Unusual presentation of more common disease/injury

Postpartum culture negative endocarditis: a case report and review of the current guidelines

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Summary

Culture-negative endocarditis (CNE) presents physicians with diagnostic and treatment challenges. Postpartum endocarditis is rare and usually culture negative. Empirical antimicrobial regimes lead to the risk of aggressive treatment with potentially toxic drugs. This paper presents a case of postpartum CNE, discussing the issues of diagnosis and treatment. European and American guidelines for CNE are then reviewed and compared.

BACKGROUND

The incidence of endocarditis is approximately 5 per 100 000 population per year with an estimated mortality of around 10%.¹ A key component to the diagnosis and treatment of infective endocarditis (IE) is the availability of blood culture results.² However culture-negative endocarditis (CNE) accounts for 20% of diagnosed cases when standard blood culture systems are used.^{3–4} The lack of an identifiable causative pathogen is often associated with either prior use of antimicrobial agent(s), inadequate microbiological techniques or presence of fastidious organism. Tricuspid valve endocarditis in low risk patients such as ours is unusual but similar reports following abortion or during pregnancy have been documented in the literature.^{5–9} Diagnosis of postpartum IE is typically delayed. The lack of clinical peripheral stigmata of IE and the lack of growth of any microorganisms in blood cultures are also consistent with previous case reports.^{5–6} Lack of advanced diagnostic tools such as serological assays and PCR in standard clinical laboratories as well as the time required to identify pathogens, makes clinical decisions to start antimicrobial agents difficult.

CASE PRESENTATION

A 29-year-old Asian female was admitted to the labour ward for the birth of her third child. She was previously healthy with no significant medical history or unusual social history. At 24 weeks of pregnancy, she was treated with amoxicillin-clavulanic acid for a presumed urinary tract infection (UTI) for 5 days. She underwent an uneventful vaginal delivery at 40 weeks, and was discharged 24 h post delivery. She complained of rigors and sweating for the next week and was later reviewed in hospital. She was empirically treated with oral amoxicillin-clavulanic acid for a suspected recurrent UTI for 2 days. High vaginal swab as well as urine and blood cultures were taken prior to discharge. Urine and blood cultures did not grow any organisms, however the vaginal swab grew group B haemolytic *Streptococci*. Methicillin-resistant *Staphylococcus aureus* (MRSA) screen was negative.

Seventeen days postpartum she was readmitted to hospital with rigors, fever and breathlessness. Despite her symptoms she generally appeared well. However on examination, she had likely left basal pneumonia with no stigmata of endocarditis. Initial investigations revealed grossly elevated inflammatory markers C-reactive protein (CRP) 315; total white count $12.1 \times 10^9/l$ (normal $4-11 \times 10^9/l$) with a neutrophilia $9.1 \times 10^9/l$ (normal $1.7-7.5 \times 10^9/l$). Plain chest radiograph showed patchy consolidation at the left base with a further small opacity at the right base suggestive of multifocal infection (figure 1). Liver function was highly abnormal with alanine transaminase 641 (normal <41 IU/l), alkaline phosphatase 259 (normal 20–130 IU/l) and bilirubin 27 (normal <21 umol/l). Ultrasound of the abdomen was unremarkable.

She was commenced on clarithromycin combined with initially oral amoxicillin before changing to intravenous amoxicillin-clavulanic acid. Despite this she remained febrile with daily spikes of her temperature up to 40°C. Blood culture results were negative in six different sets and repeated high vaginal swabs were also negative. CT of her chest confirmed the presence of multiple cavitating lung lesions (figure 2). She had bronchoscopy with bronchial washings which did not yield any pathogens. Five mls of haemorrhagic fluid was aspirated from a left pleural effusion but did not yield positive culture. Her Mantoux test, Legionella serology, viral hepatitis serology and autoantibody screen were all negative.

