIP+OP(18%)、OP(15%)、AIP(9%)和UIP(3%)。在影像学分型方面,非RP-ILD组大多为NSIP(63%),两组在NSIP和AIP分型上的差异有统计学意义(P<0.05,表3)。图4、图5为2例典型影像学征象。



A: Reticulation; B: Ground-glass opacities; C: Consolidation; D: Nodules; E: Honeycombing; F: Traction branch; G: Pneumomediastinum.

图3 RP-ILD组和非RP-ILD组各种影像学表现

Fig 3 Imaging signs in RP-ILD group and non-RP-ILD group

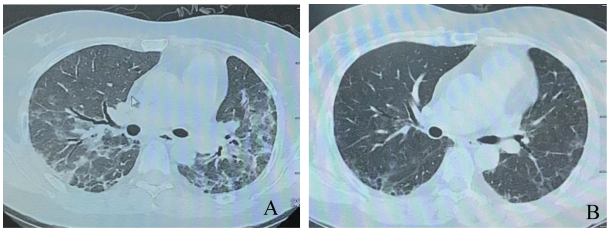
MDA5相关皮肌炎患者出现RP-ILD的多因素分析 RP-ILD组和非RP-ILD组在CADM发生率、早发ILD发生率、病初低氧血症、淋巴细胞总数、$CD3^+CD4^+$T计数、IgM、ALP、病程中纵膈气肿

表3　RP-ILD组和非RP-ILD组影像学检查比较

Tab 3　Comparison of imaging examination between RP-ILD group and non-RP-ILD group　[n（%）]

Imaging examination	RP-ILD（n=26）	Non-RP-ILD（n=41）	χ^2	P
UIP	0	2（4.88）	Fisher	0.518
NSIP	7（26.92）	24（58.54）	6.40	**0.011**
COP	5（19.23）	5（12.20）	0.19	0.663
NSIP+COP	7（26.92）	5（12.20）	1.45	0.228
AIP	6（23.08）	0	7.76	**0.005**

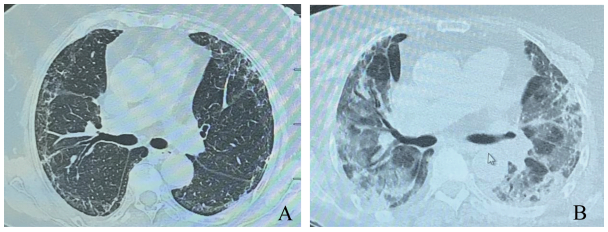
UIP：Usual interstitial pneumonia；NSIP：Nonspecific interstitial pneumonia；COP：Cryptogenic organizing pneumonia；AIP：Acute interstitial pneumonia.



A：Multiple ground glass opacities，reticulations and consolidations at the first diagnosis，consistent with the NSIP+COP classification；B：The ground glass opacities and consolidations was absorbed after the treatment of glucocorticoid and cyclophosphamide.

图4　1例44岁女性患者治疗前后的影像学表现

Fig 4　Imaging finding of a 44-year-old female patient before and after treatment



A：Sub-pleural reticulations and ground glass opacities at the initial diagnosis，consistent with the NSIP classification；B：One month later，progress was made with extensive ground glass opacities and consolidations in both lungs.

图5　1例65岁女性患者治疗前后的影像学表现

Fig 5　Imaging finding of a 65-year-old female patient before and after treatment

发生率、AIP分型方面差异有统计学意义。将CADM、早发ILD、$CD3^+CD4^+$T细胞计数下降（<0.4×10^9/L）、病初低氧血症、纵膈气肿等6个分类变量纳入多因素分析，将是否出现RP-ILD作为因变量，采用二元Logistic回归分析，显示$CD3^+CD4^+$T细胞计数下降、病初合并低氧血症是患者出现RP-ILD预后不良的因素（表4）。

