2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults[a]

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These guidelines are intended for use by infectious disease specialists, orthopedic surgeons, neurosurgeons, radiologists, and other healthcare professionals who care for patients with native vertebral osteomyelitis (NVO). They include evidence and opinion-based recommendations for the diagnosis and management of patients with NVO treated with antimicrobial therapy, with or without surgical intervention.

Keywords. spondylodiscitis; osteomyelitis; *Staphylococcus aureus*; spine infection; discitis.

EXECUTIVE SUMMARY

Native vertebral osteomyelitis (NVO) in adults is often the result of hematogenous seeding of the adjacent disc space from a distant focus, as the disc is avascular [1, 2]. The diagnosis of NVO can often be delayed several months and may initially be misdiagnosed and mismanaged as a degenerative process [3, 4]. NVO is typically diagnosed in the setting of recalcitrant back pain unresponsive to conservative measures and elevated inflammatory markers with or without fever. Plain radiographs of the spine are not sensitive for the early diagnosis of NVO. Magnetic resonance imaging (MRI) of the spine is often required to establish the diagnosis. Except in septic patients or patients with neurologic compromise, empiric antimicrobial therapy should be withheld, when possible, until a microbiologic diagnosis is confirmed. An image-guided or intraoperative aspiration or biopsy of a disc space or vertebral endplate sample submitted for microbiologic and pathologic examination often establishes the microbiologic or pathologic diagnosis of NVO [5]. NVO is commonly monomicrobial and most frequently due to *Staphylococcus aureus* [6–8]. The concomitant presence of *S. aureus* bloodstream infection within the preceding 3 months and compatible spine MRI changes preclude the need for a disc space aspiration in most patients [1, 9, 10]. Definitive therapy should be based on the results of culture and in vitro susceptibility testing. The majority of patients are cured with a 6-week course of antimicrobial therapy, but some patients may need

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[a]Guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances.

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surgical debridement and/or spinal stabilization during or after a course of antimicrobial therapy [7, 11–13]. Indications for surgery may include the development of neurologic deficits or symptoms of spinal cord compression and evidence of progression or recurrence despite proper antimicrobial therapy [6]. Most patients can be followed symptomatically and by monitoring laboratory parameters such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [14]. Repeat imaging studies should be reserved for patients failing to show clinical and or laboratory improvement [15, 16].

Summarized below are the Infectious Diseases Society of America (IDSA) recommendations pertaining to the diagnosis and management of patients with NVO. The expert panel followed a process used in the development of other IDSA guidelines, which included a systematic weighting of the strength of recommendation and quality of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system [17–20] (Table 1). A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found online in the full text of the guidelines.

RECOMMENDATIONS FOR CLINICAL DIAGNOSTICS

I. When Should the Diagnosis of NVO Be Considered?

Recommendations

1. Clinicians should suspect the diagnosis of NVO in patients with new or worsening back or neck pain and fever (strong, low).
2. Clinicians should suspect the diagnosis of NVO in patients with new or worsening back or neck pain and elevated ESR or CRP (strong, low).
3. Clinicians should suspect the diagnosis of NVO in patients with new or worsening back or neck pain and bloodstream infection or infective endocarditis (strong, low).
4. Clinicians may consider the diagnosis of NVO in patients who present with fever and new neurologic symptoms with or without back pain (weak, low).
5. Clinicians may consider the diagnosis of NVO in patients who present with new localized neck or back pain, following a recent episode of *Staphylococcus aureus* bloodstream infection (weak, low).

