Author: Susana Núñez-Pereira

QUESTION 2: When should patients with suspected infections of the spine be referred to an infectious disease department?

RECOMMENDATION: There is no data on the timing or need for a referral to an infectious disease department. We support a multidisciplinary approach to managing clinical spine infections.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Only one paper has addressed the collaboration with an infectious disease-specialized team in order to improve outcomes for patients with spinal surgical site infections (SSIs). The paper is a retrospective study reporting on 40 patients, none of whom needed implant removal [1]. The paper didn't report on the exact timing when collaboration started, but reported three main advantages related with this collaboration:

1. Efficient detection of auxiliary bacteria (reached 88%)
2. Early treatment with antibiotics
3. Appropriate duration of administration of antibiotics

There were no other papers which discussed this issue, and all subsequent searches on related articles yielded no more information on the matter.

From a theoretical point of view, referral, or at least counselling by an infectious diseases specialist, might have some advantages. Antibiotic treatments are more complex today and only specialists are adequately up-to-date on the issue. The appropriate treatment choice might be difficult in patients with allergies, multi-resistant smears or simply a low tolerance for the medication. Adjusting the choice of antibiotic, taking into account side effects and tolerance, will very likely improve compliance, which is paramount in reaching a successful treatment outcome.

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Authors: Dolors Rodriguez-Pardo, Gregory Schroeder

QUESTION 3: Which patients with vertebral osteomyelitis (VO) are suitable for outpatient management? Does any criteria exist to aid in this decision-making?

RECOMMENDATION: There are no studies aiming to identify which patients diagnosed with VO can be treated on an outpatient basis.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

VO, also known as spondylodiscitis, describes an infection of the vertebrae and intervertebral disc. By comparison, discitis describes infection limited to the intervertebral disc, however there are many who consider discitis and VO to be different stages of the same disease process. VO can arise from hematogenous seeding, contiguous spread from infection in adjacent soft tissues or direct inoculation during spinal surgery or procedures (i.e., epidural). Management of native vertebral osteomyelitis (NVO) depends on the location of the infection, disease progression and the patient's general condition including age and comorbidities.

Conservative treatment is reasonable in the early stages with no or minor neurologic deficits or in the case of severe comorbidities. However, in cases of doubt, surgical treatment should be considered. Both options require a concomitant antimicrobial therapy, initially applied intravenously and administered orally thereafter [1]. To date, there is no consistent data from randomized controlled trials to guide the optimal duration and appropriate route of antibiotic therapy. Although the optimal duration of antibiotic therapy remains controversial, it should never undercut six weeks [2]. Recent Infectious Diseases Society of America (IDSA) guidelines for the diagnosis and treatment of NVO in adults include evidence and opinion-based recommendations for the management of patients with NVO treated with antimicrobial therapy, with or without surgical intervention, but do not address the issue of which patients affected by NVO can be treated on an outpatient basis [3,4]. The extent of pursuing spinal biopsies to determine etiology, antimicrobial therapy, response to treatment and preference for surgical techniques and timing all vary widely in clinical practice with heterogeneous studies limiting comparisons. Surgery, rather than conservative approaches, is being proposed as the default management choice because in carefully-selected patients it can offer faster reduction in pain scores and improved quality of life [5–9]. Due to a

heterogeneous and often comorbid patient population and the wide variety of treatment options, no generally applicable guidelines for VO exist and management remains a challenge.

The goals of treatment include establishing a diagnosis and identifying the pathogen, eradicating the infection, preventing or minimizing neurologic involvement, maintaining spinal stability and providing an adequate nutritional state to combat infection. Often, this can be accomplished with non-operative approaches.

The mainstay treatment of pyogenic infections of the spine remains antibiotic therapy and immobilization with a proper orthosis. If nonsurgical treatment fails, however, surgical intervention may be required. Surgery is indicated in the following circumstances: to obtain a bacteriologic diagnosis when closed biopsy is negative or deemed unsafe, when a clinically significant abscess is present (spiking temperatures and evidence of sepsis), in cases of refractory to prolonged non-operative treatment where the sedimentation rate remains high or pain persists, in cases of spinal cord compression causing a neurologic deficit and in cases of substantial deformity or vertebral body destruction, especially in the cervical spine. Alton et al. reported that 75% of patients with an epidural abscess in the cervical spine who underwent medical management failed and that medical management failure was associated with a significantly increased risk of neurologic injury [10]. Patel et al. reported on 128 patients with an epidural abscess and found that 41% failed medical management. However, there were significant predictors of medical failure [11]. Four key predictors were identified, including diabetes mellitus, C-reactive protein (CRP) greater than 115, white blood cell count greater than 12.5 and positive blood culture. Patients with none of the aforementioned parameters only failed 8.3% of the time. Those with one parameter failed 35.4% of the time, those with two parameters failed 40.2% of the time and patients with three or more parameters failed 76.9% of the time.

Once the antibiotic is prescribed by oral route, if the patient is stable, the treatment could be administered in an outpatient setting. Several studies described a successful switch to oral antibiotics after 10 days, using oral agents with a high bio-availability and tissue penetration (i.e., fluorquinolones, rifampin, fusidic acid and clindamycin) [12–15]. A retrospective analysis of all patients diagnosed with NVO, at the University Hospital of Basel, Switzerland, concluded that switching to an oral antibiotic regimen after two weeks of intravenous treatment may be safe, if CRP has decreased compared to baseline CRP and epidural or paravertebral abscesses of significant size have been drained [16]. Importantly, these results do not extend to patients with endocarditis, surgical site infection, and/or vertebral implants. Also, positive blood cultures, neurological abnormalities and staphylococcal infections (compared with negative microbiology) are associated with longer intravenous courses [17].

