ISSN: 2469-567X

Chiu-Yin et al. Int J Virol AIDS 2017, 4:034
DOI: 10.23937/2469-567X/1510034
Volume 4 | Issue 1
Open Access

International Journal of Virology and AIDS

CASE REPORT

Dual Cytomegalovirus and *Aspergillus* Pneumonia Following Influenza B Infection in a Patient with Polyarteritis Nodosa

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Abstract

Polyarteritis Nodosa (PAN) is a systemic necrotizing vasculitis that might require immunosuppressive therapy. We report on a 72-year-old woman of PAN with influenza B infection, who developed dual cytomegalovirus and *Aspergillus* pneumonia in the later course. Together with steroid therapy, delayed initiation of anti-CMV and anti-fungal therapy complicated the disease course. Early diagnosis and therapy for CMV and aspergillosis in the patients post-influenza attack are important, especially in those with steroid therapy.

Keywords

Aspergillosis, Cytomegalovirus, Influenza B, Polyarteritis nodosa

Introduction

Polyarteritis Nodosa (PAN) is a form of systemic necrotizing vasculitis preferentially targeting medium muscular arteries. The clinical responses to immunosuppressive therapy support the pathogenic linkage of PAN to immunological mechanisms [1]. Cytomegalovirus (CMV) diseases frequently occur in the patients receiving immunosuppressive therapy. In addition, Invasive Pulmonary Aspergillosis (IPA) usually occurs in immunocompromised hosts, but can also happen after severe influenza infections in patients without classical predisposing factors [2]. Herein we report on a patient of PNA with influenza B infection, who subsequently developed life-threatening dual CMV and *Aspergillus* pneumonia.

Case Report

A 72-years-old woman of polyarteritis nodosa had fever, running nose, and nasal obstruction for 3 days. In emergency room, rapid influenza diagnostic test in nasopharyngeal swab was positive for influenza B on October 31, 2015. Chest X-ray (CXR) showed slight infiltration on bilateral lungs. A white blood cell count was 16,100/μL and an elevated C-Reactive Protein (CRP) level was 238.0 mg/L. Initial renal function was normal. Other data of laboratory testing were tabulated in Table 1.

Initially, zanamivir inhalation therapy and intravenous moxifloxacin were given. However, high spiking fever was still off and on. As increased CRP (315.7 mg/L), leukocytosis (24,500/μL) and worsening dyspnea, the patient was transferred to the intensive care unit on November 09. Bilevel positive airway pressure was used for non-invasive mechanical ventilation support. Antimicrobial therapy with piperacillin-tazobactam was initiated to replace moxifloxacin. Thereafter, fever was subsided. As acute renal failure occurred, continuous venovenous hemofiltration was performed.

Followed-up CXR showed newly developed consolidation over right lung fields (Figure 1A) and the sputum cultures yielded yeast-like organisms. Antimicrobial therapy was maintained with piperacillin-tazobactam. For the therapy of PAN, intravenous methylprednisolone 40 mg every 6 hours was given since November 20,

Citation: Chiu-Yin Y, Hsi-Hsing Y, Wen-Liang Y (2017) Dual Cytomegalovirus and *Aspergillus* Pneumonia Following Influenza B Infection in a Patient with Polyarteritis Nodosa. Int J Virol AIDS 3:034. doi.org/10.23937/2469-567X/1510034

Received: July 31, 2017: **Accepted:** September 18, 2017: **Published:** September 20, 2017

Table 1: Clinical course and laboratory data of the patient during hospitalization.

