

## 多发性肌炎/皮肌炎合并间质性肺炎的 临床和影像学特征及转归分析

赵云 吕玲<sup>△</sup>

(复旦大学附属华山医院风湿科 上海 200040)

**【摘要】** 目的 探讨合并间质性肺炎(interstitial lung disease,ILD)的多发性肌炎(polymyositis,PM)/皮肌炎(dermatomyositis,DM)患者的临床、影像学特征及转归。方法 回顾分析我院2005年1月1日至2008年12月31日间31例合并ILD的多发性肌炎/皮肌炎患者资料,比较其确诊时的临床表现和胸部高分辨率CT(HRCT)表现及其转归。根据HRCT表现将患者分为两组:第1组主要表现为磨玻璃样变或实变,第2组主要表现为网格状或纤维条索状。结果 第1组共10例患者,其中2例生存,8例死亡;第2组共21例患者,其中18例生存,3例死亡。两组间呼吸困难( $P=0.015$ )和初诊时低 $\text{PaO}_2$  ( $P=0.003$ )有统计学差异,两组间采用的激素冲击治疗( $P=0.045$ )及结局( $P=0.000$ )亦有明显的统计学差异。Logistic回归分析显示,呼吸困难( $\text{OR}=0.06, P=0.014$ )和初诊时低 $\text{PaO}_2$  ( $\text{OR}=1.18, P=0.049$ )是发生胸部HRCT磨玻璃样变或实变的独立危险因素。肌力水平和肌酶水平在不同的胸部HRCT表现间无明显统计学差异。通过Kaplan-Meier法和Log-rank  $t$  检验发现,第1组患者的生存率较第2组差( $P=0.000$ )。结论 胸部HRCT表现为磨玻璃样变或实变的患者比表现为纤维条索样变或网格状改变的患者预后要差。

**【关键词】** 多发性肌炎; 皮肌炎; 间质性肺炎

**【中图分类号】** R 593.26 **【文献标志码】** B

## The clinical manifestations, imaging features and prognosis of interstitial pneumonia in polymyositis/dermatomyositis

ZHAO Yun, LV Ling<sup>△</sup>

(Department of Rheumatology, Huashan Hospital, Fudan University, Shanghai 200040, China)

**【Abstract】 Objective** To study the clinical and chest imaging features of chest and the prognosis of patients with interstitial lung disease (ILD) due to polymyositis (PM)/dermatomyositis (DM).

**Methods** We analyzed the clinical manifestation and high resolution computed tomography (HRCT) manifestation of chest in 31 patients with PM/DM combining with ILD diagnosed in our hospital from January 1, 2005 to December 31, 2009. According to the manifestation of HRCT, we separated all the patients into two groups; the HRCT manifestation of patients in the first group was ground-glass change or real change, and the other was linear opacities or grid variable.

**Results** There were 10 patients in the first group with 2 alive and 8 dead. In the second group, there were 21 patients with 18 alive and 3 dead. We found that there were statistical differences between the two groups in dyspnea ( $P=0.015$ ),  $\text{PaO}_2$  ( $P=0.003$ ) at preliminary diagnosis, high-dose steroid pulse therapy ( $P=0.045$ ) and outcome ( $P=0.000$ ). Logistic regression test revealed that dyspnea ( $\text{OR}=0.06, P=0.014$ ) and  $\text{PaO}_2$  ( $\text{OR}=1.18, P=0.049$ ) at preliminary diagnosis were the independent negative factors. There was no statistical difference in the extent of muscle weakness and the level of serum creatase between the two groups. Kaplan-Meier curve and log-rank test showed that the prognosis of the first group was worse than the second group ( $P=0.000$ ).

**Conclusions** The prognosis of patients with HRCT manifestation of ground-glass change or real change was worse than those with linear opacities or grid variable HRCT manifestation.

<sup>△</sup>Corresponding author E-mail: huashanlvling@sina.com

**【Key words】** polymyositis; dermatomyositis; interstitial pneumonia

多发性肌炎(polymyositis, PM)/皮肌炎(dermatomyositis, DM)合并间质性肺炎(interstitial lung disease, ILD)是由 Mills 和 Mathews 于 1956 年首次报道的,之后的一些研究发现,是否合并 ILD 是影响 PM/DM 患者预后的重要因素。因各个报道的诊断方法不同,PM/DM 合并 ILD 的发生率为 5%~65%<sup>[1-3]</sup>。

