No concordance between bone and non-bone specimens in cases of chronic osteomyelitis: An observational study

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ABSTRACT:

Background: The correct diagnosis and treatment of the bone-infecting organism are extremely important for determining the prognosis of chronic osteomyelitis. Many people believe that non-bone specimens can replace bone cultures because the current knowledge on choosing the optimal specimen for culture is unclear. In this study, bone cultures are compared to non-bone specimens' microbiology as the gold standard for diagnosis.

Methods: A retrospective observational investigation of 50 patients with bacterial chronic osteomyelitis in a hospital in North India.COM caused by Staphylococcus aureus were analyzed independently and combined with all other etiologies. Concordance of the specimens from monomicrobial and polymicrobial COM were analyzed in relation with the site of surgical access to the bone sampled (intact skin versus infected soft tissues). Also, sequestrum and bone cultures were analyzed independently and together, to check if the first were concordant more often than the second with non-bone specimens.

Results: Concordance between both specimens for all etiologic agents was 28%, for Staphylococcus aureus 38%, and for organisms other than S. aureus 19%.After removing the majority of these potential sources of confusion, we only discovered a 28% concordance between non-bone and bone specimens. In other words, 72% of patients with COM would not benefit from antimicrobial therapy directed by antibiograms of bacteria obtained from non-bone tissues. More specifically, 36% of

patients would not need an antibiotic prescription, while 52% of patients would not receive enough of one.

Conclusions:

Because the microbiology of non-bone specimens differs significantly from that of bone, it is impossible to diagnose or treat chronic osteomyelitis using cultures of these specimens.

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INTRODUCTION

Osteomyelitis is inflammation or swelling that occurs in the bone.It can result from an infection somewhere else in the body that has spread to the bone, or it can start in the bone — often as a result of an injury.Osteomyelitis is more common in younger children (five and under) but can happen at any age.Boys are usually more affected than girls.

Antibiotics are often prescribed to treat osteomyelitis. Surgery may also be recommended in certain cases.In most nations, chronic osteomyelitis (COM) is a significant medical issue that is mostly linked to severe trauma and contemporary surgery. Due to the high costs of diagnosis, inpatient and outpatient care, rehabilitation, lost productivity, and sequelae, it is an extremely expensive disease for both the patient and society [1]. The term "cure" cannot be used to describe COM, according to authorised experts, because "the bone infection may reappear years after apparent successful treatment of the condition" [2]. Treatment must consist of the following to reduce the chance of recurrence:thorough surgical debridement and targeted antibiotic therapy that targets the infection's bacteria. The gold standard for acceptable culturing of bone specimens is based on common sense and a single classical paradigm [3]. Recent research, however, contends that non-bone samples, such as sinus tracts and superficial wounds, contain bacteria that are comparable to those found in bone specimens and that these samples are thus as effective as the diseased bone [6–8]. Despite the fact that bone cultures continue to be emphasised as the gold standard for diagnosis by the majority of specialists [4,5,9] and recent research [10], these contradicting reports point to the need for more conclusive information since uncertainty may have fuelled the no cure theory [9].

Methodology A retrospective observational investigation of 50 patients with bacterial chronic osteomyelitis in a hospital in North India.COM had been defined since 1997 as a bone infection that was worst or had not improved after one month of evolution, independent of the presence or quality of surgical and antimicrobial therapy. This definition was selected because one month is 3 times the 10-day period necessary for bone necrosis after acute infection [11] and it allowed precise selection of patients from the database. To overcome the limitation imposed by the lack of bone histopathology demonstrating COM, each case was evaluated in search of the hallmark of chronicity, that is, bone necrosis, microorganisms infecting the bone, and compromised soft tissues surrounding the infected bone [12].