After 14 days of intravenous antibiotics, her symptoms continued and her CRP remained 193. Her antimicrobial therapy was changed at this stage to intravenous piperacillin-tazobactam, vancomycin and metronidazole. Haemoglobin decreased to 7.8 g/dl with normal mean cell volume, white cell and platelet count.

An echocardiogram showed a large freely mobile mass involving the anterior tricuspid valve leaflet with a much smaller mass involving the anterior mitral valve leaflet (figure 3). The valves were preserved with no evidence of tricuspid or mitral regurgitation. A diagnosis of culture

Figure 1 Consolidation is seen at the left base with effusion along with bilateral patchy nodular opacities.

negative IE with septic emboli was made. She was then commenced on a combination of intravenous benzylpenicillin (2.4 g 6 hourly) and gentamicin (80 mg twice daily) having stopped all of her previous antibiotics. She had some improvement to her inflammatory markers (CRP 61) but high temperatures continued. The dose of benzylpenicillin was increased to 2.4 g 4 hourly and she became afebrile with CRP at 29. After 2 weeks, a reduction in dose of benzylpenicillin led to further fever and an increase in CRP to 72, so high dose benzylpenicillin was maintained for a further 4 weeks. However, discontinuation of antibiotics then led to spiking of temperature and CRP of 219. She was then referred for surgery and underwent successful

Figure 2 Lung window CT slice at the level of carina confirming nodular opacities with cavitation.

resection of the tricuspid valve vegetation (figure 4) with preservation of her native tricuspid valve.

INVESTIGATIONS

As above.

DIFFERENTIAL DIAGNOSIS

- Culture negative endocarditis
- Non-IE

Figure 3 Transoesophageal echocardiogram demonstrating tricuspid valve vegetation (measuring 2.4×1.38 cm in this view).

TREATMENT

As discussed in the case presentation.

OUTCOME AND FOLLOW-UP

Patient has remained well since her surgery with preserved valvular function on her latest follow-up at 12 months after surgery.

DISCUSSION

In the case described although no pathogens were ever grown from blood, the most likely microorganism is bacterial given the general health of the patient and initial response of clinical and inflammatory markers following intravenous antibiotics. The growth of group B *Streptococcus* in one (out of three) vaginal swab may prove significant. A number of reported cases of tricuspid valve endocarditis in pregnancy or following abortion appear to be attributable to group B *Streptococcus* (*Streptococcus agalactiae*).^{8–13} These bacteria can be isolated from the genital area in 5%–40% of women and are reported to cause neonatal sepsis, chorioamnionitis, endometritis and maternal bacteremia.^{6 14 15} Hospital acquired microorganisms such as MRSA is a possibility in this case, although initial screens were negative. The range of other causative pathogens include common microorganisms such as *Streptococci* of the viridans group and enterococci that may have been difficult to culture due to prior antibiotic use to those that are uncommon such as HACEK group, *Coxiella burnetii*, *Brucella species*, *Bartonella species*, *Legionella pneumophila*, *Chlamydia pneumoniae* and *Tropheryma whippelii* species as well as fungi.¹⁶ The most

commonly isolated microorganisms in CNE are *Bartonella quintana*, *C burnetii* and *Brucella*.¹⁷ The data comes from case report studies with identification rate accounting for 1%–10% of cases. Non-infective valvular vegetations can produce symptoms similar to CNE.^{16 18–21} Four groups of conditions have been identified as potential causes of non-infective vegetative endocarditis. These include neoplastic disease (eg, atrial myxoma, carcinoid, marantic endocarditis); autoimmune disease (antiphospholipid syndrome, rheumatic carditis, systemic lupus erythematosus, polyarteritis nodosa and Behçet's disease); postvalvular surgery and others such as myxomatous degeneration, eosinophilic heart disease and ruptured mitral cordae. Our patient did not have any clinical features for these conditions and on balance it was felt that her symptoms were likely to be related to CNE.

