

风湿性疾病合并肺孢子菌肺炎 8 例并文献复习

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[摘要] 目的:探讨风湿性疾病患者并发肺孢子菌肺炎(PCP)的危险因素、临床特点及早期诊治要点,提高医务人员对该病的认识。方法:回顾性分析上海交通大学医学院附属仁济医院 2012 年 12 月—2020 年 6 月住院诊治的 8 例风湿性疾病患者并发 PCP 的病例资料,并复习相关文献进行分析。结果:①8 例患者均为女性,年龄为 28~67 岁,5 例为系统性红斑狼疮,2 例为肌炎,1 例为成人斯蒂尔病。基础患病时间为 3~120 个月,诊断 PCP 前均使用中到大量泼尼松及免疫抑制剂治疗。5 例系统性红斑狼疮患者在发生感染肺孢子菌肺炎时处于狼疮的活动期,并且累及肾脏。②除原发病临床表现外,患者最常见临床表现为新出现的发热、干咳、气促。2 例合并曲霉,1 例合并毛霉,8 例患者中乳酸脱氢酶、1-3β 葡聚糖升高,血清白蛋白、淋巴细胞计数降低,胸部 CT 表现为双肺磨玻璃影,间质性病变为主。肺泡灌洗液六胺银染色可见肺孢子菌包囊,8 例患者的治疗过程中均使用甲氧苄氨嘧啶-磺胺甲噁唑和卡泊芬净的药物,经积极治疗后 4 例好转,3 例病情恶化自动出院,1 例死亡。结论:长期使用激素及免疫抑制剂治疗的风湿性疾病患者,原发疾病处于活动期、肾脏和肺脏受累、1-3β 葡聚糖升高及淋巴细胞绝对值减低是并发 PCP 的高危因素。

[关键词] 风湿性疾病;肺孢子菌肺炎

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Rheumatic disease complicated with pneumocystis pneumonia: eight cases report and literature review

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Abstract Objective: To investigate the risk factors and clinical characteristics of patients with rheumatic diseases complicated by pneumocystis pneumonia(PCP), as well as the main points of early diagnosis and treatment, so as to improve medical staff's understanding of the disease. **Methods:** A retrospective analysis was performed on 8 patients with rheumatic diseases complicated by PCP hospitalized in Renji Nan Hospital, Affiliated to Shanghai Jiao Tong University School of Medicine from December 2012 to June 2020, and the relevant literatures were reviewed. **Results:** ①All 8 patients were female, aged from 28 to 67 years, 5 were systemic lupus erythematosus (SLE), 2 were myositis, and 1 was adult-onset Still's disease. The basic illness period ranges from 3 to 120 months, and moderate to large amounts of prednisone and immunosuppressive therapy were used before the diagnosis of PCP. Five cases of SLE patients were in the active phase of lupus when PCP infection occurred, and their kidneys involved. ②In addition to the primary clinical manifestations, the most common clinical manifestations of the patients were emerging fever, dry cough, and shortness of breath. Two cases were combined with Aspergillus and one case was combined with Mucor. In 8 cases, lactate dehydrogenase, 1-3β glucan increased, serum albumin, and lymphocyte count decreased, and chest CT showed ground glass shadows in both lungs, mainly interstitial lesions. Pneumocystis cysts can be seen in the alveolar lavage fluid with silver hexaamine staining. Eight patients were treated with trimethoprim-sulfamethoxazole and caspofungin during the treatment process. Four cases improved after active treatment. Three cases deteriorated and were discharged automatically, and one case died. **Conclusion:** For the patients with rheumatic diseases treated with hormones and immunosuppressive agents for a long time, the risk factors for complicated by PCP are the following: the primary disease is in the active stage, the kidneys and lungs are involved, 1-3β glucan increased and the absolute value of lymphocytes is decreased.