Inclusion and Exclusion Criteria

Patients with COM, of any age and gender who had aerobic bacterial cultures from the infected bone and any of the non-bone specimens listed below that were directly related to the infected bone were eligible for inclusion. These specimens included pus aspirated from nearby soft tissues, soft tissues, surgical wounds, drainage from orifices left by orthopaedic pins, and drainage from sinus tracts. Only the bone biopsy, sequestrum, bone marrow, and aspirated subperiostic pus were considered acceptable surgical bone specimens. Additionally, it was mandated that bone samples be collected after surgery, and the surgeon had to clearly document whether the incision was done through intact skin as opposed to infected soft tissues or sinus tracts.

Comparative and intervening measures

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The gender, age, period of COM evolution, bone involved, surgical access to take a bone specimen, origin of specimens cultured, genera and species of organisms identified, and antibiograms were checked in the patient records, manual processing by standard microbiology processeswere done. It was noted whether or not there had been any antibiotic use in the 48 hours prior to the bone biopsy.

Type of analysis

Taking bone specimens as the gold standard against which non-bone specimens were compared, organisms isolated from these two different cultures in each patient were paralleled looking for concordance, first by genera and species, and then by antibiogram. Concordance was defined as the finding of exactly the same bacterial species with identical susceptibility pattern in both specimens. COM caused by Staphylococcus aureus were analyzed independently and combined with all other etiologies. Concordance of the specimens from monomicrobial and polymicrobial COM were analyzed in relation with the site of surgical access to the bone sampled (intact skin versus infected soft tissues). Also, sequestrum and bone cultures were analyzed independently and together, to check if the first were concordant more often than the second with non-bone specimens.

Statistics

The presentation of variables is in the form of means with standard deviations or percentages. Chi Square analysis with Yates correction was used to examine the statistical significance of differences between groups. Data management was carried out using Epi-Info 2000. (CDC, Atlanta, GA).

Results

The Section of Infectious Diseases attended 158 consults for COM during the study period, excluding cases of diabetic foot infections (38 months). Four patients had COM linked to decubitus ulcers, and 114 patients lacked non-bone cultures and/or adequate operating documentation. The demographic information for the remaining 50 patients who met the inclusion criteria is shown in Table 1.

In conclusion, 90% of the subjects had COM evolving from 1 to 432 months (median 3, mean 17 ±61 months) and were males aged 36 ±16 years. In 84% of patients, a violent or surgical trauma came first before bone infection. The majority of the contaminated bones (84%) were the femur, tibia, and fibula.

All of the criteria for inclusion, albeit not necessarily sequestra, needed infected bone, infected soft tissues, and radiological indications of osteomyelitis, hence 100% of the patients had these. In the surgical notes of 22 patients, the term "bone necrosis" was used, and in the notes of 27 additional patients (through x-rays, drainage of sinus tracts, or the surgeon's report), the term "sequestra" was used. Only one patient did not exhibit obvious signs of dead bone, but this patient did have a month-long Pseudomonas aeruginosa infection of the right tibia.

Table1:Demographicdataof50patientswithchronicosteomyelitis.

Variable	Data
Agerangeinyears(mean□SD)	14–80(36□16)
Males (%)	45(90)
Females(%)	5(10)
EvolutionrangeofCOM inmonths(median)	1–432 (3)
BonesaffectedbyCOM:	

Femur(%)	21(42)
Tibia(%)	20(40)
Fibulaandtibia(%)	1(2)
Otherbones(%)	8(16)
Factor associated with COM	
Trauma(%)	32 (64)
Orthopedicdevices (%)	9(18)
Contiguousinfection(%)	6(12)
Hematogenous(%)	2(4)
Orthopedicsurgery(%)	1(2)

Table 2: Description of bone and non-bone specimens from 50 patients with chronic osteomyelitis.

