

Culture Negative Abscesses at Multiple Sites: A Diagnostic and Management Dilemma in a District Hospital

Cynthia Sandanamsamy^{1,*}, Lai Nai Kiat Sean¹, Chan Weng Kit¹, Naganathan¹, Ganesh Kasinathan²

¹Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Jalan Lagoon Selatan, Bandar Sunway, Subang Jaya, Selangor, Malaysia

²Department of Medicine, Segamat Hospital, KM 6 Jalan Genuang, Segamat, Johor, Malaysia

*Corresponding author: csan18@student.monash.edu

Abstract Background: Culture negative abscesses at multiple sites are a common phenomenon. It is an important source of sepsis and septic shock in many developed and developing countries worldwide. Case Presentation: This case describes a 42 year-old Malay gentleman who presented to us with high grade fever associated with cough, foul-smelling sputum and pleurisy. He has underlying chronic Type 2 Diabetes Mellitus. He works as a rubber tapper, a smoker with a 40 pack years history, and a teetotaler. On physical examination, he had notable pyrexia with stable vital signs. He was septic looking and had obvious rigors. His dental hygiene was poor with multiple caries. Lungs were clear on auscultation. Examination of the abdomen revealed tender hepatosplenomegaly. Chest radiograph showed multiple cavitating lesions suggestive of lung abscesses. A subsequent Contrast Enhanced Computed Tomography (CECT) of the thorax, abdomen and pelvis revealed multiple lung, liver, splenic and adrenal abscesses of different sizes. A 2D transthoracic echocardiogram did not reveal any vegetation. Tuberculosis and viral screening were negative. His melioidosis serology titer was not significant. Multiple sets of blood, sputum and urine cultures did not grow any organism. He was treated for culture negative abscesses with a six week course of parenteral third generation cephalosporin antibiotics and metronidazole. Repeated imaging showed significant improvement of all abscesses and he responded well clinically. Conclusion: Effective and early management of culture negative abscesses with broad spectrum antibiotics is vital in reducing overall mortality and morbidity.

Keywords: *pyrexia, hepatosplenomegaly, tuberculosis, adrenal, metronidazole*

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1. Introduction

Culture negative abscesses are commonly seen in clinical practice. It is an important source of sepsis and septic shock in many developed and developing countries worldwide. Mortality rates remain high at 30% and rise to 60% in the presence of septic shock despite significant advancement in treatment modalities. [1] Culture negative abscesses usually carry a better prognosis than the culture positive. Blood cultures as one of the most imperative investigations should be done when bloodstream infection is suspected. Only 50% of the blood cultures are positive. [1] It is commonly thought that cultures may lack the sensitivity to detect all infecting bacteria. [2] With negative cultures, failure to administer antibiotics to which the pathogens are susceptible increases the mortality rate. [1] Here, we report a case of culture negative abscesses at multiple sites which showed adequate clinical and radiological response after being treated with broad-spectrum antimicrobials in a rural hospital setting.

2. Case Presentation

A 42 year-old Malay rubber tapper male presented to us with daily high grade fever, purulent cough, and pleurisy for a week. He has underlying chronic Type 2 Diabetes Mellitus of which he was on oral hypoglycemic agents. He had chills and rigors. He also complained of reduced effort tolerance with occasional dyspnoea. He denied having haemoptysis, vomiting, abdominal pain or change in bowel habit. There was no tuberculosis or other high risk contact. He denied consuming any traditional medications. There was no significant family history. He is a chronic smoker of 40 pack years and a teetotaler. Physical examination revealed a septic looking man. He was febrile to touch with a temperature of 38.5°C. He had a pulse rate of 110 beats per minute. His blood pressure and oxygen saturation was within normal limits. He had poor oral hygiene with multiple dental caries. Cardiovascular examination revealed normal heart sounds with no audible murmurs. Lungs were clear on auscultation. Abdominal