Key words rheumatic diseases; pneumocystis pneumonia

肺孢子菌肺炎(pneumocystis pneumonia, PCP)是由耶氏肺孢子菌引起的间质性浆细胞性肺

炎,为条件性肺部感染性疾病。本病在 20 世纪 50 年代前仅见于早产儿、营养不良婴儿,近几年随着免疫抑制剂的应用,肿瘤化疗的普及,尤其是人类免疫缺陷病毒感染^[1]的出现,发病率明显上升,已成为人类免疫缺陷病毒感染患者最常见的感染与

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致死的主要病因。风湿性疾病的治疗通常需使用大剂量激素及免疫抑制剂,导致机体长期处于免疫缺陷状态。该类患者也成为 PCP 的高危人群,PCP 也成为了该类患者感染和致死的主要病因。为此我们回顾性分析仁济南院 2012 年 12 月—2020 年 6 月期间住院确诊的 8 例风湿性疾病患者并发 PCP 病例,探讨风湿性疾病患者并发 PCP 的高危因素,为风湿性疾病并发 PCP 的早发现、早诊治提供有价值的资料。

1 对象与方法

1.1 研究对象

8 例风湿性疾病并发 PCP 的患者资料见表 1。风湿疾病的诊断:系统性红斑狼疮(systemic lupus erythematosus,SLE)^[2-3] 参照 1997 年美国风湿病

学会拟定的 SLE 分类标准,多发性肌炎(polymyositis,PM)和皮肌炎(dermatomyositis,DM)^[4-5] 参照 1975 年 B/P 标准,成人斯蒂尔病(Adult-onset still's disease,AOSD)参照 Yamaguchi 等^[6] 诊断标准。8 例患者资料见表 1。PCP 的诊断标准:在免疫低下或免疫缺陷患者出现典型的 PCP 临床与影像学表现的基础上,合格的呼吸道标本中检测到肺孢子菌。

1.2 研究方法

总结 8 例风湿性疾病并发 PCP 患者的病例资料,包括一般情况:年龄、性别、发生 PCP 前原发病的患病时间、脏器受累情况;临床表现及实验室、胸部影像学检查;治疗及预后情况。

表 1 8 例风湿性疾病并发 PCP 的患者资料

例序	年龄 /岁	基础 疾病	体温 /℃	症状	狼疮 活动期	乳酸脱 氢酶/ (U·L ⁻¹)	血清白 蛋白/ (g·L ⁻¹)	淋巴细 胞计数/ 1-3β 葡聚糖 (×10 ⁹ · L ⁻¹)	动脉氧 分压/ mmHg	胸部 CT	病原学	预后
1	67	SLE	38.4	气促、 干咳	是	721	26.8	524.8	0.39	66	肺间质 改变	肺孢 子菌 自动 出院
2	36	SLE	37.7	气促、 干咳	是	1925	23.0	264.7	0.28	81	肺间质 改变	肺孢 子菌 自动 出院
3	59	SLE	39.0	气促	是	523	21.0	2311.2	0.79	43	肺间质 改变	肺孢 子菌 好转
4	28	SLE	40.0	气促、 干咳	是	296	29.5	419.7	0.29	78	磨玻璃影	肺孢 子菌 好转
5	43	PM	39.3	气促		336	35.7	821.0	0.20	61	肺间质 改变	肺孢 子菌 好转
6	45	AOSD	37.8	气促、 咳嗽、 咳痰		619	28.4	342.3	0.54	79	肺间质 改变	肺孢 子菌 好转
7	30	SLE	37.7	气促、 干咳	是	1535	25.0	5000.0	0.22	72	磨玻璃影	肺孢 子菌 死亡
8	41	DM	39.0	气促、 干咳		795	29.5	4010.0	0.74	65	磨玻璃影	肺孢 子菌 自动 出院

