Chronic Osteomyelitis: Aetiology and Antibiotic Susceptibility Pattern

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Research Article

Abstract: **Background:** Chronic osteomyelitis is a persistent disease, difficult to treat or eradicate completely. In the absence of early diagnosis and prompt treatment or due to development of drug resistance, chronic osteomyelitis is still an important cause of high morbidity. Pus culture and sensitivity will yield the causative organism and help in selecting the appropriate antibiotics. **Methodology:** 100 pus samples taken aseptically were cultured on Blood and MacConkey agar plates aerobically at 37°C for 18-24 hrs. Culture isolates were identified by a series of standard biochemical reactions. Antibiotic susceptibility was performed as per CLSI guidelines. **Results:** Study group comprised73males and 27 females. Majority of the patients were in the age group of 11 – 50 years (77%) with trauma being the most common (44%) predisposing factor. The commonest organisms isolated were *Staphylococcus aureus* (35%) and *Pseudomonas aeruginosa* (17%). Majority of Gram positive organisms were sensitive to Amikacin, Linezolid, Vancomycin and Gram negative organisms to Amikacin and Imipenem. **Conclusion:** The wide range of causative organisms and degree of resistance to commonly used anti-microbials supports the importance of pus culture and provides important information to guide clinician's choice of empirical antibiotics.

Keywords: Chronic osteomyelitis, *S. aureus*, *P. aeruginosa,* antibiotic resistance.

Introduction

Osteomyelitis is defined as an inflammation of the bone caused by an infecting organism. The infection generally is due to a single organism, but polymicrobial infections can occur, especially in the diabetic foot.[1] Chronic osteomyelitis is a relapsing and persistent infection that evolves over months to years and is characterized by low-grade inflammation, presence of dead bone (sequestrum), new bone apposition, and fistulous tracts.[2] Chronic osteomyelitis commonly involves long bones; especially tibia and femur.[3] Microorganisms reach to the metaphysis of bone through blood flow from skin wounds and other infectious regions.Multiplication of microorganisms in metaphysis will cause congestion, oedema, exudates, leucocytosis, necrosis and abscess.[4] The most important risk factors of osteomyelitis are trauma (primarily open fractures and severe soft tissues injury), vascular insufficiency, diabetes, elderly children, obesity, surgical wound infection, mismanagement of acute osteomyelitis, haemoglobinopathies such as sickle cell diseases.[3,5] The bacteria most commonly causing chronic osteomyelitis are *S. aureus*, Coagulase negative *Staphylococcus*, *Pseudomonas* spp., *E. coli*, *Proteus* spp., *Klebsiella* spp., *Enterococcus* spp., *Enterobacter* spp. and anaerobes like *Peptostreptococcus* spp., *Bacteroides* spp., *Clostridium* spp. and rarely *Salmonella* spp. and *Actinomycetes*.[6] The still dominant role of *S. aureus* could be confirmed, but also the increasing number of gram-negative bacteria. The mixed infection is obviously determined by gram-negative bacteria with their marked resistance to antibiotics.[7] The beta-lactamases including extended spectrum beta- lactamases (ESBL), AmpC beta-lactamases and metallo-beta-lactamase (MBL), have emerged worldwide as a cause of antimicrobial resistance in gram negative bacteria.[8] The problems which are associated with beta-lactamases include multidrug resistance, difficulty in detection and treatment, and increased mortality.[9] The wide range of causative organisms and degree of resistance to commonly used anti-microbials supports the importance of extensive intra-operative sampling and provides important information to guide clinicians' choice of empirical antibiotics.[10] Traditional treatments have used operative procedures followed by 4 to 6 weeks of parenteral antibiotics. Adjunctive therapy for treating chronic osteomyelitis may be achieved by using beads, spacers, or coated implants to deliver local antibiotic therapy and/or by using hyperbaric oxygen therapy.[11] Proper management of chronic osteomyelitis requires accurate microbial isolation and appropriate antibiotic administration. Hence the present study was conducted to determine the bacterial agents causing chronic osteomyelitis and their antibiogram.

Material and Methods

One hundred clinically diagnosed patients of chronic osteomyelitis of all age groups and both sexes attending Orthopaedic outpatient department and those admitted in Orthopaedic wards were included. Pus samples were collected from depth of the wound under strict aseptic conditions. Direct smear examination was done. The sample was inoculated onto blood and MacConkey agar plates and incubated aerobically at 37^{o}C for 18-24 hrs. The isolates were identified by standard procedures.[12] Antibiotic sensitivity was done on Mueller Hinton agar by Kirby Bauer disc diffusion method using Clinical and Laboratory Standard Institute guidelines.[13] Antibiotic discs used were: Ampicillin (10µg), Gentamicin (10µg), Amikacin (30µg), Ciprofloxacin (5µg), Cotrimoxazole (1.25µg /23.75µg), Oxacillin (1µg), Cefotaxime (30µg), Ceftazidime (30µg), Imipenem (10µg), Erythromycin (5µg), Clindamycin (2µg), Linezolid (30µg), Vancomycin(30µg).

