Sp69: What are the factors that decide cessation of antibiotic course in native pyogenic spinal infections? Do patients with healed infection require periodic follow-up?

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Recommendation: Based on the available literature, authors recommend a tailored antibiotic treatment duration of at least 6 weeks for native pyogenic spinal infections. Cessation of therapy can be further guided by monitoring serum inflammatory markers (primarily ESR) for sufficient downtrend as well as resolution of associated clinical signs and symptoms of infection. There is moderate evidence for use of ^{18}F-FDG PET/CT scan to confirm success of treatment, especially when combined with serum inflammatory markers, but this should be reserved as supplementary. Although useful for diagnosis, MRI does not provide significant utility for determining antibiotic cessation.

For patient follow-up, authors suggest close monitoring up to one year for those deemed at high risk (neurological deficit, age ≥ 65, epidural/paravertebral abscess) for recurrence/sequelae based on risk factors. For patients without these factors, no such conclusion on follow-up can be drawn from the literature.

Level of Evidence: Low

Delegate Vote:

Rationale:

Several studies advocate for a standard antibiotic duration of 6-8 weeks for patients with native pyogenic spinal infections [1-3]. Bernard et al. conducted a non-inferiority randomized controlled trial of 359 patients with pyogenic vertebral osteomyelitis. Reporting on cure rate at 1 year, they found that 6 weeks of standard antibiotic therapy was not inferior to 12 weeks [2]. This was further supported by Da Nóbrega Danda et al. via a retrospective cohort study of 50 patients with pyogenic spondylodiscitis. They concluded that longer antibiotic duration did not have any advantage with respect to infection cure rate. However, recurrence in those at higher risk, identified as spinal cord compression, sensory deficit, or antibiotic commencement prior to microorganism identification, may warrant an extended course of 8+ weeks, according to the authors [3]. This notion was supported by Park et al., who retrospectively reported improvement in recurrence rate of hematogenous vertebral osteomyelitis with 8+ week antibiotic therapy, specifically for patients infected with MRSA or with undrained paravertebral/psoas abscess [4].

In addition to the antibiotic duration suggestions, cessation may be guided by lab results. The literature is inconclusive as to which lab(s) is most useful, but ESR may be the optimal test for following treatment course [1, 5, 6]. According to Osenbach et al., ESR trends downward over a longer duration than CRP and WBC count and is more consistent with the eradication of the infectious organism. Specifically, the authors found a mean ESR value of 85 mm/h at time of diagnosis with pyogenic vertebral osteomyelitis and 25 mm/h when antibiotic therapy was complete. It is important to note that ESR often remained elevated above ‘normal’ at cessation, but this did not correlate with treatment failure. Therefore, it is the downward trend that is useful for determining treatment success, not absolute value. WBC count did not follow any consistent

trend [1]. Chiang et al. further supported this claim, noting no usable trend in WBC count and a return of CRP to <5mg/dL after 2 weeks of antibiotic therapy in 79.4% of their study population with pyogenic vertebral osteomyelitis. ESR, conversely, saw a consistent decline in successful treatment over the antibiotic course and afterwards [5]. Two other studies advocate for use of both CRP and ESR to evaluate treatment success [7, 8]. However, both drew labs on only two occasions for analysis: at diagnosis and at antibiotic treatment cessation. This means the trend over time of both CRP and ESR could not be adequately evaluated, and there is no way of knowing how quickly CRP fell in these patients. Thus, testing for decreased CRP at time of cessation may still be useful, but should not be relied upon without concomitant ESR value.

Imaging is another possible tool for antibiotic cessation, but does not appear to be first-line in decision making. As noted by several studies, repeat MRI beyond diagnostic usage does not appear useful and may even lead to unnecessary surgical treatment or antibiotic extension [7, 9-12]. For example, Zarrouk et al. actually noted a persistence of positive MRI findings in many patients treated for vertebral osteomyelitis after successful antibiotic course. At 3 months (average duration of antibiotic therapy), 66% of sites still had vertebral edema, 42% had discal abscess, and 9% had paravertebral abscess. These findings decreased over time, and were not indicative of treatment failure [11]. Some studies do, however, report utility of ^{18}F-FDG PET/CT scan for evaluating treatment success in pyogenic spine infections [9, 10]. Russo et al. determined ^{18}F-FDG PET/CT to be more reliable and accurate for identifying good treatment response of vertebral osteomyelitis in comparison to MRI. Further, the authors suggest this imaging study, in combination with inflammatory markers, could be a feasible method to monitor treatment response going forward [10]. This tool does need further investigation to confirm utility, but may be a second-line metric for patients if needed.