II. What Is the Appropriate Diagnostic Evaluation of Patients With Suspected NVO?

Recommendations

6. We recommend performing a pertinent medical and motor/sensory neurologic examination in patients with suspected NVO (strong, low).
7. We recommend obtaining bacterial (aerobic and anaerobic) blood cultures (2 sets) and baseline ESR and CRP in all patients with suspected NVO (strong, low).
8. We recommend a spine MRI in patients with suspected NVO (strong, low).
9. We suggest a combination spine gallium/Tc99 bone scan, or computed tomography scan or a positron emission tomography scan in patients with suspected NVO when MRI cannot be obtained (eg, implantable cardiac devices, cochlear implants, claustrophobia, or unavailability) (weak, low).
10. We recommend obtaining blood cultures and serologic tests for *Brucella* species in patients with subacute NVO residing in endemic areas for brucellosis (strong, low).
11. We suggest obtaining fungal blood cultures in patients with suspected NVO and at risk for fungal infection (epidemiologic risk or host risk factors) (weak, low).
12. We suggest performing a purified protein derivative (PPD) test or obtaining an interferon-γ release assay in patients with subacute NVO and at risk for *Mycobacterium tuberculosis* NVO (ie, originating or residing in endemic regions or having risk factors) (weak, low).
13. In patients with suspected NVO, evaluation by an infectious disease specialist and a spine surgeon may be considered (weak, low).

III. When Should an Image-Guided Aspiration Biopsy or Additional Workup Be Performed in Patients With NVO?

Recommendations

14. We recommend an image-guided aspiration biopsy in patients with suspected NVO (based on clinical, laboratory, and imaging studies) when a microbiologic diagnosis for a known associated organism (*S. aureus*, *Staphylococcus lugdunensis*, and *Brucella* species) has not been established by blood cultures or serologic tests (strong, low).
15. We advise against performing an image-guided aspiration biopsy in patients with *S. aureus*, *S. lugdunensis*, or *Brucella* species bloodstream infection suspected of having NVO based on clinical, laboratory, and imaging studies (strong, low).
16. We advise against performing an image-guided aspiration biopsy in patients with suspected subacute NVO (high endemic setting) and strongly positive *Brucella* serology (strong, low).

IV. How Long Should Antimicrobial Therapy Be Withheld Prior to an Image-Guided Diagnostic Aspiration Biopsy in Patients With Suspected NVO?

Recommendations

17. In patients with neurologic compromise with or without impending sepsis or hemodynamic instability, we recommend immediate surgical intervention and initiation of empiric antimicrobial therapy (strong, low).

Table 1. Strength of Recommendations and Quality of the Evidence

Strength of Recommendation and Quality of Evidence	Clarity of Balance Between Desirable and Undesirable Effects	Methodological Quality of Supporting Evidence (Examples)	Implications
Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research is unlikely to change our confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Strong recommendation, low-quality quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence	Recommendation may change when higher-quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Strong recommendation, very-low-quality evidence (very rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher-quality evidence becomes available; any estimate of effect for at least 1 critical outcome is very uncertain.
Weak recommendation, high-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patients or societal values. Further research is unlikely to change our confidence in the estimate of effect.
Weak recommendation, moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation, low-quality evidence	Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced	Evidence for at least 1 critical outcome from observational studies or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Weak recommendation, very low-quality evidence	Major uncertainty in the estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least 1 critical outcome, is very uncertain.

Abbreviation: RCT, randomized controlled trial.

V. When Is It Appropriate to Send Fungal, Mycobacterial, or Brucellar Cultures or Other Specialized Testing Following an Image-Guided Aspiration Biopsy in Patients With Suspected NVO?

Recommendations

18. We suggest the addition of fungal, mycobacterial, or brucellar cultures on image-guided biopsy and aspiration specimens in patients with suspected NVO if epidemiologic, host risk factors, or characteristic radiologic clues are present (weak, low).
19. We suggest the addition of fungal and mycobacterial cultures and bacterial nucleic acid amplification testing to appropriately stored specimens if aerobic and anaerobic bacterial cultures reveal no growth in patients with suspected NVO (weak, low).

VI. When Is It Appropriate to Send the Specimens for Pathologic Examination Following an Image-Guided Aspiration Biopsy in Patients With Suspected NVO?

Recommendation

20. If adequate tissue can be safely obtained, pathologic specimens should be sent from all patients to help confirm a diagnosis of NVO and guide further diagnostic testing, especially in the setting of negative cultures (strong, low).