2 结果

2.1 一般资料及激素、免疫抑制剂使用情况

8 例患者发生 PCP 前原发病患病时间为 3~120 个月。7 例患者均有肾脏受累,5 例均由肾脏穿刺性病理诊断为Ⅳ型狼疮性肾炎。发生 PCP 时每日糖皮质激素剂量泼尼松为 35~60 mg,所有病例均在减量过程中。有 3 例发生 PCP 前 3 个月内有 200~300 mg 量不等的甲泼尼龙冲击治疗,其中 1 例接受了 2 次激素冲击治疗。7 例患者均同时使用免疫抑制剂,2 例为霉酚酸酯;2 例为环磷酰胺;2 例硫唑嘌呤;1 例为环孢素。5 例 SLE 患者在发生 PCP 感染时,处于狼疮的活动期。

2.2 临床表现及实验室检查

8 例患者均有间断发热,体温介于 37.7~40.0℃。气促为最主要的症状,但肺部听诊未闻及明显干湿啰音。6 例患者有咳嗽,以干咳为主。实验室检查方面 8 例患者淋巴细胞绝对值及白蛋白均降低,淋巴细胞绝对值范围为 (0.50±0.28)×10⁹/L、白蛋白平均值为 (23.26±2.33) U/L、乳酸脱氢酶平均值为 (969±670) U/L、1-3β 葡聚糖平均值为 (969.00±299.75) U/L 及巨细胞病毒 DNA 含量均有不同程度的升高。所有的患者均经血清学检测证实 HIV 抗体为阴性。血气分析均提示明显的低氧血症。胸部 CT 表现为双肺磨玻璃

样,以间质改变为主。

2.3 治疗及预后

8 例患者均未接受预防 PCP 治疗。在诊断 PCP 前患者同时接受了多种抗生素的治疗,但仍反复发热,效果欠佳。明确 PCP 诊断后,8 例患者均接受了甲氧苄胺嘧啶磺胺甲噁唑(TMP-SMZ)加卡泊芬净的治疗,疗程为 3 周以上。非 HIV 患者 PCP 治疗方案参考文献[7]。所有患者均继续使用糖皮质激素,剂量维持在 20~50 mg 泼尼松,3 例较前减 10 mg 泼尼松,其余剂量基本一致。2 例继续使用免疫抑制剂,其余均停止使用免疫抑制剂。2 例患者因发生 I 型呼吸衰竭进展至急性呼吸窘迫综合征,行气管插管呼吸机辅助通气。预后:1 例因严重呼吸衰竭死亡,3 例病情进一步恶化自动出院,其余 4 例经过治疗后气促均明显缓解,未再发热,痊愈出院。

3 讨论

糖皮质激素被广泛应用于风湿免疫性疾病的治疗中,当激素不能减量或原发病控制不佳时会合并应用免疫抑制剂如环磷酰胺、利妥昔单抗等^[8-10]的治疗,但上述药物长期应用易造成患者免疫抑制,肺部感染风险显著增高,甚至很快进展至呼吸衰竭。

目前,AOSD 合并肺部感染的大样本多中心研究报道较少,仅见于病例及单中心回顾性研究,查阅国内外文献 AOSD 合并细菌、病毒、曲霉^[11-15]感染均有报道,但合并 PCP 感染仅见国内学者张祎等^[16]有报道。黄絮等^[17]报道非 HIV 患者 PCP 合并巨细胞病毒感染比例高达 58%。本研究中,患者肺泡灌洗液培养不仅找到了肺孢子菌,同时也合并曲霉感染和疑似病毒感染。张祎等^[16]报道的 5 例 AOSD 合并 PCP 感染患者,乳酸脱氢酶和 1-3β 葡聚糖均升高,本例患者 LDH 和 1-3β 葡聚糖也是升高的,1-3β 葡聚糖可以作为辅助诊断肺孢子菌肺炎的指标之一,Engsbro 等^[18]报道 1-3β 葡聚糖试验诊断肺孢子菌肺炎的敏感度为 83%~89%、特异度为 64%~74%。乳酸脱氢酶升高有助于 PCP 的诊断,尤其对 HIV^[19]患者,但乳酸脱氢酶无特异性,因此,乳酸脱氢酶是否是 AOSD 并发 PCP 感染的危险因素,鉴于病例数的限制,以及查阅国内外文献并未发现这方面的报道,值得进一步探讨。本例中患者并发 PCP 发生在激素减量过程中,非 HIV 的风湿性疾病患者激素用量的调整方案并没有指南或专家共识出台。笔者推测本例 AOSD 患者处于稳定期,激素减量过程中 PCP 所诱发的机体免疫平衡被再次打破是造成肺损伤的主要因素,因此维持甚至适当增加激素剂量,可能会抑制过度炎症反应,改善预后。当 AOSD 患者长期服用激素及免疫抑制剂时,出现发热、干咳、气促,乳酸脱

