Postoperative *Candida* Osteomyelitis in Femoral Fracture: A Case Report

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Introduction

Though *Candida* osteomyelitis is described as a rare manifestation of candidemia, non-hematogenous *Candida* osteomyelitis is seldom reported[1]. We have revently experienced a case of non-hematogenous *Candida* osteomyelitis complicating an open femoral fracture.

Case Report

A 70-year-old man was admitted to our hospital in November 1992 for evaluation of postoperative femoral pain. He was diagnosed as having diabetes mellitus in 1985, when he had received an oral hypoglycemic agent. In March 1992 he suffered a left femoral open fracture in a traffic accident, which was soon repaired with a plate and screws in a local hospital. He was discharged in August with the help of a stick. In September a purulent discharge from the wound was seen, which ceased with local treatment. But local pain and a burning sensation were present. He rejected the proposal of a reoperation and visited us. There was no history of persistent fever or central catheterization.

Examination revealed a normal temperature and a well-healed left femoral operation scar, with heat and tenderness. The deep tendon reflex and vibration sense were diminished. Diabetic retinopathy was observed by fundic examination by an ophthalmologist. Laboratory data revealed a hematocrit of 33.7%, leukocyte count of 11,600/mm^3, C-reactive protein of 4.7 mg/dl, erythrocyte sedimentation rate of 117 mm per hour, postprandial serum glucose of 356 mg/dl, and HbA1c of 15.0%. A test for fecal occult blood was positive. An X-ray film of the left femur revealed a condylar fracture. Around the metal some osteolytic lesions were seen (Fig. 1). Chronic osteomyelitis and loosening of the fixation were highly suspected and diabetic control with insulin therapy was begun. Soon a gastric cancer was found by endoscopic examination, and a gastrectomy was performed in December without complications. In February 1993 an operation on the femur was performed. Yellowish granulomatous tissue, containing pus, was seen around the fracture site and the metal. Nonunion and osteomyelitis were confirmed. Removal of metal, debridement and external fixation were performed. Gomori methenamine silver stain revealed yeast in granulation tissue (Fig. 2). Cultures of both sequestral and granulation tissues grew a yeast, which was identified as *Candida glabrata* by the API System S.A.®, France, in which the organism assimilated only glucose and trehalose without formation of pseudohyphae. Combination therapy consisting of 1084-mg course of amphotericin-B over 8 weeks and

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Fig. 1 Tomography of the femur, showing osteolytic lesions.

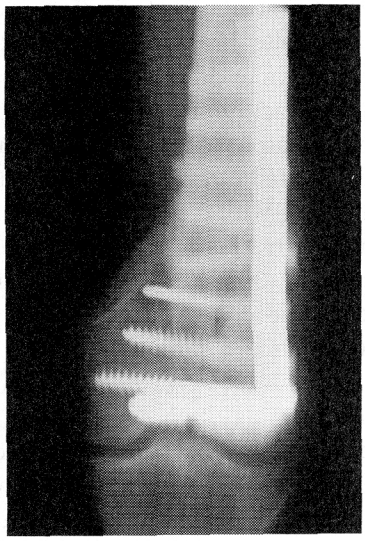
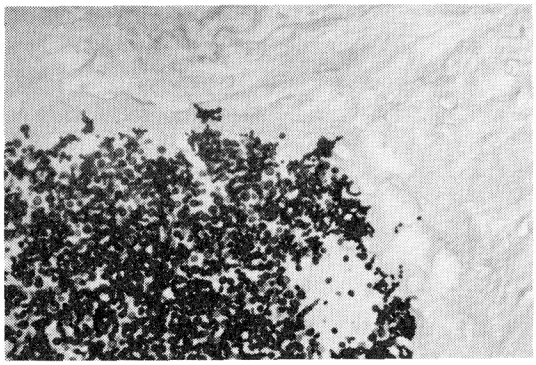


Fig. 2 Photomicrograph of the granulomatous tissue, showing microabscess with yeasts (Gromori methenamine silver stain, ×400).



flucytosine (100 mg/kg body weight) over 40 days[1] was begun 2 days after the operation, and resulted in a completely healed wound without pain. Four months after the operation, the external fixator was removed and he was discharged without a stick. Follow-up evaluation 10 months later found the patient to be asymptomatic.

Discussion

As catheter-associated candidemias have been increasing recently, *Candida* osteomyelitis, recognized as a sequela of candidemia[1], may become more common. In contrast non-hematogenous or contiguous *Candida* osteomyelitis is still very rare; only 9 cases (Table 1) have been reported in the