Results

The highest incidence of chronic osteomyelitis (77%) was seen in the 11-50 yr age group. Male patients were more than female with ratio of 2.7:1.The commonest bone affected was femur (48%) with trauma being the commonest predisposing factor (44%). Other predisposing factors include post-operative infections, orthopaedic implants and diabetes mellitus. Out of 100 samples, 87% was culture positive and 13% culture negative, monomicrobial flora was seen in 67% and polymicrobial flora 20%.Of 107 culture smears studied by Gram's staining, 49 (45.8%) were Gram positive and 58 (54.2%) were Gram negative. Out of 35 *Staphylococcus aureus* isolated, 14 (40%) were Methicillin Resistant *Staphylococcus aureus***.** Most of the Gram positive isolates were sensitive to Vancomycin, Linezolid and Amikacin and Gram negative isolates to Imipenem, Amikacin and Ciprofloxacin.

Table 1: Various organisms isolated from cases

Organisms	**No. of organisms**	**Percentage (%)**
Staphylococcus aureus	35	32.9
Coagulase negative staphylococcus	14	13.0
Pseudomonas aeruginosa	17	15.8
Escherichia coli	12	11.2
Klebsiella pneumoniae	14	13.0
Enterobacter cloacae	12	11.2
Proteus mirabilis	3	2.9
Total	**107**	**100**

Table 2: Predisposing factors for chronic osteomyelitis

Predisposing factor	**No. of cases**	**Percentage (%)**
Trauma	44	44
Orthopaedic implants	21	21
Post operative infection	23	23
Implant / Diabetes mellitus	4	4
Post operative infection / Diabetes mellitus	3	3
Trauma / Diabetes mellitus	5	5
Total	**100**	**100**

Table 3: Involvement of various bones

Bone involved	**No. of cases**	**Percentage (%)**
Femur	48	48
Tibia	23	23
Humerus	9	9
Radius	3	3
Ulna	4	4
Fibula	1	1
Malleoli	3	3
Patella	2	2
Metatarsals	3	3
Metacarpals	4	4
Total	**100**	**100**

Table 4: Antibiotic sensitivity pattern of Gram positive organisms

Organisms	No. of isolates	Antibiotics									
		A No. (%)	G No. (%)	AK No. (%)	CF No. (%)	CO No. (%)	E No. (%)	CD No. (%)	LZ No. (%)	VA No. (%)	OX No. (%)
S. aureus	35	3(8.5)	20(57.1)	31(88.5)	13(37.1)	22(62.8)	14(40.0)	20(57.1)	34(97.1)	35(100)	14(40)
Coagulase negative staphylococcus	14	0(0)	9(64.2)	13(92.8)	5(35.7)	6(42.8)	5(35.7)	8(57.1)	13(92.8)	14(100)	-
Total (%)	**49**	**3(6.1)**	**29(59.1)**	**44(89.7)**	**18(36.7)**	**28(57.1)**	**19(38.7)**	**28(57.1)**	**47(95.9)**	**49(100)**	14(40)

A – Ampicillin, G – Gentamicin, AK – Amikacin, CF – Ciprofloxacin, CO – Cotrimoxozole, E – Erythromycin,CD - Clindamycin, LZ – Linezolid, VA – Vancomycin, OX –Oxacillin

Table 5: Antibiotic sensitivity pattern of Gram negative organisms

Organisms	No. Of isolates	Antibiotics							
		A No.(%)	G No. (%)	AK No. (%)	CF No. (%)	CO No. (%)	CE No.(%)	CA No.(%)	IPM No. (%)
P. aeruginosa	17	0(0)	4(23.5)	10(58.8)	5(29.4)	4(23.5)	2(11.7)	1(5.8)	13(76.4)
E. coli	12	0(0)	4(33.3)	7(58.3)	4(33.3)	4(33.3)	3(25.0)	0(0)	10(83.3)
K. pneumonia	14	0(0)	0(0)	9(64.2)	9(64.2)	0(0)	1(7.1)	1(7.1)	11(78.5)
E. cloacae	12	0(0)	4(33.3)	5(41.6)	4(33.3)	4(33.3)	1(8.3)	0(0)	10(83.3)
P. mirabilis	3	0(0)	1(33.3)	2(66.6)	1(33.3)	1(33.3)	1(33.3)	1(33.3)	3(100)
Total (%)	**58**	**0(0)**	**13(22.4)**	**33(56.8)**	**23(39.6)**	**13(22.4)**	**8(13.7)**	**3(5.1)**	**47(81.0)**