The original Duke criteria for diagnosing IE makes great emphasis for positive blood culture results as well as echocardiography findings with a combination of alternative minor criteria.²² Thus based on the original Duke criteria our patient would fulfil only one major criteria (echocardiography findings) and one minor criteria (fever $>38^{\circ}\text{C}$). The diagnosis then would at best be classified as 'possible' IE. Recent additions to the original Duke criteria has resulted in a 'modified' Duke criteria in the hope of making it more sensitive and particularly useful in CNE by applying serological data (for *C burnetii*) and making some refinements to the minor criteria, in particular, echocardiography findings are now part of major criteria.²³ These changes reflect our increasing understanding of IE

Figure 4 Vegetation attached to leaflet of tricuspid valve.

Table 1 Guidelines for the use of empirical antimicrobials in CNE

British Society for Antimicrobial Chemotherapy

Acute presentation: flucloxacillin + gentamicin

Indolent presentation: penicillin + gentamicin

Penicillin allergic/prosthetic valve/suspected MRSA: vancomycin + gentamicin + rifampicin

European Society of Cardiology

Native valve: vancomycin + gentamicin

Prosthetic valve: vancomycin + gentamicin + rifampicin

American Heart Association

Prior use of antibiotics: ampicillin-sulbactam + gentamicin

Suspected fastidious organisms: ceftriaxone + gentamicin +/- doxycycline

Prosthetic valve:

≤1 year: vancomycin + gentamicin + cefepime

≥1 year: ceftriaxone + gentamicin +/- doxycycline

but highlights some of the limitations still exist in using diagnostic criteria in IE. Indeed some of the basic problems remains, that in routine clinical laboratories serological testing is not done and often takes considerable time making clinical decisions the more important while waiting for these results. Applying the modified Duke criteria would still classify our patient as 'possible' and not 'definite' IE. In a study of 1 998 suspected cases of IE, the application of serological tests according to the modified Duke criteria reclassified approximately 9% of 'possible' IE to 'definite' IE and 7% of 'rejected' IE to 'possible' IE.²⁴ The organisms isolated included *C burnetii*, *Bartonella*, *Legionella* and *Aspergillus* species. With advancing diagnostic techniques and application to CNE, particularly PCR, the likelihood of identifying microorganisms will be higher than currently. However PCR-based techniques are most reliable when done on direct histological specimens (cardiac valves)^{25–28} and requires further validation and standardisation before

it can be applied in routine clinical practice. Additionally, there remains a methodological problem of identifying bacterial DNA and linking it to the causative microorganism as background and persistent bacterial DNA even after therapy may make interpretations of results some what difficult.^{29 30} Nonetheless this technique and others are likely to be very useful diagnostic tools in CNE.

Currently recommended empirical antimicrobial regimes aim to cover common as well as rare pathogens in patients with predictable risk factors. In low risk groups (structurally normal heart, no use of intravenous drugs and no major medical illnesses) the selection of appropriate antimicrobial regimes is often not so clear. In general, empirical antimicrobial treatment in CNE should take into account length of symptoms and presentation, nature of valve (native vs prosthetic) and other risk factors such as intravenous drug use and recent intervention likely to produce bacteraemia. Current guidelines for the use of empirical antimicrobial agents vary (table 1).

The British Society for Antimicrobial Chemotherapy recommendations are based primarily on presentation.³¹ In acutely unwell patients, a combination of flucloxacillin (8–12 g daily in 4–6 divided doses) plus gentamicin (1 mg/kg every 8 h) is used. If the presentation is more indolent then a combination of penicillin (7.2 g daily in six divided doses) or ampicillin/amoxicillin (2 g 6 hourly) plus gentamicin is recommended. In penicillin allergic patients or those with valve prosthesis or MRSA, vancomycin (1 g 12 hourly) plus rifampicin (300–600 mg 12 hourly) plus gentamicin (1 mg/kg 8 hourly) is advised. This is in contrast to the recommendations set out by the European Society of Cardiology which are based on the nature of valve(s) involved.³² Hence in native valve endocarditis, a combination of vancomycin (15 mg/kg 12 hourly) plus gentamicin (1 mg/kg 8 hourly) is recommended. In prosthetic valve

endocarditis, the recommendations are similar to the British Society for Antimicrobial Chemotherapy.

