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CASE REPORT

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Mucormycosis spondylodiscitis after lumbar disc puncture

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Abstract Vertebral osteomyelitis due to mucormycosis is a rare but fulminant and fatal disease. Only one case has been reported in literature, with postmortem diagnosis. The present paper reports a female case of mucormycosis spondylodiscitis and vertebral osteomyelitis after lumbar disc puncture and radio frequency nucleoplasty. She subsequently underwent two surgical debridements, continuous local irrigation and drainage, together with local and systemic Amphotericin B treatments. The infection was controlled 4 months after the second debridement; however, there was no improvement in the neurological function at the most recent follow-up, 16 months after the surgery. The experience of this patient, though a single case, supports early recognition, surgical debridement, systemic and local antifungal treatment, closed irrigation and drainage as the keys to successful treatment.

Keywords Mucormycosis · Osteomyelitis · Spine · Spondylodiscitis · Treatment

Introduction

Mucormycosis is the most acute, fulminant and fatal of all fungal infections in humans. Mucormycosis, also known as phycomycosis or zygomycosis, is an infection caused by fungi of the class *Zygomycosis* and order *Mucorales*, usually *Rhizopus, Absidia, Mortierella* and *Mucor* [1]. They exist in the soil and air. Most of these pathogenic fungi require oxygen, and are capable of growth in anaerobic and microaerophilic conditions [2]. Although the fungi show minimal intrinsic pathogenicity to normal persons, they can initiate aggressive and fulminant infections under certain clinical conditions [1]. Most reported cases of mucormycosis occurred in patients who were immunologically predisposed to infection. These conditions include hematologic malignancy, organ transplants, severe burns, end-stage renal disease or diabetes mellitus [2–4]. The portals of entry in these cases were the nasopharynx or paranasal sinuses, with direct involvement of the orbit, meninges and the brain. They could cause a diversity of pathologic clinical manifestation, including rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system (CNS), disseminated and miscellaneous syndromes [3–6]. However, spondylodiscitis and vertebral osteomyelitis due to mucormycosis is very rarely presented. A PubMed search of the literature from 1975 to 2004 in the English language revealed only one case report diagnosed in the postmortem [7]. The present report describes a case of spondylodiscitis and vertebral osteomyelitis due to mucormycosis after a lumbar disc puncture, which, to our knowledge, has not been previously described. We re-

viewed the clinical, radiographic and operative findings in the case and the literature regarding this unusual lesion.

Case report

A 57-year-old woman was admitted with severe low back pain, fever, weakness and numbness of the lower extremities. She had been suffering from low back pain and right lower extremity pain for 5 years before she underwent a percutaneous CT-guided L4–5 disc puncture and radio frequency nucleoplasty in a local hospital . Her symptoms improved for 3 days postoperatively followed by an aggravation of pain and rising of body temperature. Despite the vigorous antibiotic treatment with cephoradine (6 g/day) and clindamycin (1.2 g/day), the patient's symptoms deteriorated and she was referred to the authors' hospital. She had no other medical or family history.

Physical examinations on admission showed that her body temperature was 38.9°C. Her lumbar spinal movements were severely restricted, and there was tenderness at the spinous processes of the fourth and fifth lumbar vertebrae. Muscle strength grading was: quadriceps 3/5, hamstrings 2/5, ankle dorsiflexion or plantar flexion 0/5. A sensory examination revealed a slightly dull sensation to touch below the knee level and the sensation was completely lost below the ankle level on both sides. The patella reflex decreased and the ankle reflex was totally lost. The laboratory examinations revealed the following results: WBC 16×10^9/l, N 92%, ESR 104 mm/h.

The plain radiographs showed that the L4 and L5 appear slightly decreased in density in contrast to the other vertebral bodies (Fig. 1). Magnetic resonance image (MRI) scanning revealed a low signal intensity on T1-weighted and patches of high signal intensity on T2-weighted images in the L4/5 disc level (Fig. 2).

Surgical treatment was planned with one-stage anterior radical debridement and autologous bone graft transplantation with posterior fixation. The operation started from posterior decompression and exploration; during the surgery, the paraspinal muscle appeared edematous with abscesses found on both sides of the vertebral column. The abscesses were connected with the L4–5 vertebral bodies anteriorly. Pus was also found inside the vertebral canal where the extra-dural fat became liquefied and nerve roots appeared dark gray and edematous. Purulent pus could also be seen within the laminae and spinous processes. Samples from different locations were sent for bacterial and fungal culture and for pathologic analysis. Debridement of vertebral elements and affected disc tissue was carried out until the bleeding bone was encountered. Due to the extensiveness and uncertainty of the infection, an autologous bone