Outpatient parenteral antibiotic therapy (OPAT) has become an option allowing for early discharge of hospitalized patients who have infections without a reliable oral alternative and requires lengthy antibiotic therapy. It provides numerous benefits, some of the most remarkable being that OPAT permits early discharge and reduces costs, avoids hospitalization trauma in children or immobilization syndrome in the elderly and reduces nosocomial infections by multidrug resistant organisms [17]. OPAT also allows for self-administration of antibiotics using elastomeric pumps [18,19]. Different retrospective studies and case series have reviewed the experience with OPAT in several countries [17,19–27]. β-Lactam antibiotics are commonly used in OPAT with higher treatment success among those treated with ceftriaxone and ertapenem, while oxacillin was associated with a higher rate of antimicrobial discontinuation because of antimicrobial-related complications [17,20,26]. Other alternatives are teicoplanin, telavancin or daptomycin in the case of gram-positive infections [17,25,28]. All this data regarding OPAT confirms that infection management in an outpatient setting is safe, clinically efficacious, and acceptable for treating a wide range of infections with high levels of patient satisfaction and substantial cost savings. Therefore, OPAT could be considered an effective alternative for appropriately selected elderly patients with vertebral osteomyelitis.

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QUESTION 4: What is the optimal treatment of spinal infections caused by *Propionibacterium acnes* (*P. acnes*)?

RECOMMENDATION: When possible, patients should undergo complete removal of implants after *Cutibacterium acnes* (*C. acnes*) (formerly *P. acnes*) infection, especially in the setting of latent infection. Antibiotic regimens typically involve specific parenteral antibiotics for a period of greater than two weeks, with the most common antibiotic duration being six weeks of multiple parenteral and/or oral agents. However, the duration of antibiotic treatment is highly variable. It is unclear in which setting patients may be successfully treated with antibiotic therapy alone and instrumentation may be retained. Penicillin is currently the standard of care, but other non beta-lactam antibiotics should be considered based on the susceptibility profile.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 73%, Disagree: 7%, Abstain: 20% (Super Majority, Strong Consensus)

RATIONALE

P. acnes is an anaerobic, gram-positive bacillus existing as normal flora of the skin and sebaceous glands and was originally considered a common contaminant of blood cultures as well as an uncommon cause of brain, pulmonary and dental infections [1]. *C. acnes* infections are commonly thought to originate from patient skin approximation with surgical sites, are frequently poly-microbial, require an extended incubation period in culture media for diagnosis and form a resistant biofilm, making treatment with antibiotics alone difficult [2–4].

P. acnes infection of the spine was first reported as an etiology of spine infection by Serushan et al. in 1982 [5]. The patient presented with osteomyelitis of the cervical spine and was treated with 40 days of intravenous penicillin with resolution of his fever and neck pain. *C. acnes* has subsequently been implicated in vertebral osteomyelitis and discitis and may present with insidious onset of back pain, fever and/or neurologic symptoms, with treatment typically involving administration of parenteral antibiotics. Additional debridement or percutaneous drainage of abscesses occurs in rare cases [6–8]. Duration of antibiotics ranged from 2-28 weeks in one series, and typically involved multiple agents due to the frequency of co-infection with other pathogens including *Staphylococcus,* Lactobacillus and Enterococcus species [9].

Tsai et al. reported on successful treatment of two cases of *C. acnes* osteomyelitis of the cervical spine with anterior debridement, decompression and fusion with autograft and treatment with a combination of oral and parenteral antibiotics for 6-16 weeks [10]. Overall, the decision to treat *C. acnes* vertebral osteomyelitis and discitis with surgery, antibiotics or a combination of these approaches has been made on a case-by-case basis. No well-defined, widely-applicable treatment regimen was identified in the literature.

C. acnes also frequently presents as a delayed infection after spinal instrumentation, which has been attributed to its low virulence and slow growth rate, and is common in instrumented pediatric scoliosis surgery [4,11–17]. Viola et al. reported a series of eight patients with delayed infection, one of which had *C. acnes* infection and was treated with irrigation and debridement, removal of instrumentation and six weeks of cefotetan with good results and no loss of balance or alignment at midterm follow-up. Of 23 patients with delayed infections after posterior TSRH instrumentation, Richards and Emara found that the causative agent in delayed infections was *C. acnes* in 12 (52.1%). Patients underwent removal of instrumentation with either primary or delayed closure and parenteral antibiotics (two to five days) followed by a course of oral antibiotics for an additional two to four weeks [18]. Tribus reported on a delayed infection with *Staphylococcus epidermidis* and *C. acnes* resulting in laminar erosions seven years after TSRH instrumentation. The patient was treated with removal of instrumentation and seven weeks of intravenous vancomycin and oral rifampin with resolution of pain and infection [12]. In cases of late implant infections, successful treatment typically involved implant removal and greater than two weeks of a combination of parenteral and oral antibiotics.

In the largest single study evaluating treatment of *C. acnes* infection after Cotrel-Dubousset instrumentation, Bemer et al. conducted a retrospective study investigating various treatment regimens including complete or partial implant removal, implant replacement and maintenance of implants with irrigation and debridement, both with and without antibiotics. Patients who underwent partial removal with antibiotic monotherapy or absence of antibiotic therapy were more likely to develop a secondary infection. Ultimately, wide variation in treatment regimens prevented more mean-