The American Heart Association (AHA) guidelines on the other hand aims to distinguish between two groups of patients with native valve CNE.³³ The first group are those who received antimicrobial treatment prior to collection of blood cultures. In this group, one suggested treatment would be a combination of ampicillin-sulbactam (3 g 6 hourly) plus gentamicin (1 mg/kg 8 hourly). The second group of patients are those with fastidious or slow-growing microorganisms. In this group, emphasis is made to cover for one of the common pathogens *Bartonella* with ceftriaxone (2 g daily) plus gentamicin (3 mg/kg daily in three divided doses) with or without doxycycline (200 mg daily in two divided doses). In penicillin allergic patients, furthermore in native valve endocarditis vancomycin (30 mg/kg daily in two divided doses) plus gentamicin (3 mg/kg daily in three divided doses) plus ciprofloxacin (1000 mg po daily or 800 mg intravenous daily in two divided doses) may be used. For prosthetic valve endocarditis, the duration of the implant is also considered in the AHA guidelines. In patients with so called early (≤ 1 year since implant) prosthetic valve endocarditis, vancomycin (30 mg/kg daily in two divided doses) plus gentamicin (3 mg/kg daily in three divided doses) plus cefepime (6 g daily in three divided doses) plus rifampicin (900 mg daily in three divided doses) can be used. Whereas in late (> 1 year since implant) prosthetic valve endocarditis, regimes such as ceftriaxone (2 g od intravenous or intramuscular as one dose) plus gentamicin (3 mg/kg intravenous or intramuscular in three divided doses) with or without doxycycline (200 mg intravenous or intramuscular in two divided doses) are recommended in suspected *Bartonella* infection.

The duration of antimicrobial therapy according to all three guidelines is between 4 and 6 weeks, with longer duration of therapy in complicated or prosthetic valve patients. However in right-sided endocarditis, shorter course of antimicrobial therapy has been advocated in a number of clinical trials of intravenous drug addicts.^{34–36} What is clear from these recommendations that no single antimicrobial regime is most appropriate for all patients with CNE and therapy will have to be patient-tailored. Practically this may mean initiating one type of antimicrobial regime with the strong possibility that it may need to be changed to another if there is little clinical improvement. Treatment regimes are based on data from case reports and met-analysis with limited data from randomised controlled trials. In particular, combination treatment with β -lactam and aminoglycoside are favoured over monotherapy even when dealing with gram positive bacteria (*Staphylococcus* and *Streptococcus*).³⁷ This treatment paradigm has recently been challenged in two independent met-analyses. The findings by Falagas *et al*³⁸ and Paul *et al*³⁹ show that the addition of aminoglycoside to β -lactam does not affect mortality, treatment success or relapse of endocarditis. Instead there is increased risk of nephrotoxicity with combination therapy versus β -lactam monotherapy. Given the increased incidence of MRSA, should we also use antimicrobial agents empirically to cover for MRSA in CNE? Vancomycin has been the first line therapy for MRSA suspected IE. But recent studies of new antimicrobial agent daptomycin suggest that the drug is as equally

