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Case Report/รายงานผู้ป่วย

Fulminant Aspergillus Pneumonitis in a Healthy Child with Chronic Granulomatous Disease.

Anantasit N, MD.[1], Khositseth A, MD.[1],
Sirikulchayanonta V, MD.[2], Sirinavin S, MD.[1]

[1] Department of Pediatric, [2] Department of Pathology,
Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400 Thailand.

Abstract

Chronic granulomatous disease (CGD) is an inherited immunodeficiency characterized as defect in one of the 4 subunits of the nicotinamide adenine dinucleotide phosphate oxidase complex affecting phagocytosis activities. Patients' symptoms are usually gradual onset or asymptomatic. The authors report a girl with rapidly progressive pneumonia in previously healthy child who not response empirical antibiotic.

Keywords: chronic granulomatous disease, aspergillus

Corresponding author: Anantasit N, MD.
Division of Critical Care, Department of Pediatric, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, 10400, Thailand
Tel: 66-2-201-2949 Email: nattachai032@hotmail.com

Introduction

The clinical courses of chronic granulomatous disease patients are usually asymptomatic or gradual onset but this case had acute severe onset. A previously healthy 20 months girl presented with rapidly progressive community-acquired pneumonia and failed to empirical treatment. Therefore, fungal infection should be considered. Early investigation and aggressive treatment of fungus are recommended.

Case report

A previously healthy 20-month-old girl was transferred to our tertiary center with respiratory failure secondary to pneumonia, preceded by fever and rhinorrhea for 3 days with progressive dyspnea. Empirical antimicrobial agents administered were ceftriazone, cloxacillin, and amikacin. Physical examination revealed BT 37.5°c, HR 157/min, BP 83/38 mmHg, equal breath sounds with rales bilaterally. Investigations showed leukocytosis (WBC of 33.0 $x10^3$/μL with 91% neutrophil), thrombocytosis (platelet 516,000/μL), coagulopathy (aPTT 125 s, PT 16 s, INR 1.39 and TT > 200 s), and negative anti-HIV. A chest film revealed patchy - nodular infiltration of both lungs with minimal pnemothorax at left upper lung field (Fig. 1). Arterial blood gas confirmed severe respiratory acidosis with hypoxemia (pH 7.0, PCO_2 100 mmHg, PO_2 61.3 mmHg, and HCO_3 25.2 mmol/L). Severe pneumonia with ARDS was the initial diagnosis from which point treatment with ciprofloxacin, amikacin, and amphotericin B commenced. Two hours later, hypotension developed requiring fluid resuscitation, inotropic and vasopressor drugs and stress-dose of hydrocortisone. Her vital signs were stabilized. However, 7 hours later, her respiratory failure deteriorated with increased pneumothorax requiring high frequency oscillatory ventilator resulting in decreased pneumothorax. On 19th hof admission, the patient developed tension pneumothorax requiring bilateral intercostal drainages. Fiberoptic bronchoscopy (FOB) revealed sticky and cotton liked mucous at left lower bronchus. KOH from Bronchoalveolar lavage (BAL) fluid revealed dichotomous branching septate hyphae. After 48 hours of admission, her clinical was not improved. The tracheal culture confirmed *Aspergillus fumigatus* and amphotericin B was therefore changed to intravenous voriconazole. Subsequent dihydrorhodamine-123 (DHR) assay taken showed autosomal recessive form CGD. Her vital signs deteriorated further and she died at 59 hours after admission. The autopsy performed showed severe pulmonary edema and pneumonia bilaterally with multiple abscesses and fungal balls (Fig. 2).

Discussion

A previously healthy child with community-acquired pneumonia with pulmonary nodule but rapidly progressed to respiratory failure under empirical antibiotic was unusual. This was highly suggestive of an underlying disease, which therefore required prompt treatment with fungal infection and extensive inves-tigation including high resolution computerized tomography (HRCT), FOB with BAL, and transthoracic percutaneous needle aspiration should be recommended. This patient was not stable enough to perform neither HRCT nor percutaneous needle aspiration. Bedside FOB with BAL was feasible and perhaps, provided useful information for the diagnosis as demonstrated sticky and cotton liked mucous and positive fluid culture for *A.fumigatus,* highly suggestive of IPA, although definitive diagnosis requires histo-pathological documentation from sterile site but probable diagnosis in immunocompromised host consists of surrogate non culture based method i.e. positive galactomannan assay, present of β-D-glucans in serum, BAL, and compatible CT finding(air crescent sign or halo sign)[1,2]. The chest film in IPA is often non-specific but multiple small nodules at pleural-based provides a more specific to diagnosis of fungal disease[3]. IPA is predominantly seen in prolonged

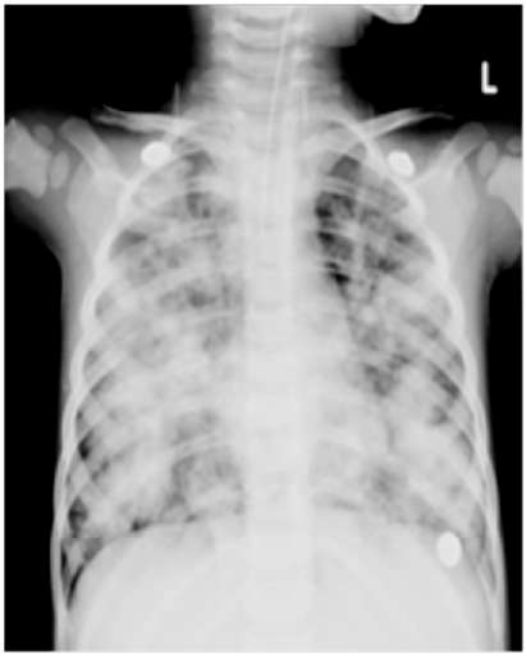

Fig.1 *Chest film demonstrated extensive patchy nodular infiltration bilaterally with minimal pneumothorax at left upper lung field.*