Bonespecimens,n(%)	**Non-bonespecimens,n(%)**
Bone,38(76)	Softtissuessurroundingbone,30(60)
Sequestrum,10(20)	Surgicalwound,11(22)
Bonemarrow,1(2)	Sinustract,5(10)
Subperiosticpus,1(2)	Pussecretedthroughpinsorifices,2(4)
	Pus aspirated fromsurrounding tissues2(4)
Total,50(100)	Total,50(100)

Table 2 provides specifics regarding the origin of the cultured samples, which are distinguished as bone and non-bone specimens. 76% of patients had a bone biopsy, 20% had sequestrum, 2% had bone marrow, and 2% had subperiostic pus. Pus leaked by pin orifices (4%), pus aspirated from soft tissues surrounding the infected bone (4%), surgical incisions (22%), sinus tracts (10%), and sinuses were the next most frequent findings in non-bone specimens.

Table 3 displays the concordance analysis for 50 patients and their 100 cultures. 68 and 57 bacterial isolates, respectively, were generated by cultures from bone and non-bone specimens. For 3 and 7 individuals, respectively, sterile non-bone and bone specimens were used (only 1 patient had sterile cultures from both specimens). In 20 patients (40%) both specimens grew the same genus and species, however six of these showed different susceptibility patterns, indicating distinct strains of the same species. Consequently, there was 28% concordance between bone and non-bone specimens (14 of 50 patients). 26 patients had 35 bone isolates missed by cultures from non-bone materials (52% false negative rate), whereas 18 patients had 36% false positives for 23 isolates that were not present in the diseased bone.

Percent distribution of bacterial species isolated from the bones of 50 patients with chronic osteomyelitis.

Table3:Concordanceanalysisbetweenboneandnon-bonespecimensfor50patientswithchronicosteomyelitis

Variable	BoneSpecimens	Non-boneSpecimens	Concordance:
	(n=68)	**(n =57)**	**#Patients(%)**

Negativecultures	3	7	1of3(33)
Monomicrobialcultures	29	32	11of29(38)
Polymicrobialcultures	18	11	2of18(11)
Staphylococcusaureus	21	20	8of21(38)
OtherGram-positivecocci	19	9	4of19(21)
AllGram-positivecocci*	**40**	**29**	**11of40(28)**
Enterobacteriaceae coli	11	13	1of11(9)
Pseudomonasaeruginosa	8	10	2of8(25)
Other Gram-negativebacilli	3	1	0of3(0)
AllGram-negativebacilli	**27**	**28**	**3of27(11)**
Allbacteria	**68**	**57**	**14of50(28)**

Table4:Concordanceanalysis betweenbone and non-bone specimens for 21 patientswithchronic osteomyelitis by *Staphylococcusaureus*.

Variable	Bone Specimens(n=68)	·bone imens(n =57)	Concordance:#Pat ients(%)
IsolatesdifferenttoS.aureus	47	37	5of26(19)
CulturespositiveforS.aureus	21	20	8of21(38)
S.aureusinpureculture	14	14	7of14(50)
S.aureusplusotherspecies	**7**	**6**	**1of6(17)**

Ten individuals had sequestra cultured as bone samples; three of the cultures were monomicrobial and seven were polymicrobial. S. In 5 cases, aureus was isolated, with 3 involving another pathogen and 2 in pure culture. In three of these ten individuals (30%), non-bone specimens were consistent with sequestra. In 5 out of 50 patients, drainage from sinus tracts was cultured as non-bone specimens; one was consistent with bone specimens (20%). All patients received thorough descriptions of the surgical access. In 12 patients, access to the bone was through healthy skin, whereas in 38 patients, it was through infected soft tissues. In the first group, the percentage of polymicrobial bone cultures was 50%, while in the second group, it was 32% (p = 0.6469).

At the time of the bone biopsy, 26 patients (52%) were taking 1 to 3 intravenous antibiotics; 14 of these patients' bone isolates were resistant to the antibiotics administered. 24 patients (48%) did not receive antibiotic therapy, and 10 cases of unanticipated antibiotic resistance in bone iso- lates (p = 0.5633). The average exposure time was 23 19 days, with exposure times ranging from 2 to 70 days. 15 and 11 patients, respectively, had exposure times under and over 21 days for antibiotics. Eight of the first group and six of the second group had resistant bone iso- lates (p = 0.7362); The concordance between bone and non-bone specimens was unaffected by antibiotic therapy: 4 patients (15%) with and 10 (42%) without antibiotics exhibited concordant cultures (p = 0.0797).