Laboratory data (normal limits)	Oct 31	Nov 3	Nov 6	Nov 9	Nov 16	Nov 20	Nov 25	Nov 30	Dec 3	Dec 10
Admission	Ward	Ward	Ward	ICU	ICU	ICU	ICU	ICU	ICU	ICU
Temperature (peak, °C)	39.2	40.4	39.2	37.8	37.2	36.8	36.8	36.8	36.8	36.0
Antibiotic therapy	A	B	B	C	C	C	D	D	D	D
Influenza A antigen	Negative									
Influenza B antigen	Positive									
Urine RBC/HPF	30-49	30-49		20-29						
Urine WBC/HPF	10-19	30-49		30-49						
Urine culture	NG	NG		NG						
Blood culture	NG	NG	NG							
Sputum culture					Yeast					
Blood WBC count/μL	16,100	14,500	19,600	24,500	34,500	31,100	18,100	17,300	19,200	9,000
Blood platelet count/μL	449,000	435,000	495,000	600,000	214,000	173,000	99,000	89,000	41,000	55,000
Blood hemogram (g/dL)	12.4	10.8	9.9	8.1	6.9	6.1	8.6	8.8	8.8	9.3
CRP (< 5 mg/L)	238.0	319.1	296.0	315.7	183.6	175.0	34.7	22.8	72.6	62.7
Procalcitonin (< 0.05 ng/mL)				7.23		24.22			1.14	
BUN (6-20 mg/dL)		13		61	117	63	54	162	43	93
Creatinine (0.57-1.11 mg/dL)	0.77	0.82		4.52	8.72	4.01	1.46	5.09	1.28	2.16
AST (5-34 U/L)	34									53
ALT (2-40 U/L)	37									69
CMV-PCR						Positive		Positive		
Aspergillus Ag (< 0.5 index)							0.32			6.37

ICU: Intensive Care Unit; Antibiotic A: Cefuroxime (for 4 days); Antibiotic B: Moxifloxacin (for 5 days); Antibiotic C: Piperacillin-tazobactam (for 16 days); Antibiotic D: Piperacillin (for 18 days); RBC: Red Blood Cell; WBC: White Blood Cell; HPF: High Power Field; NG: No Growth; CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; CMV-PCR: Cytomegalovirus-Polymerase Chain Reaction.

