Sp53: **What is the optimal management of patients with pyogenic spinal infection who have failed one regimen of antibiotic treatment**

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Recommendation: Once treatment failure has been established, surgical intervention becomes the primary approach. Surgery offers several advantages, including reducing the infective load, removing and replacing diseased tissue, obtaining biopsy samples for culture and histopathology, and addressing stability and deformity.

However, in cases of medical management failure, it is essential to reassess the diagnosis by revisiting biopsy, cultures, and imaging to establish a credible underlying cause before proceeding with further treatment.

Strength of Recommendation: Low

Delegate Vote:

Rationale:

The overall quality of evidence is quite poor; nonetheless recommendations do exist based on systematic reviews, expert opinion and similar case scenarios.

Some of the key observations of this Review of literature are as follows in terms of answering the question- What is the optimal management of patients with pyogenic spinal infection who have failed one regimen of antibiotic treatment?

Antibiotic therapy is the mainstay of treatment of pyogenic spondylodiscitis with 72-85.7% success rate (Gregori). Typically failure of drug therapy is defined as persistence, progression or recurrence (after initial relief) after 6 weeks of antibiotic therapy for pyogenic spondylodiscitis (Tong). Others (Blecher) have defined it as failure of clinical and/or serological resolution and progress of deformity and/or neurological deficit . Flury has recommended that persistence of clinical, laboratory abnormalities with related readmissions or death be used as an appropriate definition. Several risk factors have been suggested such as < 4 weeks of drug therapy (Skaf), epidural abscess, cervical and dorsal lesions, and >3 vertebrae affection (Jin). Pola et al also proposed a negative culture as a poor prognostic factor while Li et al suggested that a positive blood culture and abscess formation are indicative of possible treatment failure. Serial monitoring of CRP has been shown to be a reliable predictor of healing (Ibrahim, Legrand) as well as X rays (Legrand) though MRI has not been recommended frequently. A reduction of CRP by 50% per week is a good prognostic factor (Duarte). FDG PET is an evolving modality that has shown some promise (Duarte) in monitoring patients.

Prevention of such failure of medical management is important and the recommendations are varied. Several authors suggest 6-12 weeks of antibiotics (Tavarisingam) of which 2-4 weeks is IV (particularly if MRSA is diagnosed) (Al Nammari) followed by oral upto 18 weeks total. Passerini et al reported the IDSA guidelines which suggests that suggests 6 weeks of IV antibiotics and goes to demonstrate that 2 weeks IV followed bu oral is as effective as 6 weeks IV. In culture positive cases 6 weeks therapy is shown to be as effective as 12 weeks (Bernard) where as in blood culture negative cases Li suggests 3 weeks of antibiotic therapy (If concurrent

surgery is elected). Other suggestions to prevent failure is the usage of 2 synergistic bactericidal antibiotics simultaneously for 12 weeks(Grados). For culture negative cases Guoliouris et al recommends the addition of Rifampicin or Fucidin to the primary antibiotic to enhance cure rates. The systematic review by Rutges et al have recommended the usage of Daptomycin to improve healing rates particularly in MRSA infections.

Once failure has been established the treatment is largely surgical (Skaf, Blecher, Beretta, Valancius etc). The advantages of surgery are that the infective load can be reduced, diseased tissue removed and replaced, biopsy culture histopathology obtained and stability and deformity corrected (Rutges , Duartes, Grados). Early surgery can reduce mortality and morbidity by 40% (Tavarjasingam). Several other modalities have been reported with individual success rates like hyperbaric Oxygen therapy (Korpinar), paravertebral muscle infiltration of antibiotics (Bonura), etc. Duarte and Vacarro in their algorithm of management suggest that failure of medical management should mean that one goes back and start all over again with biopsy, cultures and imaging to try and reestablish a credible cause.

References:

1. Skaf GS et al 2010, Lebanon. <4 weeks is a risk factor; >12 weeks rarely needed; Failure of conservative (not defined) is n indication for surgery
2. Tong YJ et al. 2019, China. Definition- Progression, persistence or recurrence of disease despite 6 weeks of antimicrobial therapy.
3. Korpinar S. Turkey 2019. N=19; Failure 4-6 weeks of antibiotics; Hyper baric O2 is a good adjuvant. Not RCT. Only SSI
4. Tavarjasingam SG. Et al. UK Germany, 2023, Systematic review. N=10954 from 21 studies. Failure of conservative Rx not defined; Drug therapy was 4-12 weeks; early surgery had 40% risk reduction in terms of mortality and morbidity.
5. Al Nammari SS et al 2007. UK. N=13. Only MRSA diskitis; 2-4 weeks of IV followed by oral for 6-18 weeks total. Failure not defined.
6. Flury BB et al. 2014. Switzerland. N=61. Failure- persistence of signs and symptoms, lab signs and neurology + related readmission or related death.
7. Bernard L et al France 2015. RCT 6 vs 12 weeks of antibiotics. N=176 vs 175. 6 is non inferior to 12. Only culture + cases included.
8. Blecher R et al . 2023. USA. N=42. Failure- Non responsiveness to Rx, Progress of deformity or neurology. Surgery
9. Beretta RS et al. 2023. USA. N= 9983; Retrospective cohort study. 45.5% MR S Aureus, 31.02% surgical cases. 37.29% re-op at 1 year.
10. Passerini M et al 2022 USA. IDSA guidelines 2015 is 6 weeks of IV antibiotics (Berbari et al); Systematic review and MA (N=14 studies 1078 patients);<2 weeks was early switch from IV to oral. No evidence of benefit of IV over oral.
11. Gregori et al. Italy 2019. 72-85.7% succeeds with antibiotics alone. Clinical, Lab imaging for failure.
12. Bonura EM et al 2019 Italy. Paravertebral muscle injection of antibiotics.
13. Jin Y et al 2022. USA. N=242. Risk factors for surgery are presence of epidural abscess, Cervical and Dorsal spine affection and >3 vertebrae affection.
14. Pola E et al. 2018. Italy. N=207. Microbial Diagnosis was the main predictor for success. Neg culture was the most common neg prognostic factor.
15. Duarte RM Vacarro AR. Portugal 2013. Management algorithm. Suggest in their algorithm that if response is poor go back and restart with biopsy. Gallium scan or FDG PET for follow up (not MRI); CRP reduction of 50% per week is good response.

16. Valancius K et al. 2012, Denmark. N=196. Failure means surgery.
17. Li YD et al Taiwan 2018. N=59. +ve blood culture and abscess formation are risk factors and need longer antibiotic Rx; if not 3 weeks is enough in surgical patients
18. Grados F et al France 2006. N=85 articles reviewed. Initial Rx is 2 synergistic bactericidal antibiotics; total duration is 12 weeks. Grade D recommendation X-ray follow up 3 months after stopping antibiotics.
19. Gouliouris T et al 2010. UK. Adding Rifampicin, or Fucidin as combination drugs in culture negative cases.
20. Legrand E et al. 2001. France N=110. Blood culture +vs in 47.3% Biopsy culture +ve in 63.6%. Outcome measures- clinical, radiological and serological (ESR CRP)
21. JPHJ Rutges et al. 2015. Netherlands. Systematic Review N=25 studies. 6 weeks antibiotic strong recommendation. Minimum 8 weeks in MRSA and Daptomycin usage has better results than Vancomycin in MRSA.
22. Ibrahim A. et al 2024. Egypt. N=38. CRP is a good guide for success of medical management