MDA5相关皮肌炎患者死亡情况分析　67例患者中，29例（43.3%）死亡，均死于ILD及其并发症。26例RP-ILD患者中有23例在诊断后4个月内死亡，3例经治疗后病情控制，41例未出现RP-ILD的患者中，3例在病情控制半年到1年后，激素及免疫抑制剂减量过程中出现ILD进展死亡，3例在治疗过程中出现重症感染死亡。死亡时患者的平均年龄为54.7（39～86）岁，诊断至死亡的平均时间为2.8（0.5～14）个月。对性别、年龄、病程、关节痛、皮肌炎分型、发热、皮肤溃疡、皮疹类型、早发ILD、ALT、AST、LDH、ALP、GGT、ALB、免疫球蛋白、补体、CK、血沉、CRP、淋巴细胞分类计数、抗MDA5抗体、RO52抗体、病初低氧血症、ILD类型等39个因素进行单因素分析，发现年龄、病初合并低氧血症、淋巴细胞总数、$CD3^+CD4^+$T细胞计数、$CD3^+CD8^+$T细胞计数、抗MDA5抗体滴度、影像分型为AIP等7个因素差异上的有统计学意义（表5）。排除年龄和抗MDA5抗体滴度等混杂因素后，病初低氧血症和$CD3^+CD4^+$T计数与死亡风险相关（表6）。

表4　MDA5相关皮肌炎患者出现RP-ILD的预后不良因素分析

Tab 4　Analysis of poor prognostic factors for RP-ILD in patients with anti-MDA5 antibody-positive dermatomyositis

Factor	β	SE	Wald	P	OR	95%CI
$CD3^+CD4^+$T	1.651	0.799	4.274	0.039	5.213	1.089-24.942
Hypoxemia	2.438	0.801	9.275	0.002	11.453	2.385-55.008

讨　论

抗MDA5抗体是CADM常见的MSA，该抗体由Sato等[8]于2005年在一名日本患者中首次检出。抗MDA5抗体相关皮肌炎在亚裔女性中多见，且病情更严重[9]，本组病例男女比例为1∶2.5，且多为CADM患者（74.6%），虽然很多患者主诉有乏力和肌肉酸痛，但客观检查并无肌力下降或仅有轻度肌力下降。在出现RP-ILD的患者中CADM比例更高（96.15%），这也和以往研究认为CADM易出现急性ILD相符。本组中，超过半数患者有肝酶（ALT、AST、LDH）升高，但未发现肝功能损害与RP-ILD相关。Nagashima等[10]研究发现，肝功能损害是抗MDA5抗体阳性的CADM患者常见的肌肉外表现，但与急进性死亡无关。

亚裔成人抗MDA5抗体相关皮肌炎患者的ILD发生率高达90%～95%[11]，部分患者早期出现

表5 MDA5相关皮肌炎患者死亡相关的单因素COX分析

Tab 5 COX single factor regression analysis of death-related factors in patients with anti-MDA5 antibody-positive dermatomyositis

Factor	B	SE	χ^2	*P*	HR (95%CI)
Age	0.033	0.015	4.606	0.032	1.034 (1.003-1.065)
Hypoxemia	1.505	0.395	14.515	<0.001	4.504 (2.077-9.768)
Total lymphocytes	-2.235	0.700	10.201	0.001	0.107 (0.027-0.422)
$CD3^+CD4^+T$	-6.274	1.654	14.393	<0.001	0.002 (0.000-0.048)
$CD3^+CD8^+T$	-6.141	2.563	5.743	0.017	0.002 (0.000-0.327)
Anti-MDA5 (+++) *vs.* (+/++)	2.198	1.020	4.646	0.031	9.011 (1.221-66.520)
AIP	1.339	0.479	7.832	0.005	3.817 (1.494-9.751)

Refer to Tab 3.