之前的报道大多关注 PM/DM 患者合并 ILD 的预测因素及对预后的影响<sup>[4-6]</sup>,尽管报道的预后差别较大,但一致认为 ILD 是 PM/DM 不良预后因素之一。Pawel 等<sup>[7]</sup>报道,抗 Jo-1 抗体阳性(64.2% vs. 11.1%),有关节炎症状(64.2 vs. 18.1%)及雷诺现象(38% vs. 0%)的患者更容易发生 ILD。有研究表明<sup>[8]</sup>,抗 Jo1 抗体、呼吸困难及咳嗽是间质性肺病 3 个独立的危险因素,而高水平的 LDH(>400 U/L)与间质性肺病的发生呈负相关。但近来陆续有报道显示,并不是所有合并 ILD 的 PM/DM 患者的预后都很差,ILD 的类型与患者的预后密切相关<sup>[9-11]</sup>。Jin 等<sup>[11]</sup>根据临床特点将 PM/DM 患者间质性肺炎分为急性和慢性两种,急性的定义为在确诊前 1 个月内出现呼吸困难和低氧血症并呈进行性加重,或需插管护理,其他的归为慢性间质性肺炎,72%的急性患者尽管进行了强化治疗,还是在 1~2 个月内死于呼吸衰竭;而慢性患者 3 年的死亡率与没有并发间质性肺炎的患者没有统计学上的差异。而 Olivier 等<sup>[12]</sup>初步探讨了 PM/DM-ILD 的影像学特点,指出 PM/DM-ILD 的 HRCT 主要表现为磨玻璃样变、网格状改变、蜂窝状改变、实变等,并认为蜂

窝状改变的患者预后较差。

但目前国内外将 PM/DM 患者的临床表现与 ILD 的特点结合起来共同研究如何影响患者的预后的报道很少见。本研究以合并 ILD 的 PM/DM 患者的肺部 HRCT 表现为焦点,结合患者的临床表现,研究 PM/DM 合并的 ILD 的特点及其与预后之间的关系,是本领域研究的一个新的方向。

## 对象和方法

### 研究对象

**一般情况** 回顾分析 2005 年 1 月 1 日至 2008 年 12 月 31 日年间我院风湿科诊断、治疗,并在出院后保持随访的 31 例合并 ILD 的 PM/DM 患者。所有患者均符合 1975 年 Bohan 和 Peter 提出的特发性炎症性肌病(idiopathic inflammatory myopathies, IIM)的诊断标准<sup>[13]</sup>。所有患者在诊断后均予每天 0.5~1 mg/kg 的激素治疗,并给予环磷酰胺 0.8 mg/m<sup>2</sup> 每月 1 次,连用半年,之后每 3 个月 1 次,连用 1 年。治疗过程中根据患者病情需要行激素冲击治疗或换用环孢素等其他免疫抑制剂,激素冲击治疗方案为 500 mg/d,连用 3~5 d,或 1 g/d,连用 3 d。

**分组** 根据患者胸部 HRCT 表现分为 2 组:第 1 组(CT1)主要表现为磨玻璃样变或实变(图 1A、B),第 2 组(CT2)主要表现为网格状或纤维条索状(图 1C、D)。

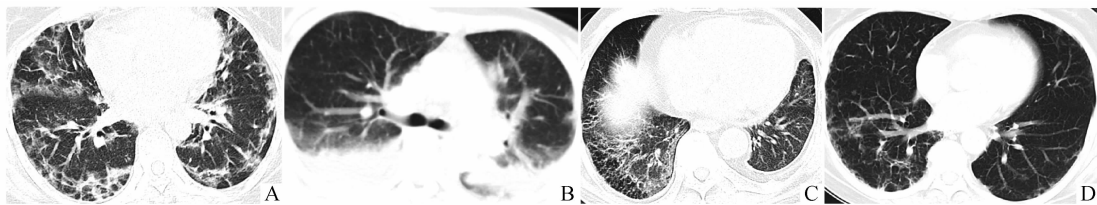


图 1 PM/DM 患者肺部 HRCT 表现

Fig 1 Representative CT scan of four PM/DM patients

A: Ground-glass change covered tow lungs symmetrically; B: Real chang was showed in tow lungs dissymmetrically; C: Grid variable change was mainly found in the basilar part of tow lungs; D: Linear opacities was was also mainly found near the basilar part of tow lungs.