effective against MRSA as the combination of vancomycin plus gentamicin.^{40 41}

Learning points

- CNE remains a clinical problem both in terms of diagnosis and treatment. Serological testing may help identify some of the difficult to grow pathogens and may guide treatment options. Antimicrobial regimes vary between current published guidelines further adding to the difficulty in choosing empirical therapies with combination treatment being favoured overall. Newer antimicrobial agents may prove useful in therapies and could make guidelines more uniform and simpler to apply.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Engl J Med* 2001;**345**:1318–30.
2. Raoult D. Etiological diagnosis of blood-culture-negative endocarditis. *Enferm Infect Microbiol Clin* 2006;**24**:295–6.
3. Werner M, Andersson R, Olaison L, *et al*. A clinical study of culture-negative endocarditis. *Medicine (Baltimore)* 2003;**82**:263–73.
4. Tunkel AR, Kaye D. Endocarditis with negative blood cultures. *N Engl J Med* 1992;**326**:1215–7.
5. Sexton DJ, Rockson SG, Hempling RE, *et al*. Pregnancy-associated group B streptococcal endocarditis: a report of two fatal cases. *Obstet Gynecol* 1985;**66**(3 Suppl):44–7S.
6. Crespo A, Retter AS, Lorber B. Group B streptococcal endocarditis in obstetric and gynecologic practice. *Infect Dis Obstet Gynecol* 2003;**11**:109–15.
7. Shimoni Z, Pitlik S, Szyper-Kravitz M, *et al*. Tricuspid valve endocarditis in adult patients without known predisposing factors. *Eur J Clin Microbiol Infect Dis* 2001;**20**:49–51.
8. Shimoni Z, Ben David M, Niven MJ. Postpartum group B streptococcal tricuspid valve endocarditis. *Isr Med Assoc J* 2006;**8**:883–4.
9. Palys EE, Li J, Gaut PL, *et al*. Tricuspid valve endocarditis with Group B Streptococcus after an elective abortion: the need for new data. *Infect Dis Obstet Gynecol* 2006;**2006**:43253.
10. Kangavari S, Collins J, Cercek B, *et al*. Tricuspid valve group B streptococcal endocarditis after an elective termination of pregnancy. *Clin Cardiol* 2000;**23**:301–3.
11. Felice PV, Salom IL, Levine R. Bivalvular endocarditis complicating pregnancy. A case report and literature review. *Angiology* 1995;**46**:441–4.
12. Nkousa JL, Gombet T, Kimbally-Kary G, *et al*. [Tricuspid infectious endocarditis in Brazzaville. Apropos of 12 cases]. *Ann Cardiol Angeiol (Paris)* 1993;**42**:550–3.
13. Atri ML, Cohen DH. Group B streptococcus endocarditis following second-trimester abortion. *Arch Intern Med* 1990;**150**:2579–80.
14. Seaworth BJ, Durack DT. Infective endocarditis in obstetric and gynecologic practice. *Am J Obstet Gynecol* 1986;**154**:180–8.
15. Krohn MA, Hillier SL, Baker CJ. Maternal peripartum complications associated with vaginal group B streptococci colonization. *J Infect Dis* 1999;**179**:1410–5.
16. Berbari EF, Cockerill FR 3rd, Steckelberg JM. Infective endocarditis due to unusual or fastidious microorganisms. *Mayo Clin Proc* 1997;**72**:532–42.
17. Rolain JM, Brouqui P, Koehler JE, *et al*. Recommendations for treatment of human infections caused by *Bartonella* species. *Antimicrob Agents Chemother* 2004;**48**:1921–33.
18. DeLong CE, Roldan CA. Noninfective endocarditis in rheumatoid arthritis. *Am J Med* 2007;**120**:e1–2.
19. Einav E, Gitig A, Marinescu LM, *et al*. Valvulitis requiring triple valve surgery as an initial presentation of systemic lupus erythematosus. *J Am Soc Echocardiogr* 2007;**20**:1315.e1–3.
20. Joffe II, Jacobs LE, Owen AN, *et al*. Noninfective valvular masses: review of the literature with emphasis on imaging techniques and management. *Am Heart J* 1996;**131**:1175–83.