氢酶和 1-3β 葡聚糖均升高,结合肺部影像学间质性改变,需警惕合并 PCP 可能。尽快获取病原学依据,有助于提高诊治效率。

本研究中 2 例 DM/PM 患者临床表现为发热、咳嗽、气促,同时存在低氧血症表现,胸部 CT 出现间质性渗出改变,同时肺泡灌洗液病原学检查证实为肺孢子菌感染,研究报道显示,PCP 的感染多发生在风湿性疾病使用激素及免疫抑制剂治疗后,淋巴细胞计数减低、肺间质改变是 DM/PM 并发 PCP 的危险因素^[10,20-22],本篇 2 例患者服用糖皮质激素及免疫抑制剂,同时伴有肺间质改变及淋巴细胞数减低,存在并发 PCP 的危险因素,临幊上 PCP 病程进展较快;肺部体征及影像学表现与气促程度不相称是其特征之一。持续性低氧血症是 PCP 患者最主要特点,胸部 CT 常表现为双肺斑片状或弥漫性密度增高影。PCP 诊断的金标准在免疫低下或免疫缺陷患者出现典型的 PCP 临幊与影像学表现的基础上,合格的呼吸道标本中检测到肺孢子菌。新的辅助检查如二代测序(mNGS)也是强有力的数据,但 mNGS 也有其局限性。正常情况下,肺孢子菌可以定植于人体呼吸道。而 mNGS 不能区分肺孢子菌的定植与感染,因此 mNGS 检测到肺孢子菌只能提供微生物学证据,并不能排除肺孢子菌定植的可能。临幊工作者必须在综合考虑患者的免疫低下高危因素、临床症状以及影像学表现的基础上,才能诊断 PCP。本研究 2 例患者 PCP 均发生于免疫抑制剂治疗过程中,出现发热、干咳和气促,淋巴细胞计数和血清白蛋白降低,乳酸脱氢酶和 1-3β 葡聚糖均升高。在支气管肺泡灌洗液中找到肺孢子菌,故确诊为 PCP。临幊工作中需警惕 PM/DM 合并 PCP 可能。尽快获取病原学依据,有助于提高诊治效率。

5 例 SLE 并发 PCP 的患者均为女性,基础患病时间 3~120 个月,均处于原发病活动期、累及肾脏(肾脏穿刺提示狼疮性肾炎)、胸部影像提示肺间质病变并且正在使用糖皮质激素和免疫抑制剂、辅助检查提示周围淋巴细胞计数和白蛋白偏低、乳酸脱氢酶和 1-3β 葡聚糖偏高,Wang 等^[23]报道认为长期使用糖皮质激素和免疫抑制剂、淋巴细胞计数低、肾功能损害易并发严重的 PCP,Kageyama 等^[24]报道认为淋巴细胞计数低是 SLE 并发 PCP 死亡的高危因素;Esteves 等^[25]报道认为乳酸脱氢酶和 1-3β 葡聚糖可联合作为 HIV 感染患者并发 PCP 的生物标志物,乳酸脱氢酶升高有助于 PCP 的诊断,尤其对 HIV 患者^[20],但乳酸脱氢酶无特异性;另外本篇有 3 例患者巨细胞病毒(CMV)DNA 量明显升高。Faure 等^[26-27]报道认为肾移植后巨细胞病毒感染是发生 PCP 的关键危险因素,Yong 等^[28]发现实体器官和干细胞移植受者发生