Lastly, clinical signs and symptoms (or lack thereof) consistent with successful antibiotic therapy and disease cure should be heavily considered for determining when to stop medical treatment [1, 7, 9, 12-14]. Presence of such does not necessarily mean treatment failure, but should prompt deeper consideration as to whether cessation is warranted.

Regarding post-infection follow-up, the literature is inconclusive on whether follow-up should be routine. However, one study does suggest close follow up for those deemed at high risk for recurrence/sequelae based on risk factors (neurological deficit, age ≥ 65, epidural/paravertebral abscess) [15]. For patients without these factors, no such conclusion on follow-up can be drawn from the literature.

References:

1. Osenbach, R.K., P.W. Hitchon, and A.H. Menezes, Diagnosis and management of pyogenic vertebral osteomyelitis in adults. Surg Neurol, 1990. **33**(4): p. 266-75.
2. Bernard, L., et al., Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial. Lancet, 2015. **385**(9971): p. 875-82.
3. Da Nóbrega Danda, G.J., de Castro, C.N., PYOGENIC SPONDYLODISCITIS: RISK FACTORS FOR THERAPEUTIC FAILURE AND RECURRENCE. Coluna/ Columna, 2023. **22**(2).

4. Park, K.H., et al., Optimal Duration of Antibiotic Therapy in Patients With Hematogenous Vertebral Osteomyelitis at Low Risk and High Risk of Recurrence. Clin Infect Dis, 2016. **62**(10): p. 1262-1269.
5. Chiang, H.Y., et al., First-4-week erythrocyte sedimentation rate variability predicts erythrocyte sedimentation rate trajectories and clinical course among patients with pyogenic vertebral osteomyelitis. PLoS One, 2019. **14**(12): p. e0225969.
6. Carragee, E.J., et al., The clinical use of erythrocyte sedimentation rate in pyogenic vertebral osteomyelitis. Spine (Phila Pa 1976), 1997. **22**(18): p. 2089-93.
7. Euba, G., et al., Long-term clinical and radiological magnetic resonance imaging outcome of abscess-associated spontaneous pyogenic vertebral osteomyelitis under conservative management. Semin Arthritis Rheum, 2008. **38**(1): p. 28-40.
8. Özdemir, M.B., Serkan & Başaran, Seniha & Karalar, Şahin & Korkmaz, Murat & Akgül, Turgut & Eraksoy, Ömer, Annals of Clinical and Analytical Medicine Original Research Evaluation of the success of conservative treatment in spondylodiscitis patients with relevant laboratory findings. Annals of Clinical and Analytical Medicine, 2022. **14**.
9. Raghavan, M., E. Lazzeri, and C.J. Palestro, Imaging of Spondylodiscitis. Semin Nucl Med, 2018. **48**(2): p. 131-147.
10. Russo, A., et al., Management of vertebral osteomyelitis over an eight-year period: The UDIPROVE (UDIne PROtocol on VErtebral osteomyelitis). Int J Infect Dis, 2019. **89**: p. 116-121.
11. Zarrouk, V., et al., Imaging does not predict the clinical outcome of bacterial vertebral osteomyelitis. Rheumatology (Oxford), 2007. **46**(2): p. 292-5.
12. Okumura, N., et al., Effectiveness of oral cephalexin in antibiotic-course completion for methicillin-susceptible Staphylococcus aureus-induced bacteremic vertebral osteomyelitis. BMC Infect Dis, 2023. **23**(1): p. 307.
13. Al-Nammari, S.S., J.D. Lucas, and K.S. Lam, Hematogenous methicillin-resistant Staphylococcus aureus spondylodiscitis. Spine (Phila Pa 1976), 2007. **32**(22): p. 2480-6.
14. Dholoo, F., et al., Spondylodiscitis-a cohort analysis of its identification and management. Int Orthop, 2023. **47**(3): p. 813-818.
15. Lee, Y.M., et al., Factors associated with sequelae after treatment of hematogenous pyogenic vertebral osteomyelitis. Diagn Microbiol Infect Dis, 2019. **94**(1): p. 66-72.