Discussion

The majority of medical professionals concur that COM is truly curable as long as proper parenteral antibiotic medication is started for at least 4-6 weeks, comprehensive surgical debridement is performed, and osteosynthesis material is removed [4,5]. COM, especially in trauma patients, may necessitate antimicrobial therapy for months to years, occasionally with antibiotics essential to the hospital environment, like glycopeptides and carbapenems. Because of this circumstance, proper pathogen identification is absolutely essential for successful antimicrobial therapy. In terms of resistance, various side effects, diverse medical issues, repeated therapeutic failures (no treatment), and sequelae, prescribing any needless antibiotic or failing to treat any bacteria infecting the bone would have major epidemiological and clinical repercussions. Therefore, it is essential to have a thorough understanding of how to choose the appropriate specimen for microbiological diagnosis. In 1978, Mackowiak et al. [3] established bone specimen cultures as the de facto method for COM microbiological diagnosis. They came to the conclusion that only bone specimens were reliable to identify the aetiology of COM after doing a well-done retrospective examination of sinus- tract and bone cultures of 40 patients. Recent studies have come to the opposite conclusion by taking the same issue and approaching it from various definitions. Three articles describing the microbiological agreement between bone and non-bone specimens were published between 1991 and 1997, accounting for 145 individuals with osteomyelitis [6-8]. In one investigation, non-bone specimens had 89% sensitivity and 96% specificity, while cultures were consistent in 47–62% of patients [6]. These papers came to the similar conclusion that non-bone specimens are suitable to determine the aetiology of COM. First, there was frequently a mixture of both acute and chronic osteomyelitis. This is significant because, over time, the dynamics of bacterial populations in soft tissues and bone vary greatly [3]. Second, cultures from wound swabs and sinus tracts were compared using debridement material rather than bone cultures as the diagnostic gold standard. Third, two weeks before debridement, needle bone biopsies were collected through the sinus passage. During such a surgery, there is a chance that organisms will be introduced and may then be recovered during the debridement process two weeks later. Fourth, all types of tissues that were removed during surgical debridement were regarded as reliable diagnostic samples.

Five, susceptibility patterns weren't taken into account. After removing the majority of these potential sources of confusion, we only discovered a 28% concordance between non-bone and bone specimens. In other words, 72% of patients with COM would not benefit from antimicrobial therapy directed by antibiograms of bacteria obtained from non-bone tissues. More specifically, 36% of patients would not need an antibiotic prescription, while 52% of patients would not receive enough of one.

Sterile bone cultures were obtained from three patients with COM histories and pictures, and one patient additionally had sterile non-bone cultures. Before the specimen sampling, two of them were taking antibiotics. S. was detected through prospective monitoring using both aerobic and anaerobic bone cultures. A. aureus in the initial. The second patient had the calcoaceticus-baumannii complex, while the third patient had Propionibacterium acnes. Because this study was retrospective in nature, it was impossible to control for important factors including the usage of antibiotics at the time of sampling, the method used to collect uncontaminated samples, and the calibre of the microbiology. Decubitus ulcers and COM resulting from diabetic foot infections were omitted because the value of bone cultures in the first condition [13] and its uncertainty in the second condition [14] respectively.

Polymicrobial bone cultures were not more frequently associated with accessing the bone through infected soft tissues than through healthy skin. This result was unexpected because bone contamination is made easier by simultaneous manipulation of colonised soft tissues, which is typical in patients with

COM related to trauma and polymicrobial colonisation of soft tissues [15,16]. It may be explained by the high rates of trauma (84%) and polymicrobial COM (36%), as well as the fact that in the majority of our patients (76%), bone was reached through contaminated soft tissues. Antibiotic use prior to specimen collection did not seem to have an impact on patterns of susceptibility or agreement between bone and non-bone specimens.

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