CMV 感染时,易合并感染曲霉病和肺孢子菌肺炎,由于本篇患者未进行 PCR 检测,无法明确诊断,但结合临床症状合并病毒感染可能性大。综上,巨细胞病毒、乳酸脱氢酶是否可作为风湿性疾病患者感染 PCP 的危险因素需要进一步研究。SLE 并发 PCP 并无特殊的临床表现,给临床治疗带来了一定的困难,目前诊断的金标准仍然依赖于在合格的痰液或肺泡灌洗液标本中找到肺孢子菌。

综上,风湿性疾病患者在长期使用激素及免疫抑制剂情况下,淋巴细胞绝对值减低、1-3 β 葡聚糖升高、原发疾病的活动期、肾脏和肺脏受累是并发 PCP 的高危因素。临幊上出现发热、干咳、气促、快速进展为低氧血症等症状,应警惕肺孢子菌肺炎,早期诊断、早期治疗可降低病死率。

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277例老年患者坏疽性阑尾炎腹腔镜下手术经验总结*

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[摘要] 目的:总结近10年来首都医科大学宣武医院针对老年坏疽性阑尾炎患者腹腔镜手术的经验。方法:对2010年1月—2020年6月期间于首都医科大学宣武医院因坏疽穿孔性阑尾炎行腹腔镜手术治疗的65岁以上老年患者的临床资料进行回顾性分析,所有患者均经手术确诊为坏疽性阑尾炎。手术方式主要采用以右上腹切口为主操作孔的三孔法腹腔镜阑尾切除术,少数行开腹手术治疗及单孔腹腔镜手术治疗。结果:本研究共纳入277例次患者,平均年龄为(71.35±8.35)岁,所有手术均顺利完成;三孔法手术时间平均56 min,平均出血量25.3 mL,术后腹腔脓肿发生率3.12%;单孔法手术时间平均75 min,平均出血量28.3 mL,术后腹腔脓肿发生率13.04%。三孔法与单孔法比较,手术时间缩短,术后腹腔脓肿发生率降低。结论:针对老年急性坏疽性阑尾炎患者以采用右上腹为主操作孔的三孔法腹腔镜阑尾切除方式可取得较好疗效及较低的围术期并发症。

[关键词] 腹腔镜;坏疽性阑尾炎;阑尾切除术;老年患者

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Experience of laparoscopic appendectomy in elderly patients with gangrenous appendicitis

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Abstract Objective: To summarize the experience of laparoscopic surgery for elderly patients with gangrenous appendicitis in Xuanwu Hospital of Capital Medical University in recent 10 years. **Methods:** From January 2010 to June 2020, elderly patients over 65 years old with gangrenous perforated appendicitis who underwent laparoscopic surgery in Xuanwu Hospital of Capital Medical University were retrospectively analyzed. Three hole laparoscopic appendectomy with right upper abdominal incision as the main operation hole was used as the main operation method, and a few laparotomy and single hole laparoscopic appendectomy were used. **Results:** A total of 277 patients were included in this study, the average age was 71.35 ± 8.35 years old, all operations were successfully completed; the average operation time of three hole method was 56 minutes, the average blood loss was 25.3 mL, the incidence of postoperative abdominal abscess was 3.12%; the average operation time of single hole method was 75 minutes, the average blood loss was 28.3 mL, the incidence of postoperative abdominal abscess was 13.04%. Compared with single hole method, the three hole method can shorten the operation time and reduce the incidence of postoperative abdominal abscess. **Conclusion:** For elderly patients with acute gangrenous appendicitis, laparoscopic appendectomy with right upper abdomen as the main operating hole can achieve better curative effect and lower perioperative complications.

Key words laparoscopic surgery; gangrenous appendicitis; appendectomy; elderly patient

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