VII. What Is the Preferred Next Step in Patients With Nondiagnostic Image-Guided Aspiration Biopsy and Suspected NVO?

Recommendations

21. In the absence of concomitant bloodstream infection, we recommend obtaining a second aspiration biopsy in patients with suspected NVO in whom the original image-guided aspiration biopsy specimen grew a skin contaminant (coagulase-negative staphylococci [except *S. lugdunensis*], *Propionibacterium* species, or diphtheroids) (strong, low).
22. In patients with a nondiagnostic first image-guided aspiration biopsy and suspected NVO, further testing should be done to exclude difficult-to-grow organisms (eg, anaerobes, fungi, *Brucella* species, or mycobacteria) (strong, low).
23. In patients with suspected NVO and a nondiagnostic image-guided aspiration biopsy and laboratory workup, we suggest either repeating a second image-guided aspiration biopsy, performing percutaneous endoscopic discectomy and drainage (PEDD), or proceeding with an open excisional biopsy (weak, low).

RECOMMENDATIONS FOR CLINICAL THERAPY

VIII. When Should Empiric Antimicrobial Therapy Be Started in Patients With NVO?

Recommendations

24. In patients with normal and stable neurologic examination and stable hemodynamics, we suggest holding empiric antimicrobial therapy until a microbiologic diagnosis is established (weak, low).
25. In patients with hemodynamic instability, sepsis, septic shock, or severe or progressive neurologic symptoms, we suggest the initiation of empiric antimicrobial therapy in conjunction with an attempt at establishing a microbiologic diagnosis (weak, low).

IX. What Is the Optimal Duration of Antimicrobial Therapy in Patients With NVO?

Recommendations

26. We recommend a total duration of 6 weeks of parenteral or highly bioavailable oral antimicrobial therapy for most patients with bacterial NVO (strong, low).
27. We recommend a total duration of 3 months of antimicrobial therapy for most patients with NVO due to *Brucella* species (strong, moderate).

X. What Are the Indications for a Surgical Intervention in Patients With NVO?

Recommendations

28. We recommend surgical intervention in patients with progressive neurologic deficits, progressive deformity, and spinal instability with or without pain despite adequate antimicrobial therapy (strong, low).
29. We suggest surgical debridement with or without stabilization in patients with persistent or recurrent bloodstream infection (without alternative source) or worsening pain despite appropriate medical therapy (weak, low).
30. We advise against surgical debridement and/or stabilization in patients who have worsening bony imaging findings at 4–6 weeks in the setting of improvement in clinical symptoms, physical examination, and inflammatory markers (weak, low).

RECOMMENDATIONS FOR CLINICAL FOLLOW-UP

XI. How Should Failure of Therapy Be Defined in Treated Patients With NVO?

Recommendation

31. We suggest that persistent pain, residual neurologic deficits, elevated markers of systemic inflammation, or radiographic findings alone do not necessarily signify treatment failure in treated NVO patients (weak, low).

XII. What Is the Role of Systemic Inflammatory Markers and MRI in the Follow-up of Treated Patients With NVO?

Recommendations

32. We suggest monitoring systemic inflammatory markers (ESR and or CRP) in patients with NVO after approximately 4 weeks of antimicrobial therapy, in conjunction with a clinical assessment (weak, low).
33. We recommend against routinely ordering follow-up MRI in patients with NVO in whom a favorable clinical and laboratory response to antimicrobial therapy was observed (strong, low).
34. We suggest performing a follow-up MRI to assess evolutionary changes of the epidural and paraspinal soft tissues in patients with NVO who are judged to have a poor clinical response to therapy (weak, low).

XIII. How Do You Approach a Patient With NVO and Suspected Treatment Failure?

Recommendations

35. In patients with NVO and suspected treatment failure, we suggest obtaining markers of systemic inflammation (ESR and CRP). Unchanged or increasing values after 4 weeks of treatment should increase suspicion for treatment failure (weak, low).
36. We recommend obtaining a follow-up MRI with emphasis on evolutionary changes in the paraspinal and epidural soft

tissue findings in patients with NVO and suspected treatment failure (strong, low).

37. In patients with NVO and clinical and radiographic evidence of treatment failure, we suggest obtaining additional tissue samples for microbiologic (bacteria, fungal, and mycobacterial) and histopathologic examination, either by image-guided aspiration biopsy or through surgical sampling (weak, very low).
38. In patients with NVO and clinical and radiographic evidence of treatment failure, we suggest consultation with a spine surgeon and an infectious disease physician (weak, very low).

Notes

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