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ETIOLOGICAL FACTORS CAUSING RESISTANT BONE INFECTIONS

Medical Science

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ABSTRACT

Chronic osteomyelitis remains a daunting challenge to orthopaedic surgeons. It is often described as a disease that can never truly be cured, particularly when the biological characteristics of the causative organism are taken into account. a single center retrospective cohort study was performed among 75 patients diagnosed with chronic osteomyelitis admitted and Bone and soft tissues were collected for cultures. Patient, injury, surgery associated variables, and microbiological records were reviewed for risk factors associated with chronic osteomyelitis. The focus of data collection was to compare characteristics of patients according to outcome.

KEYWORDS

osteomyelitis

INTRODUCTION

Chronic osteomyelitis remains a daunting challenge to orthopaedic surgeons. It is often described as a disease that can never truly be cured, particularly when the biological characteristics of the causative organism are taken into account. The two main routes of infection in osteomyelitis are through either haematogenous or contiguous bacterial inoculation. It is estimated that approximately 10 to 30% of acute haematogenous osteomyelitis may become chronic in nature. Chronic haematogenous osteomyelitis is an age-old problem, illustrated by the fact that the palaeopathological analysis of an Australopithecus africanus hominid skeleton, from Sterkfontein, South Africa, revealed evidence of chronic infectious disease of the skeleton. The oldest medical text, known as the Edwin Smith Papyrus from the sixteenth century BC also describes cases of 'pus pouring from bone', probably in reference to osteomyeilits. Despite the advent of antibiotic therapy and advances in the management of acute haematogenous osteomyelitis, the incidence of chronic osteomyelitis has steadily climbed, particularly during the past century. This is likely as a result of the increased incidence of high velocity skeletal trauma, as well as the increased use of surgical implants.

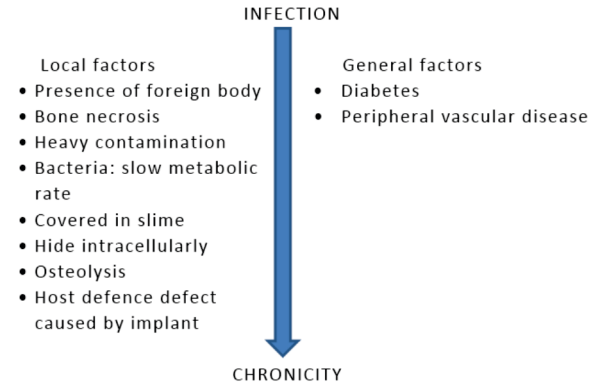
Open fractures can lead to the development of contiguous Osteomyelitis in 3–50% of cases, depending on the severity of the injury and quality of the subsequent management. The surgical management of closed fractures may result in postoperative osteomyelitis in 1–5% of cases, while the estimated risk of infection complicating an elective primary hip or knee replacement is in the region of 0.5–2%. This risk is, however, significantly higher in revision surgery (5%) and, in the case of second stage revision for periprosthetic infection, the infection rate climbs to approximately 20%. Overall, infectious complications occur in approximately 5% of orthopaedic cases during the life-time of the prosthesis or implant. Socio-economically underdeveloped regions carry a particularly heavy burden in terms the prevalence of osteomyelitis. This may be attributed to, among other factors, the high incidence of osteomyelitis in childhood, immunosuppression, malnutrition and the high incidence of trauma.

A clinician treating a patient with a suspected infected wound will usually send a superficial pus swab to the laboratory and institute antibiotic therapy accordingly. Particular problems, however, exist for wounds that are in fact sinuses overlying a focus of chronic osteomyelitis. Mackowiack in 1978 demonstrated the low positive predictive value of sinus tract swabs; in a retrospective analysis of 40 patients, only 44% of the soft tissue swabs contained the same pathogen as that obtained from a bone sample at the time of operation. However, isolation of Staphylococcus aureus from the sinus tract swab had a higher positive predictive value than for other bacteria (78%). The same study found 60% of chronic osteomyelitis to be due to S aureus, followed by Enterobacteriaceae (23%), pseudomonas (9%) and streptococcus (9%).3 Similar results with regards to the inaccuracy of wound swabs were obtained in prospective studies on diabetic foot infection4 and on post-traumatic chronic osteomyelitis.5 The latter study also demonstrated the poor positive predictive value of Craig needle biopsy specimens. Accurate identification of the micro-organism and its sensitivity can therefore only be obtained by an open surgical procedure, and there appears little (if any at all) place for non-invasive diagnostic methods.