examination revealed tender hepatosplenomegaly. There were no palpable lymph nodes or skin abscesses seen. His complete blood count, renal and liver function tests are as shown in Table 1. Multiple sets of blood, sputum and urine cultures did not grow any organisms. Tuberculosis and viral screening were negative. Melioidosis serology titer was not significant. His serum tumor markers were not elevated. A 2D transthoracic echocardiogram did not reveal any vegetations. Chest radiograph showed multiple cavitating lesions suggestive of lung abscesses (Figure 1). A subsequent CECT of the thorax, abdomen and pelvis revealed multiple lung, liver, splenic and adrenal abscesses of different sizes (Figure 2 & Figure 3). He was started on parenteral amoxicillin/clavulanate which he did not respond to adequately. He was subsequently switched to a six week course of parenteral ceftazidime and metronidazole. Repeated imaging post treatment showed good resolution of abscesses at all affected sites. There were no bronchial lavage or biopsy taken as this service was not available at our centre.

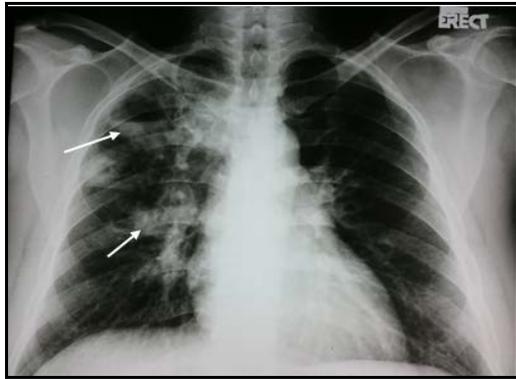


Figure 1. Pre-treatment Chest Radiograph shows multiple cavitating lesions suggestive of multiple lung abscesses (shown by the arrow)

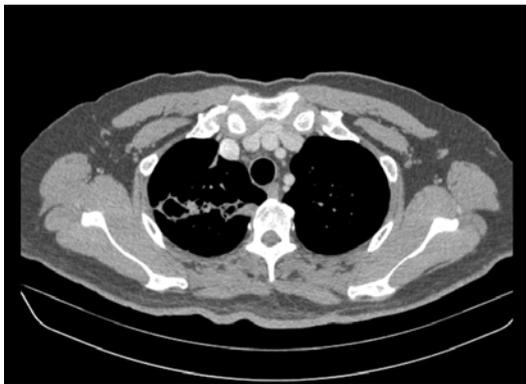


Figure 2. CECT Thorax shows multiple right lung abscesses



Figure 3. CECT of the abdomen shows multiple abscesses of varying sizes in the liver, spleen and adrenal gland.

Table 1. Serum Biomarkers

Serum Biomarkers (International Units)	Values (Normal range)
Hemoglobin (g/dL)	10.4 (11.5-18.0)
White Cell Count ($10^9/L$)	12.5 (4-11.0)
Platelet ($10^9/L$)	152 (150-400)
Sodium (mmol/L)	140 (130-145)
Potassium (mmol/L)	3.35 (3.3-5.1)
Serum creatinine (umol/L)	36.0 (40-80)
Total bilirubin (umol/L)	3.8 (0-21)
Total protein (g/L)	72.7 (66-87)
Albumin(g/L)	32.9 (39.7-49.4)
Random Blood Sugar (mmol/L)	4.0 (4 – 7.8)
Alkaline Phosphatase (U/L)	110 (40-129)
Alanine Transaminase (U/L)	9.0 (0-41)
C-Reactive Protein (mg/L)	154.8 (<5)
Erythrocyte Sedimentation Rate (mm/hr)	115 (<20)