肺部 HRCT 扫描时患者取仰卧位,屏气状态下自肺尖至肺底扫描。先作常规 CT 扫描,层厚 10.0 mm,螺距 1.5,间隔 10.0 mm,然后在感兴趣区作 HRCT 扫描,层厚 1.5~2.0 mm,间隔 1.5~2.0 mm。为消除背部血管坠积效应,部分患者加做俯卧位扫描。所有普通胸片及 HRCT 片结果均经 2

名有经验的放射科医师阅片讨论,并作出诊断。

**统计方法** 计量资料采用 *t* 检验,计数资料采用  $\chi^2$  检验,多因素分析采用 Logistic 回归分析确定独立危险因素,通过 Kaplan-Meier 法和 Log-rank *t* 检验比较两组患者的生存曲线, $P < 0.05$  时认为有统计学差异。统计软件采用 Stata 7.0。

## 结 果

**一般情况** 所有患者随访至 2009 年 5 月 31 日止。第 1 组共 10 例患者,其中男性 1 例,女性 9 例,年龄为(53.34 ± 3.59)岁,生存患者 2 例,死亡患者

8 例。第 2 组共 21 例患者,其中男性 7 例,女性 14 例,年龄为(52.03 ± 2.85)岁,生存患者 18 例,死亡患者 3 例。两组患者临床表现间的差异见表 1,两组患者实验室检查间的差异见表 2,两组患者的大剂量激素冲击治疗情况及结局见表 3。

表 1 两组 PM/DM 患者的临床表现

Tab 1 The clinical manifestations of the PM/DM patients in the two groups

Item		CT1	CT2	$\chi^2$	P
Sex	male	1	7	1.926	0.165
	female	9	14		
Age (y)		53.34 ± 3.59	52.03 ± 2.85	0.269	0.790
Subset	PM	1	8	2.595	0.107
	DM	9	13		
Cough	yes	8	10	2.917	0.088
	no	2	11		
Dyspnea	yes	8	7	5.907	0.015
	no	2	14		
Upper limb strength	I - II°	3	5	0.136	0.713
	III - IV°	7	16		
Lower limb strength	I - II°	4	5	0.862	0.353
	III - IV°	6	16		
Neck flexor strength	I - II°	4	6	3.876	0.584
	III - IV°	6	14		

CT1: The group of patients whose HRCT manifestation was ground-glass change or real change; CT2: The group of patients whose HRCT manifestation was linear opacities or grid variable.

表 2 两组 PM/DM 患者的实验室检查

Tab 2 The laboratory examination of the PM/DM patients in two groups

Item		CT1	CT2	$\chi^2$ or <i>t</i>	P
ANA	(+)	7	14	0.034	0.853
	(-)	3	7		
Anti-Jo1 antibody	(+)	2	5	0.056	0.813
	(-)	8	16		
ESR (mm/h)		34.0 ± 10.69	29.0 ± 6.38	0.420	0.678
CRP (mg/L)		13.4 ± 4.73	16.1 ± 4.01	-0.408	0.687
PaO <sub>2</sub> (mmHg)		80.9 ± 4.14	93.23 ± 1.77	-3.227	0.003
CK (U/L)		725.2 ± 251.6	1780.4 ± 902.7	1.480	0.150
LDH (U/L)		471.0 ± 51.09	534.6 ± 91.15	0.657	0.6565
Respiratory infection	yes	2	1	1.800	0.180
	no	8	20		

1 mmHg = 0.133 kPa; ANA: Antinuclear antibody; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; PaO<sub>2</sub>: Partial pressure of oxygen in artery; CK: Creatine kinase; LDH: Lactate dehydrogenase; CT1: The group of patients whose HRCT manifestation was ground-glass change or real change; CT2: The group of patients whose HRCT manifestation was linear opacities or grid variable.

表 3 两组 PM/DM 患者的大剂量激素冲击治疗情况及结局

Tab 3 The condition of impact of glucocorticoid and the outcome of the PM/DM patients in two groups

Item		CT1	CT2	$\chi^2$	P
Methylprednisolone pulses	yes	4	2	4.031	0.045
	no	6	19		
Outcome	alive	2	18	12.778	0.000
	dead	8	3		

CT1: The group of patients whose HRCT manifestation was ground-glass change or real change; CT2: The group of patients whose HRCT manifestation was linear opacities or grid variable.

由表1可见, $\chi^2$ 检验显示,在 $\alpha=0.05$ 的水平,呼吸困难( $P=0.015$ )在不同的胸部HRCT表现间有统计学差异,而性别( $P=0.165$ )、年龄( $P=0.790$ )、肌炎的类型( $P=0.107$ )、咳嗽症状( $P=0.088$ )及肌无力程度(上肢 $P=0.713$ ,下肢 $P=0.353$ ,颈屈肌 $P=0.584$ )在两组间未显示出有统计学差异。

从表2可以看出,在 $\alpha=0.05$ 的水平,实验室检查中只有初始治疗时 $\text{PaO}_2$ 水平( $P=0.003$ )在两组间有显著的统计学差异,第1组要低于第2组。