A – Ampicillin, G – Gentamicin, AK – Amikacin, CF – Ciprofloxacin, CO – Cotrimoxozole, CE – Cefotaxime,CA – Ceftazidime, IPM –Imipenem

Discussion

Chronic osteomyelitis is notoriously resistant to treatment and requires aggressive surgical debridement in addition to antibiotic therapy.[14] The advent of prosthetic joints has added new dimensions to the challenges of septic arthritis and osteomyelitis, as these are prone to become infected by a wide range of organisms including low grade pathogens.[15] Chronic osteomyelitis may require antimicrobial therapy for months to years, sometimes with antibiotics that are invaluable for the hospital environment, such as glycopeptides and carbapenems. This situation makes the accurate identification of the pathogen an absolute cornerstone of antimicrobial therapy.[16] Widespread use of antibiotics has altered aetiological pattern of infections and antibiotic susceptibility. Hence continuous monitoring of susceptibility pattern needs to be carried out in individual setting so as to detect the true burden of antibiotic resistance among organisms and prevent their further emergence by judicious use of drugs.[15] In our study chronic osteomyelitis was commonly seen in males of 11-50 yrs age group with trauma being the commonest cause. Other causes included post-operative infections, orthopaedic implants and diabetes mellitus. The establishment of chronic osteomyelitis as a result of inoculation by bacteria from environment depends on size of the inoculum, virulence of the bacteria and loss of resistance of the host tissues caused by their disruption. The incidence is about 5% for open fractures and 1% for closed fractures.[8] 87% was culture positive and 13% culture negative. Collection of specimen before the administration of antibiotics, use of proper transport media and other factors play a role in incidence of positive culture.[17] Monomicrobial flora was seen in 67%, polymicrobial flora 20%and the commonest bone affected was femur 48% which is consistent with the studies by Zuluaga AF *et al.* [2] and Perry CR *et al.* [18.] Most osteomyelitis in diabetic foot infections and ischemic ulcers is polymicrobial and includes mixtures of aerobic and anaerobic organisms. Use of broad-spectrum agents such as ampicillin-sulbactam, piperacillin-tazobactam, or a carbapenem will provide empiric activity against most potential aerobic and anaerobic pathogens, but even these broad-spectrum agents may be inadequate, especially if MRSA is a concern.[19] *Staphylococcus aureus* with MRSA (40%) followed by *Pseudomonas aeruginosa* was common organisms isolated which is similar to study by Patzakis MJ *et al.* [20]. Also in study by Saurabh A *et al.* [21] *Staphylococcus aureus* was the commonest organism isolated from both sinus track cultures and sequestrum cultures. High prevalence rate of anaerobic bone infection was found especially in chronic cases. Thus, conventional treatment measures may not be beneficial and special type of management should be applied for these cases. Hence anaerobic culture is also recommended for all cases with osteomyelitis.[22] *Clostridium difficile, Propionibacterium acne, Bacteroides urealyticus, Porphyromonas* species, *Peptostreptococcus prevotii and Clostridium perfringens* were isolated in study by Zuluaga AF *et al.*.[2] In our study most of the gram positive organisms were sensitive to vancomycin, linezolid and amikacin and gram negative to imipenem, amikacin and ciprofloxacin. Combination oflinezolid plus rifampin or vancomycin plus rifampin is efficacious in MRSA chronic osteomyelitis.[23] Systemic daptomycin is also as active as vancomycin in the treatment of experimental

MRSA osteomyelitis.[24] While antimicrobial therapy is desirable in the control of chronic osteomyelitis, surgery remains the diagnostic and therapeutic procedure, which should be carried out early to resolve the condition.[5] Appropriate therapy of posttraumatic tibial osteomyelitis includes adequate drainage, thorough debridement, obliteration of dead space, stabilization when necessary, wound protection, and specific antimicrobial therapy.[25]

Conclusion

Chronic osteomyelitis is the common form of osteomyelitis in adults and is usually the sequel of trauma. Isolation of causative organism and performance of antibiotic sensitivity studies are critical in the selection of antimicrobial agents. Resistant causative organisms are frequently isolated. Carefully selected antibiotic therapy guided by culture and sensitivity is an effective treatment modality. This will prevent development of drug resistance and indiscriminate use of antibiotics.

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