表6 MDA5相关皮肌炎患者死亡风险的多因素COX分析

Tab 6 COX multivariate regression analysis of death-related factors in patients with anti-MDA5 antibody-positive dermatomyositis

Factor	β	SE	χ^2	*P*	HR (95%CI)
Hypoxemia	1.115	0.419	7.067	0.008	3.049 (1.340-6.936)
$CD3^+CD4^+T$	-3.805	1.673	5.172	0.023	0.022 (0.001-0.591)

RP-ILD,是最主要的死亡原因。本组中所有患者均合并ILD。病初低氧血症和$CD3^+CD4^+T$降低是出现急进性进展及死亡的预后不良因素。本组出现RP-ILD的26例患者中,17例在就诊时合并严重低氧血症,虽经呼吸支持,强化免疫抑制及大剂量激素治疗,症状无好转,短期内死亡(2周至4个月),死亡率高与急进性病程及治疗时间有关,若已出现低氧血症甚至呼吸衰竭,则治疗反应极差。在自身免疫性疾病中,外周血淋巴细胞亚群的评估可用于指示疾病活动及判断预后,$CD3^+CD4^+T$作为辅助性T细胞在免疫疾病中发挥重要作用。有研究报道,合并ILD的抗MDA5抗体阳性皮肌炎患者肺泡灌洗液中存在大量淋巴细胞,且CD4/CD8比例升高[12],推测大量血清中的CD4淋巴细胞迁移到肺泡,激活细胞因子形成炎症风暴,最终导致呼吸衰竭而死亡。同时,$CD4^+T$细胞降低增加了机会性感染的风险,本组有3例患者病初未出现RP-ILD,但后期出现重症感染死亡,这3例患者初诊时$CD4^+T$均<0.3×10^9/L。皮肌炎合并ILD患者后期常继发真菌感染(主要白念和卡肺),这也是导致死亡的重要原因,建议$CD4^+T$低下患者可预防性使用复方磺胺甲恶唑。血清抗MDA5抗体滴度被认为与疾病活动性显著相关,且可作为评估疗效的指标[13]。高滴度的血清抗MDA5抗体和急性死亡相关,低滴度的慢性病程患者预后和无抗MDA5抗体的皮肌炎患者类似[14]。我们的单因素分析也发现抗MDA5抗体滴度增高和死亡风险相关。近期报道显示,RO52、抗MDA5抗体双阳性的皮肌炎患者较单纯抗MDA5抗体阳性的患者预后更差,死亡率更高[15-16]。本组中70.1%的患者抗MDA5抗体、RO52双抗体阳性,但并未发现RO52抗体与死亡的相关性,有待今后延长随访时间、扩大样本量继续观察。

病理学研究表明[17],NSIP和OP是DM-ILD最常见的类型,且NSIP和OP常共存。本组67例患者的HRCT表现,以磨玻璃影和网线状影发生率最高,符合NSIP的分型。RP-ILD组实变影更多见,提示肺泡渗出明显,符合OP、NSIP+OP分型,少数RP-ILD患者在初诊时有明显咳喘、发热,影像学表现为广泛的磨玻璃影和实变影,分型为AIP,均在短期内死亡。Meta分析显示[18],抗MDA5抗体相关皮肌炎患者纵膈气肿发生率明显增加,常和不良预后相关。推测其发生机制是肺泡损伤导致其膨胀,气体从肺泡进入间质,然后沿脉管系统向肺门和纵膈流注。本组中有8例(11.9%)在病程中出现纵膈气肿,其中6例发生RP-ILD死亡,纵隔气肿与RP-ILD风险相关。

抗MDA5抗体相关皮肌炎合并RP-ILD目前缺乏统一的治疗方案,多基于经验性治疗。文献报道较多的是大剂量激素联合钙调磷酸酶抑制剂、环磷酰胺三联方案。一项日本的多中心前瞻性研究显示,在RP-ILD早期给予三联方案可显著提升6个月生存率[19]。有小样本研究提示对于激素和免疫抑制剂无效的RP-ILD患者,加用托法替布可改善预后[20]。仁济医院的一项单中心研究也表明,托法替布可以显著提高早期抗MDA5抗体相关CADM-ILD患者的生存率[21]。本组中部分患者就诊时皮疹轻微,但已有明显低氧血症甚至呼吸衰竭,给予三联方案效果欠佳,短期内死亡,所以对于此类患者,临床上应给予足够重视,早期完善CT、肌炎抗体、淋巴细胞免疫功能、血气、肺功能等,综合评估病

情，早期诊断，精准干预，提高生存率。

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