从表3可以看出,两组不同的胸部HRCT表现间采用的激素冲击治疗( $P=0.045$ )及结局( $P=0.000$ )有显著的统计学差异。

由上可知,单因素分析显示呼吸困难( $P=0.015$ )和初始治疗时 $\text{PaO}_2$ 水平( $P=0.003$ )在两组间有统计学差异。进一步通过Logistic回归分析显示呼吸困难( $\text{OR}=0.06, P=0.014$ )和初始治疗时 $\text{PaO}_2$ 水平( $\text{OR}=1.18, P=0.049$ )亦是PM/DM患者发生胸部HRCT磨玻璃样变或实变的独立危险因素(表4)。

表4 Logistic回归分析确定PM/DM患者独立危险因素

Tab 4 To determine the independent negative factors of PM/DM patients through Logistic regression test

Item	OR	95%CI	$\chi^2$
Dyspnea	0.58	0.003-0.986	0.049
$\text{PaO}_2$	1.18	1.033-1.344	0.014

OR:Odds ratio; CI:Confidence interval.

通过Kaplan-Meier法(图2)和Log-rank  $t$ 检验发现,肺部HRCT表现为磨玻璃样变或实变的患者的生存率较表现为纤维条索状或网格状的患者预后差( $P=0.000$ )。

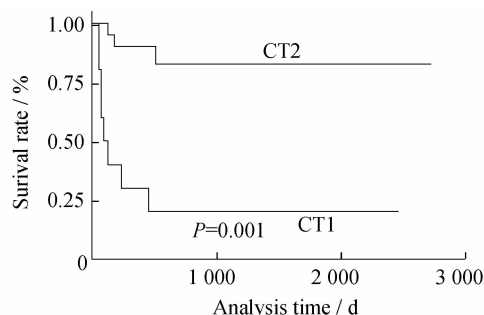


图2 两组PM/DM患者的生存曲线比较

Fig 2 The comparison of survival curves of the PM/DM patients in the two groups

CT1: The group of patients whose HRCT manifestation was ground-glass change or real change; CT2: The group of patients whose HRCT manifestation was linear opacities or grid variable.

## 讨 论

PM/DM是累及全身骨骼肌为主的炎症性肌病,其确切发病机制未明,临床表现多样。ILD是PM/DM主要的并发症,且是引起患者死亡的主要原因之一。但目前尚未报道PM/DM患者合并ILD特异性的影像学改变。美国胸科协会(ATS)和欧洲呼吸学会(ERS)一致认为特发性间质性肺炎(idiopathic interstitial pneumonia, IIP)的分型也可以应用于结缔组织病(connective tissue diseases, CTD)合并的ILD<sup>[14]</sup>。2002年ATS发表的对ATS/ERS IIP的亚型重新界定分类:①寻常型(普通型)ILD/特发性肺纤维化(UIP/IPF);②非特异性间质性肺炎(nonspecific interstitial pneumonia, NSIP);③隐源性机化性肺炎(cryptogenic organizing pneumonia, COP);④急性间质性肺炎(acute interstitial pneumonia, AIP);⑤呼吸性细支气管炎性间质性肺疾病(respiratory bronchiolitis associated interstitial lung disease, RBILD);⑥脱屑性间质性肺炎(desquamative interstitial pneumonia, DIP);⑦淋巴样间质性肺炎(lymphoid interstitial pneumonia, LIP)。但大多数文献报道的PM/DM合并的ILD主要是影像学的描述,而很难将其归为某一特定类型。Leslie等<sup>[15]</sup>报道,PM/DM患者并发的ILD常见的HRCT表现为毛玻璃样变、线状影、斑片影、支气管充气征、肺实质微结节、蜂窝样改变。

本文报道的31例患者中,10例胸部HRCT主要表现为密度较高的磨玻璃样变或实变影,21例患者主要表现为双下肺网格状或纤维条索状及蜂窝状改变,虽然治疗上激素及免疫抑制剂的应用原则一致,而且由于病情的需要,前10例患者中更多采用了超大剂量激素的冲击治疗( $P=0.045$ ),但前10例患者中最终有8例死亡,而后21例患者中只有3例死亡,死亡比例前组明显高于后组。死亡患者可能为Jin等<sup>[11]</sup>报道的AIP,而病情稳定组为其报道的慢性间质性肺炎。这可能就表明11例死亡患者存在急性的肺泡损伤,因此,PM/DM相关的ILD引起的急性肺泡损伤可能是引起患者死亡的主要原因。本研究中,呼吸困难( $P=0.015$ )和初诊时低 $\text{PaO}_2$ ( $P=0.003$ )在不同的胸部HRCT表现间有统计学差异。进一步通过Logistic回归分析得出呼吸困难( $\text{OR}=0.06, P=0.014$ )和初始治疗时 $\text{PaO}_2$ 水平( $\text{OR}=1.18, P=0.049$ )是PM/DM患者发生肺部HRCT磨玻璃样变或实变的独立危险因素。因此可根据上述两个指标来判断合并ILD的PM/DM