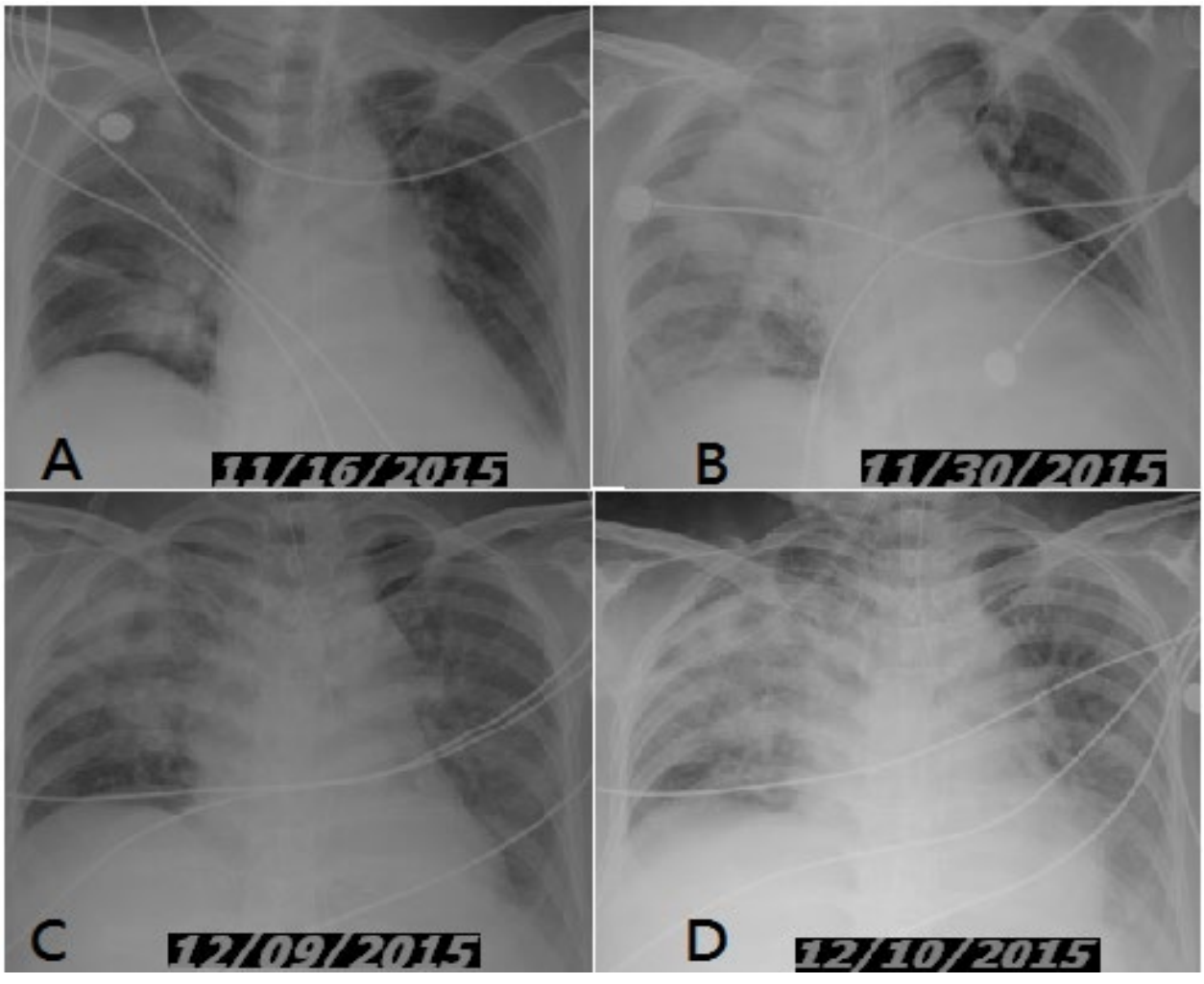

Figure 1: A) CXR is showing consolidation in right lung fields; B) Worsening in right upper lung field; C) Progress in cavity formation; D) Into more extensive consolidation.

which had been maintained for more than 3 weeks until death. Meanwhile, blood CMV-DNA testing by Polymerase Chain Reaction (PCR) showed positive. The serum *Aspergillus* antigen index revealed 0.32 (normal, < 0.5) on November 25, 2015. However, the CXR showed extended consolidation over right upper lung field on November 30 (Figure 1B). Followed-up blood CMV-PCR testing remained positive and thus ganciclovir was given since December 01. Nonetheless, CMV antigenemia revealed 8 positive cells per 200,000 leukocytes on December 08. The CXR revealed cavity formation over right upper lung field (Figure 1C) with progression to more extensive consolidation (Figure 1D). Family decided comfort therapy for the patient. The serum *Aspergillus* antigen index was elevated to 6.37 on December 10, 2015. The patient passed away on December 12, 2015. Anti-fungal therapy was not given in time.

Discussion

The current patient with PAN developed dual CMV and IPA following influenza B infection. While pneumonia was worsening, only blood CMV DNA but not *Aspergillus* antigen was detectable, it could indicate development of CMV pneumonia. However, initiation of antiviral therapy was hesitated. The occurrence of CMV infection due to the use of corticosteroid or immunosuppressive therapy for PAN is often life-threatening, so prompt intravenous antiviral treatment is recommended [3]. Oral cyclophosphamide and prednisone are standard treatment for PAN. However, Mayer, et al. referred to the effectiveness of less aggressive treatment without immunosuppressants for immunogenic vasculitis concurrent with CMV infection [4]. Because our patient had no proteinuria, renal damage (initially), cardiomyopathy, gastrointestinal manifestations, and/or central nervous system involvement, she was also treated with corticosteroid alone without immunosuppressants, which led to partial improvement of clinical condition, such as decreasing inflammatory markers (leukocyte count, CRP and procalcitonin). Nonetheless, CMV pneumonia and subsequent identified IPA still complicated the disease course, even though aggressive cytotoxic treatment was not given for PAN.

It should be noticed that post-influenza A status has been recognized as a risk host for IPA in many countries [2]. Post-influenza IPA could be fatal, even on aggressively intensive care and management [5,6]. Besides, we recently reported a 76-year-old patient with influenza B pneumonia coexisting with IPA [7]. Although rarely reported, influenza B might predispose to IPA in our patient with PAN on steroid therapy. Therefore, several factors including influenza B, PAN, steroid use, CMV infection and aspergillosis could all contribute to a lethal disease in our patient. Early diagnosis and treatment of CMV and *aspergillus* infection is of the utmost importance to avoid morbidity and mortality. The use of piperacillin-tazobactam or piperacillin before *Aspergillus* antigen testing should not be a concern for false positivity in our institute [8].

In conclusion, we report a patient of PAN who developed dual CMV and *Aspergillus* pneumonia following the influenza B infection. Physicians should be highly alert to the unusual occurrence. Repeated laboratory tests could not be neglect. Our case highlights the CMV and *Aspergillus* dual infection as the possible complication of influenza B in a patient treated with steroid therapy. Early diagnosis and therapy for suspected CMV and *Aspergillus* infections are indeed important.

Acknowledgement

None declare.

Conflict of Interests

The authors declare that they have no conflict of interest and no financial support regarding this work. The above study has been granted exemption from review by the Institutional Review Board of Chi-Mei Medical Center (application no.10501-E01).

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