From cultures of operative specimens, S aureus is the main causative agent of chronic bacterial osteomyelitis, accounting for about two thirds of the isolates, followed by pseudomonas and enterobacteriaceae. 3 5 6 Osteomyelitis complicating diabetic foot infection, however, is typically polymicrobial, with mixed aerobes, facultative anaerobes, and strict anaerobes being isolated at operation.4 Coagulase negative Staphylococcus spp, such as S epidermidis, are responsible for the majority of chronic osteomyelitis associated with orthopaedic implants and for 90% of pin tract infections.7 8 Other less common micro-organisms isolated include salmonella (more frequent in developing countries), and anaerobes such as clostridium and Pasteurella multocida.

PREDISPOSING FACTORS

Healthy bone tissue is extremely resistant to infection.13 14 The presence of bone necrosis, heavy contamination or foreign bodies, as well as general predisposing factors such as diabetes and peripheral vascular disease tip the balance in favour of the bacterium. Trauma or surgery can produce devitalised bone fragments. The other single most potent bone necrotising factor is indeed ischaemia. In the chick model of haematogenous osteomyelitis, patchy ischaemic bone necrosis occurs when the infective process occludes the vascular tunnels. This creates an ideal culture medium for bacteria, and at 48 hours, abscesses are formed. A sequestrum develops within eight days.



CHRONICITY ASSOCIATED WITH IMPLANT

Bacterial persistence is the rule in chronic osteomyelitis associated with a foreign body such as plate and screws or joint replacement.

In such cases antimicrobial therapy alone is often unsuccessful, and the infection is cured only by implant removal and debridement of necrotic bone. Southwood et al, working with an animal model (rabbit) of orthopaedic implant infection, found that as few as 50 organisms contaminating the operative site after a cemented hemiarthroplasty had been implanted resulted in infection, whereas 10 000 organisms were necessary to produce infection in the absence of a foreign body.28 After adherence on the implant via fibronectin receptors, usually on surface irregularities, coagulase negative staphylococci develop a slimy coat that protects the colony fro+ host defence mechanisms and antibiotics.29 There is also evidence for a local host defence defect in the pathogenesis of foreign body infection. Polymorphonuclear leucocytes (PMLs) extracted from tissue fluid surrounding a foreign body are unable to kill catalase positive S aureus despite optimal opsonisation.30 The same PMLs also exhibit a decreased production of superoxide and have lower content of enzymatic granules, an indication of impaired response to infection. The in vitro interaction of PMLs with Teflon leads to respiratory burst and exocytosis of enzymatic granules. The end result is a PML population composed of exhausted cells, with lower granule content, and less killing capacity.30 A similar study also demonstrated that also the opsonisation of S aureus in the presence of a foreign body is dramatically reduced at 20 hours.31 Since S aureus is mainly killed by opsonisation and subsequent phagocytosis by PMLs, the host defence defects described above are particularly relevant to the development of chronic osteomyelitis associated with internal fixation or joint replacement.