患者肺部 HRCT 的表现及其预后。本研究亦发现,肌无力程度及肌酶水平在不同的胸部 HRCT 表现患者间无统计学差异,因此可认为,不能根据患者骨骼肌受累的严重程度来推测患者肺部的损伤程度。本研究还发现,在两组不同的胸部 HRCT 表现间采用的激素冲击治疗( $P = 0.045$ )及结局( $P = 0.000$ )亦有明显的统计学差异,这说明在肺 HRCT 为磨玻璃样变或实变的患者可能存在激素抵抗而对激素冲击治疗反应较差。而且可能是过度的免疫抑制使得本身就存在免疫紊乱的机体更易被感染而增加了患者的死亡风险。由于本研究为回顾性研究,尚缺乏患者定期随访肺部 HRCT,所以无治疗后肺部 HRCT 的变化情况。

#### 参 考 文 献

- [1] Meyer O, Hayem G, Palazzo E, et al. Interstitial lung disease in polymyositis and dermatomyositis [J]. *Clin Exp Rheumatol*, 2005, 23(5): 724 - 732.
- [2] Kang EH, Lee EB, Shin KC, et al. Interstitial lung disease in patients with polymyositis, dermatomyositis and amyopathic dermatomyositis[J]. *Rheumatology*, 2005, 44(10): 1 282 - 1 286.
- [3] Chen IJ, Wu YJJ, Lin CW, et al. Interstitial lung disease in polymyositis and dermatomyositis[J]. *Clin Rheumatol*, 2009, 28: 639 - 646.
- [4] O'Callaghan AS, Horrillo ML, Gall XM, et al. Polymyositis/dermatomyositis associated lung disease: analysis of a series of 81 patients[J]. *Lupus*, 2005, 14: 534 - 542.
- [5] Marie I, Hachulla E, Cherin P, et al. Interstitial lung disease in polymyositis and dermatomyositis[J]. *Arthritis Rheum*, 2002, 47(6): 614 - 622.
- [6] Fathi M, Dastmalchi M, Rasmussen E, et al. Interstitial lung disease, a common manifestation of newly diagnosed polymyositis and dermatomyositis[J]. *Ann Rheum Dis*, 2004, 63: 297 - 301.
- [7] Pawel M, Ewawiesik S, Marzena O, et al. Clinical features and prognosis of patients with idiopathic inflammatory myopathies and anti-Jo-1 antibodies[J]. *Autoimmunity*, 2006, 39(3): 243 - 247.
- [8] Chen YJ, Wu CY, Shen JL, et al. Predicting factors of interstitial lung disease in dermatomyositis and polymyositis [J]. *Acta Derm Venereol*, 2007, 87: 33 - 38.
- [9] Maryam F, Jenny V, Marianne B, et al. Interstitial lung disease in polymyositis and dermatomyositis: longitudinal evaluation by pulmonary function and radiology[J]. *Arthritis Rheum*, 2008, 59(5): 677 - 685.
- [10] Leblond IT, Wislez M, Valeyre D, et al. Interstitial lung disease and anti-Jo-1 antibodies: difference between acute and gradual onset[J]. *Thorax*, 2008, 63: 53 - 59.
- [11] Jin WH, Dong SK, Chang KL, et al. Two distinct clinical types of interstitial lung disease associated with polymyositis-dermatomyositis[J]. *Respir Med*, 2007, 101: 1 761 - 1 769.
- [12] Olivier B, Gilbert F, Olivier C, et al. Serial chest CT findings in interstitial lung disease associated with polymyositis/dermatomyositis[J]. *Europ J Radiol*, 2004, 49: 235 - 244.
- [13] Bohan A, Peter JB. Polymyositis and dermatomyositis[J]. *N Engl J Med*, 1975, 292(7): 344 - 347.
- [14] American Thoracic Society and European Respiratory Society. American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification of the idiopathic interstitial pneumonias[J]. *Am J Respir Crit Care Med*, 2002, 165: 277 - 304.
- [15] Leslie KO, Trahan S, Gruden J. Pulmonary pathology of the rheumatic diseases[J]. *Semin Respir Crit Care Med*, 2007, 28: 369 - 378.

(收稿日期: 2009 - 12 - 02; 编辑: 张秀峰)