3. Discussion

Negative cultures are common and they pose a diagnostic dilemma in the field of medicine. There are various reasons for culture negative abscesses. The postulated reasons are cultures lack the sensitivity to detect all kinds of bacteria, insufficient blood samples, prior administration of antibiotics, sampling error, poor transport conditions and slow growing fastidious bacteria. [1] Some insights into other possibilities for negative cultures in this case are (i) Hidden bacteria within macrophages, (ii) quantity of certain organisms may be less than the minimum limit of detection, (iii) organism may no longer be in the blood stream and clinical signs may be due to the by-products of the organism, (iv) inappropriate media used, and (v) inadequate temperatures utilised during process of incubation. The main routes of abscess formation are by haematogenous embolization of the pathogen, haematogenous spread during concurrent bacteraemia, contiguous spread or by direct trauma. [3] Lung abscess are most commonly caused by the aspiration of anaerobic bacteria found in the gingival crevices. [4] The most probable route of lung abscess formation in this patient is his poor dental hygiene with gingival crevices. The dissemination of abscesses involving other organ sites in this case could be attributable to the haematogenous embolization of pathogen from the lung. Other secondary causes which predispose a patient into developing lung abscess include Lemierre's syndrome, septic embolization from right sided bacterial endocarditis and peripheral septic thrombophlebitis. [4] An untreated simple pneumonia can progress to lung abscess depending on the pathogen involved, host factors and the underlying condition of the lung. [13] Immunosuppressed patients with an underlying illness are at risk of developing *Bacteroides* bacteraemia. [5] A sour taste and foul smelling sputum is characteristic of anaerobic infection. [4] Among the anaerobic organisms involved are *Peptostreptococcus*, *Prevotella*, *Bacteroides* and *Fusobacterium* sp. [4] Non-anaerobic organisms include *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Legionella* and *Burkholderia pseudomallei*. [4] The problems in identifying anaerobic bacteria by

sputum culture and bronchial lavage may be due to contamination by upper respiratory tract organisms which make it unsuitable for culture. [4] Abscesses at a specific location or organ are associated with certain types of organisms. An organism known to cause culture negative abscesses is *Streptococcus anginosus* group (SAG). [6] SAG has been known for its association with bacterial intracerebral abscesses but may also form local suppurative infections in multiple areas of the body. [6] *Streptococcus Intermedius*, a subtype of SAG is the most pathogenic due to its capability of causing deep seated abscesses in multiple sites even in young and healthy individual by spreading hematogenously. [6] Other common differential diagnoses in the case of multiples abscesses include tuberculosis, Acquired Immunodeficiency Syndrome (AIDS), and infective endocarditis. [7] However, after these diseases have been ruled out with specific tests, melioidosis may be a possible differential in multiple abscesses with travel history to areas endemic with gram negative bacilli *Burkholderia pseudomallei* such as South East Asia, India and Australia where they present with multiple splenic and foot abscesses. [7] Another causative agent that may cause negative microbiological sample associated with multiple abscesses is *Aggregatibacter aphrophilus*, a gram-negative coccobacillus that belongs to HACEK group. [8] Cultures of HACEK group has high incidence of negative sample results due to requiring specific condition such as special medium, long incubation time, slow growth on chocolate blood agar and requiring of 5% carbon dioxide for primary isolation. [8] As such, 16S rRNA PCR is an alternative useful test for culture negative samples which is suggestive of HACEK group organisms or other anaerobic organisms. [8] However, introduction of broad range amplification and sequencing technique especially 16S rRNA gene sequences has been widely used to identify various culture-negative microorganisms. [9] 16S rRNA gene polymerase chain reaction diagnosis showed a sensitivity, specificity, positive predictive value, and negative predictive value of 42.9%, 100%, 100%, and 80.2%. [10] Abscess can be treated medically or surgically either by percutaneous drainage or by open drainage. Abscess of different size and sites require different interventions and not all abscesses necessitate surgical intervention. [4] The standard treatment for anaerobic lung infection is clindamycin (600 mg IV every eight hours, followed by 150 to 300 mg orally four times daily). [4] Beta lactams such as ampicillin-sulbactam are used in view of increasing resistance to penicillin. [4] The use of metronidazole monotherapy is not encouraged because of its high failure rate of 50%. [11] Treatment duration is from four to six weeks depending on the radiological findings and clinical discernment of the treating team as reflected on the patient's response to therapy. [4] Surgical intervention is seldom indicated for uncomplicated cases. Splenic abscess on the other hand are typically managed using a combination of antibiotic therapy and splenectomy. [3] Percutaneous drainage is increasingly being used as it is less invasive and it allows for the preservation of the organ. [3]

4. Conclusion

Organism identification in abscesses at multiple sites can be challenging. Early treatment with broad spectrum antimicrobials confers an advantage in reducing mortality and morbidity in this group of patients.

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None.

Statement of Competing Interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

List of Abbreviations

None.

Informed Consent

Informed consent was obtained from the patient for the publication of the study.

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