CHRONICITY NOT ASSOCIATED WITH AN IMPLANT

Chronic osteomyelitis has been shown to result from persistence of the acute haematogenous form in 4.4% of children in a recent Scottish study.32 Waldvogel et al in 1970 reported development of chronicity in 15% of adults.2 Chronic osteomyelitis may present as a recurrent or intermittent disease, with periods of quiescence of variable duration. Relapses of the disease several decades after the acute episode are well known (fig 3).33 Late reactivation of osteomyelitis up to 80 years after the primary illness had been “cured” have been reported.34 35 In a series of 12 patients with a minimum latent period of 20 years, no definite predisposing factor was identified, and both haematogenous and post-traumatic infections seemed equally to be involved.36 It is easy to understand the reasons behind the failure of medical treatment of osteomyelitis in the presence of dead bone: the infection will self perpetuate until all sequestra have been debrided. But what causes the same failure of antibiotic treatment in healthy individuals, with normal host defence mechanisms and negative radiology for abscesses or sequestra? And what causes late reactivation? Is osteomyelitis a lifelong disease? S aureus, mainly non-encapsulated variants, can be internalised by chick osteoblasts37 and endothelial cells38 in vitro and survive intracellularly, protected from host defence mechanisms and antibiotics. This might explain the known problem of a flare up of osteomyelitis with no identifiable causative organism. Furthermore, staphylococci can also acquire a very slow metabolic rate, in a phenotypic alteration named small colony variant. Slow growing bacteria have been known to be resistant to antibiotics since 1942, active cell wall synthesis being necessary for penicillin to be bactericidal.39 40 Small colony variants of S aureus were described for the first time in 1932 by Hoffstadt and Youmans as minuscule bacterial colonies (less than 1 mm) that grew very slowly and often required magnification to be seen.41 Small colony variants were found to be resistant to penicillin one year after its discovery by Fleming.39 Small colony variants may indeed account for the frequent failure to identify the causative micro-organism in chronic osteomyelitis: these strains may be easily missed or overgrown in a busy laboratory. They may also account for the frequent clinical presentation of chronic osteomyelitis as a slow, indolent infection that causes little inflammatory response and persists despite prolonged antimicrobial therapy.

Study Method: Between sept 01, 2013 to sept 1, 2018, a single-center retrospective cohort study was performed among 75 patients diagnosed with chronic osteomyelitis admitted and . Bone and soft tissues were collected for cultures. Patient, injury, surgery-associated variables, and microbiological records were reviewed for risk factors associated with chronic osteomyelitis. The focus of data collection was to compare characteristics of patients according to outcome (treatment success or failure).

PARTICIPANTS/ STUDY SUBJECTS

Eighty patients with chronic osteomyelitis were selected for the study of which 5 patients were excluded due to loss of follow up. Inclusion criteria were patients older than 10years of age and with at least one year of follow-up after the surgical procedures. Patients with incomplete medical records and loss of follow up (5 patients) were excluded from our study. A total of 75 patients diagnosed with chronic osteomyelitis were eligible for our study.

Description of experiment, treatment, or surgery We considered patients in remission of infection when there was absence of clinical, laboratory, or radiological signs of infection evaluated during the last medical visit (minimum of one year of follow-up), and in cases in which there was no need for reoperation or administration of an extra course of antibiotic therapy for the same site of infection following the end of therapy [11, 15]. Treatment failure or recurrent infection was defined as infection at the same site that had been previously controlled and required reoperation and/or a second complete course of parenteral antibiotic therapy. For the purpose of study analysis, we included only the first episode of recurrence and subsequent episodes were further excluded.

Variables, outcome measures, data sources, and bias In order to identify potential risk factors associated with failure of treatment of PTO, several variables (patient comorbidities, injury, microbiological findings, and surgery associated variables) were assessed by reviewing medical, intra-operative, and microbiological records. Demographics, comorbidities, smoking, alcohol consumption, diabetes and American Society of Anesthesiologists (ASA) classification were also analyzed. Injuryassociated variables assessed included time elapsed from admission to the first dose of antibiotic and to surgery, anatomical site of fracture, mechanism of trauma such as low-energy injury vs high-energy (based on the energy of the mechanism), and Gustilo type. Surgeryrelated factors analyzed were type of surgical procedure (open reduction and internal fixation or two-stage fixation with temporary external fixator), duration of surgery, and the need for blood transfusion. In addition, we assessed the need to perform supplementary surgical debridement for infected wounds. Specimen collection for microbiology and pathology was performed in the OR with a minimum of three tissue samples from infected bone and soft tissues at the time of surgical debridement.

CONCLUSION

Chronic bacterial osteomyelitis remains a major challenge despite advances in antibiotic engineering and better aseptic techniques in the operating theatre. The physiological status of the host determines not only the clinical extent of the disease, but also the treating physician's ability to effect cure.Higher rates of recurrence in patients who develop PTO were seen in elderly patients,diabetics and infections caused by P. aeruginosa.

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