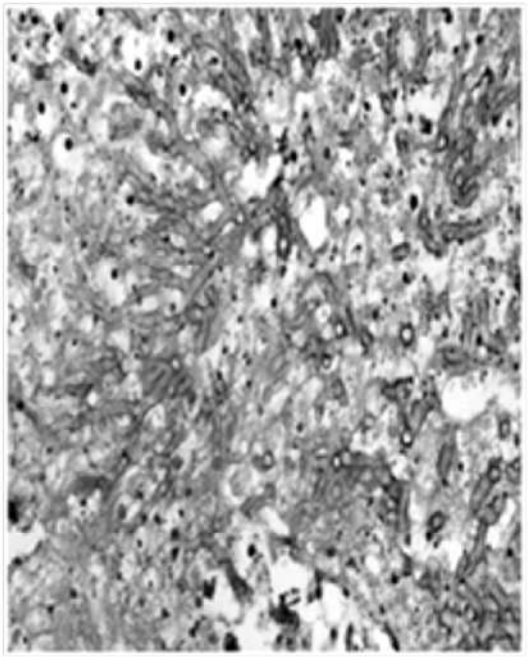

Fig.2 *Photomicrograph (H&E; original magnification x40) demonstrated fungal ball with dichotomous branching of septate hyphae of aspergillous species interspersed among acute inflammatory cells and necrotic debris.*

neutropenic patients. However, IPA can occur in non-neutropenic patients such underlying disease as primary immune deficiency and those on cortico-steroid and other immunosuppressive therapy[4]. The diagnosis of CGD is often suggested by a micro-biologic diagnosis, since the majority of infections in this disease are due to five catalase-producing microorganisms[5]: *S. aureus, B. cepacia, S.marcescens, Nocardia* species and *Aspergillus* species. In addition, when a diagnosis of IPA is made in the absence of known risk factors, CGD should be in the differential diagnosis of the underlying diseases, even in a previously healthy child[6]. A review of aspergillosis in CGD patients at NIH indicates one third was asymptomatic at diagnosis and only 20% were febrile[7]. X-linked recessive (XR) CGD is more common than autosomal recessive (AR)[8]. XR patients have worse clinical phenotype and more infections than AR forms[9]. The mean age of diagnosis in AR female form was 8.13 years[8]. An AR form of CGD in this case was exceptional as she presented in a severe condition and deteriorated rapidly in younger age. This demonstrated that AR form of CGD can have severe manifestation of IPA. The dihydrorhodamine 123 (DHR) assay, a quantitative measure of nico-tinamide dinucleotide phosphate (NADPH) oxidase subunitsduring the respiratory burst of phagocytic cells, is the diagnostic test for CGD[10]. In this case, the assay showed a broad peak of fluorescence that was lower than that of normal neutrophils, a pattern typically associated with AR variants of CGD. Unfortunately, we did not have blood test in her parents. Recom-mended treatment for pediatric IPA is voriconazole, or alternatively, amphotericin B[11].This patient received the latter initially and changed to the former 48 hours later but did not survive.

Conclusion

This case demonstrated an unusual case of first diagnosed and severe AR form of CGD presented with IPA in a previous healthy child.

Potential conflict of Interest: None.

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Original Articles/นิพนธ์ต้นฉบับ

การติดเชื้อปอดอักเสบรุนแรงจากเชื้อ Aspergillus ในเด็กเล็กที่เป็น chronic granulomatous disease

ณัฐชัย อนันตสิทธิ์, พบ.[1], อนันต์ โฆษิตเศรษฐ, พบ.[1], วรชัย ศิริกุลชยานนท์, พบ.[2], สยมพร ศิรินาวิน, พบ.[1]

[1] ภาควิชากุมารเวชศาสตร์, [2] ภาควิชาพยาธิวิทยา
คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กรุงเทพฯ 10400

บทคัดย่อ

โรค Chronic granulomatous disease เป็นโรคที่มีความผิดปกติทางภูมิคุ้มกันแต่กำเนิด จากการขาดสาร nicotinamide adenine dinucleotide phosphate oxidase ทำให้การจับกินเชื้อโรคผิดปกติ โดยปกติมักค่อยๆ แสดงอาการ หรือไม่มีอาการผิดปกติชัดเจน ผู้นิพนธ์ได้รายงานผู้ป่วยเด็กหญิงไทยอายุ 20 เดือน แข็งแรงดี ที่มาด้วยปอดอักเสบรุนแรง ซึ่งไม่ตอบสนองกับการให้ยาปฏิชีวนะเบื้องต้น

Corresponding author: ณัฐชัย อนันตสิทธิ์ พบ.
หน่วยเวชบำบัดวิกฤต ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี
มหาวิทยาลัยมหิดล ถนนพระราม 6 เขตราชเทวี กรุงเทพฯ 10400
โทรศัพท์ 02-201-2949 Email nattachai032@hotmail.com