Table 1 Reported cases of contiguous *Candida* osteomyelitis

Patient	Age/Sex	Clinical background	Location	Other organism	Therapy	Outcome	Reference
1	62/M	Median sternotomy for CABG and wound dehiscence	Sternum	*S. aureus*	Debridement,then AMPH-B(720 mg), AMPH-B wound irrigation,and 5-FC(8 g/day for 42 days)	cured	[2]
2	22/M	Periodontitis and tooth extraction	Mandibular ramus	none	Debridement,then AMPH-B wound irrigation and 5-FC(6 g/day for 180 days)	cured	[3]
3	52/M	Median sternotomy for CABG, wound dehiscence, and repeated purulent discharge	Sternum	none	Debridement, then 5-FC(150 mg/kg/day for 90 days)	cured	[4]
4	58/F	DM, alcoholism, and decubital ulcer	Femur	none	AMPH-B	worsened	[5]
5	49/M	Repeated compound fractures and operations	Metacarpus	*C.freundii* *S.marcescens*	AMPH-B(2 g) and 5-FC(5 g/day for 14 weeks)	recurrent	[6]
6	64/M	Lumbar surgery	L4-L5	none	AMPH-B(1000 mg)	cured	[1]
7	68/M	Median sternotomy for CABG and repeated debridement of wound infection	Sternum	CNS	Debridement and AMPH-B(896 mg),then KCZ(200 mg/day for 270 days)	cured	[1]
8	69/M	Median sternotomy for CABG and MVR	Sternum	none	AMPH-B(1011 mg),then KCZ(200 mg/day)	cured	[1]
9	3/M	Cut and closed fracture	Phalanx	none	KCZ(50 mg/day for 4 months)	cured	[7]
10	70/M	DM, gastric cancer, open fracture, operation, and purulent discharge	Femur	none	Debridement and external fixation, then AMPH-B(1084 mg) and 5-FC(100 mg/kg/day for 40 days)	cured	Present report

CABG: coronary bypass surgery; DM: diabetes mellitus; CNS: coagulase-negative *Staphylococcus*; KCZ: ketoconazole; MVR: mitral valve replacement

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English literature to our knowledge[1)~7)]. Those cases were regarded as non-hematogenous when there was no evidence of candidemia and the location of osteomyelitis was the same as that of the traumatized or operated area. In our case there was no history of central catheterization or continuous fever suggesting candidemia and osteomyelitis occurred in the site of an open fracture. *Candida* seemed to have invaded the site contiguously during the perioperative or draining period. This is the first case of contiguous *Candida* osteomyelitis seen in a femoral fracture, to our knowledge.

In contrast with hematogenous *Candida* osteomyelitis, non-hematogenous *Candida* osteomyelitis is said to have little recognized predisposition to the usual deep-seated *Candida* infection[1)], and may have a concomitant bacterial infection (Table 1). This may interfere with recognition of the isolated *Candida* as the etiologic agent. According to the literature, administration of antifungal agents was more or less delayed after isolation of *Candida* from the lesion in 3 cases[1)~3)]. *Candida* might be recognized as a contaminant though a clear statement about the recognition was given in only one report[3)]. Nevertheless, it may be said that we must think of *Candida* as a rare pathogen of therapy-resistant, contiguous osteomyelitis.

On reviewing the 10 cases, we found that the clinical course was often complicated. Wound dehiscence, repeated spontaneous drainage, repeated injury, or non-healing decubital ulcers were seen in 6 cases including ours. Though it could not be known whether those troublesome wounds were the result of or predisposition to *Candida* infection, it may be said that a complicated wound infection is a clinical reason to suspect non-hematogenous *Candida* osteomyelitis. We must not forget that the most effective therapy against wound infection is prophylaxis. Whether the wound is infected or not, we must keep it as clean as possible to protect it against an opportunistic invader.

Poorly controlled diabetes mellitus with angiopathy and neuropathy was seen in 2 cases including ours (Table 1). As osteomyelitis in a diabetic patient is often complicated and diabetes is a predisposing factor for systemic candidiasis, these 2 cases may tell us that diabetes is a predisposing factor for non-hematogenous *Candida* osteomyelitis.

Candida osteomyelitis, hematogenous or not, usually has a good therapeutic response to sequestrectomy and other procedures used in the standard therapy of bacterial osteomyelitis[1)]. Our unique case was also successfully treated by the standard therapy of infected nonunion with hardware, which was composed of metal removal, debridement, external fixation, and administration of appropriate antimicrobial agents. Amphotericin-B, with or without flucytosine, is the antifungal agent of first choice in this disease[1)]. Alternative agents, such as fluconazole, are promising[8)] and easily used with few adverse reactions. Future controlled clinical studies are awaited.

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開放性大腿骨骨折術後にカンジダ骨髄炎を合併した1例

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要　旨

70歳，血糖コントロール不良な糖尿病男性が開放性左大腿骨骨折の術後11カ月に同部位の骨髄炎のために手術を受けた．金属板が除去され掻爬と創外固定がおこなわれた．肉芽様組織内に酵母の微小膿瘍が認められ，腐骨と肉芽様組織の培養から *Candida glabrata* が分離同定された．術後2日目からamphotericin-Bの点滴静注とflucytosineの内服が開始され，順調に治癒した．血行性カンジダ骨髄炎はカンジダ血症の続発症として知られるが非血行性カンジダ骨髄炎の報告はまれであり，特に本例は大腿骨骨折の術後に合併した第一例目と考えられる．創傷離開，排膿，繰り返す外傷，難治性の褥瘡，といった創部のトラブルが本症を疑う手掛かりになるかもしれない．また微小血管症を有する血糖コントロール不良な糖尿病は本症の背景因子といえるかもしれない．カンジダ骨髄炎の治療は血行性，非血行性いずれも細菌性骨髄炎の治療に準じておこなわれ，予後は良好とされる．本例でも感染性偽関節の標準的治療で順調に治癒が得られた．

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