21. **Hojnik M**, George J, Ziporen L, *et al*. Heart valve involvement (Libman-Sacks endocarditis) in the antiphospholipid syndrome. *Circulation* 1996;**93**:1579–87.
22. **Durack DT**, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994;**96**:200–9.
23. **Li JS**, Sexton DJ, Mick N, *et al*. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;**30**:633–8.
24. **Raoult D**, Casalta JP, Richet H, *et al*. Contribution of systematic serological testing in diagnosis of infective endocarditis. *J Clin Microbiol* 2005;**43**:5238–42.
25. **Goldenberger D**, Künzli A, Vogt P, *et al*. Molecular diagnosis of bacterial endocarditis by broad-range PCR amplification and direct sequencing. *J Clin Microbiol* 1997;**35**:2733–9.
26. **Grijalva M**, Horváth R, Dendis M, *et al*. Molecular diagnosis of culture negative infective endocarditis: clinical validation in a group of surgically treated patients. *Heart* 2003;**89**:263–8.
27. **Gauduchon V**, Chalabreysse L, Etienne J, *et al*. Molecular diagnosis of infective endocarditis by PCR amplification and direct sequencing of DNA from valve tissue. *J Clin Microbiol* 2003;**41**:763–6.
28. **Bosshard PP**, Kronenberg A, Zbinden R, *et al*. Etiologic diagnosis of infective endocarditis by broad-range polymerase chain reaction: a 3-year experience. *Clin Infect Dis* 2003;**37**:167–72.
29. **Branger S**, Casalta JP, Habib G, *et al*. Streptococcus pneumoniae endocarditis: persistence of DNA on heart valve material 7 years after infectious episode. *J Clin Microbiol* 2003;**41**:4435–7.
30. **Rovero C**, Greub G, Lepidi H, *et al*. PCR detection of bacteria on cardiac valves of patients with treated bacterial endocarditis. *J Clin Microbiol* 2005;**43**:163–7.
31. **Elliott TS**, Foweraker J, Gould FK, *et al*. Guidelines for the antibiotic treatment of endocarditis in adults: report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother* 2004;**54**:971–81.
32. **Horstkotte D**, Follath F, Gutschik E, *et al*. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary; the task force on infective endocarditis of the European society of cardiology. *Eur Heart J* 2004;**25**:267–76.
33. **Baddour LM**, Wilson WR, Bayer AS, *et al*. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;**111**:e394–434.
34. **Torres-Tortosa M**, de Cueto M, Vergara A, *et al*. Prospective evaluation of a two-week course of intravenous antibiotics in intravenous drug addicts with infective endocarditis. Grupo de Estudio de Enfermedades Infecciosas de la Provincia de Cádiz. *Eur J Clin Microbiol Infect Dis* 1994;**13**:559–64.
35. **Fortún J**, Navas E, Martínez-Beltrán J, *et al*. Short-course therapy for right-side endocarditis due to Staphylococcus aureus in drug abusers: cloxacillin versus glycopeptides in combination with gentamicin. *Clin Infect Dis* 2001;**33**:120–5.
36. **Chambers HF**, Miller RT, Newman MD. Right-sided Staphylococcus aureus endocarditis in intravenous drug abusers: two-week combination therapy. *Ann Intern Med* 1988;**109**:619–24.
37. **Korzeniowski O**, Sande MA. Combination antimicrobial therapy for Staphylococcus aureus endocarditis in patients addicted to parenteral drugs and in nonaddicts: A prospective study. *Ann Intern Med* 1982;**97**:496–503.
38. **Falagas ME**, Matthaiou DK, Bliziotis IA. The role of aminoglycosides in combination with a beta-lactam for the treatment of bacterial endocarditis: a meta-analysis of comparative trials. *J Antimicrob Chemother* 2006;**57**:639–47.
39. **Paul M**, Silbiger I, Grozinsky S, *et al*. Beta lactam antibiotic monotherapy versus beta lactam-aminoglycoside antibiotic combination therapy for sepsis. *Cochrane Database Syst Rev* 2006;**1**:CD003344.
40. **Fowler VG Jr**, Boucher HW, Corey GR, *et al*. Daptomycin versus standard therapy for bacteremia and endocarditis caused by Staphylococcus aureus. *N Engl J Med* 2006;**355**:653–65.
41. **Kanafani Z**, Boucher H, Fowler V, *et al*. Daptomycin compared to standard therapy for the treatment of native valve endocarditis. *Enferm Infecc Microbiol Clin* 2010;**28**:498–503.

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