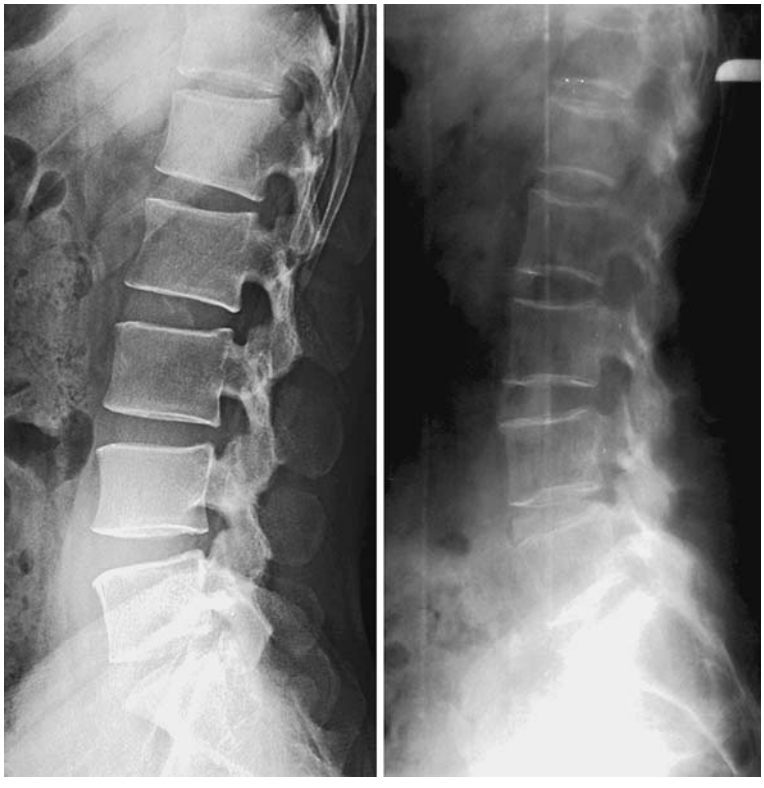

Fig. 1 Plain lateral radiographs before (*left*) and after (*right*) the L4/5 puncture and nucleoplasty procedure. There are no signs of inflammation or tumor (*left*). In the right picture, L4 and L5 appear slightly decrease in density in contrast to the other vertebral bodies

graft implantation and internal fixation were abandoned. Instead, inlet and outlet tubes were placed in the abscess cavity for closed irrigation and drainage. The wound was closed thereafter. The patient was immobilized externally with a clamped thoracolumbosacral orthosis and was given empirical antibiotics (cefuroxime 2.25 g bid and ciprofloxacin 200 mg bid) postoperatively. Abscess cavities were irrigated with saline containing gentamycin (8×10^4 U/500 ml). The patient's body temperature fell and back pain attenuated after the operation. However, a white fuzzy film started appearing in the irrigation drainage tube from the third postoperative day onward. The amount was about 40 g/day. Cultures rapidly developed thick white mycelia forms that were identified as *Rhizopus rhizopodoformis*. Aerobic and anaerobic bacterial cultures were negative for pathogens. A microscopic examination of the histological section confirmed the presence of broad, nonseptate branching hyphae characteristic of a Mucorales infection (Fig. 3). The blood, urine and respiratory culture were repeatedly negative. The patient was started on a regime of Amphotericin B (AmB) at dosage of 5 mg/day intravenously. The dosage was increased by 5 mg/day to a final dosage of 20 mg/day. Oral flucytosine 5 g/day was added to AmB for a period of 3 weeks. AmB colloidal dispersion (ABCD, Amphocil; InterMune Pharmaceuticals, USA) 3 mg/kg/day (120 mg/day) was used later on to replace AmB due to the increased serum creatinine level that was noted. In addition, local application of AmB (10 mg AmB in 10 ml normal saline) was carried out by clamping the outlet tube for 3 h after filling it from the inlet tube every other day. The treatment regime continued for 8 weeks. The white fuzzy film in the drainage decreased slowly. Three months after the debridement, there was still about 20 g of white fuzzy film in the drainage. However, the patient improved clinically with much less back pain, reduction of ESR to 87 mm/h and normal body temperature. The WBC count was 6.0×10^9/l with the neutrophils count as 75.4%. The plain radiography showed L4 grade I spondylolisthesis and bony destruction. Repeated CT and MRI showed that the progression of the soft tissue inflammation had halted, but the bony destruction increased at L4 and L5 (Figs. 4, 5). Upon the request of the patient, she was transferred to another hospital, where she received another surgical debridement. The same posterior incision was taken for the second debridement, small abscesses were found inside the paraspinal muscles and were filled with necrotic tissue and the fuzzy substance. A radical debridement was given up because the tissue structure was totally unclear. After clearing off the necrotic tissue and the fuzzy substance, the wound was closed and the irrigation and drainage tubes were set up again. The treatment regime was much the same as in the authors' hospital.

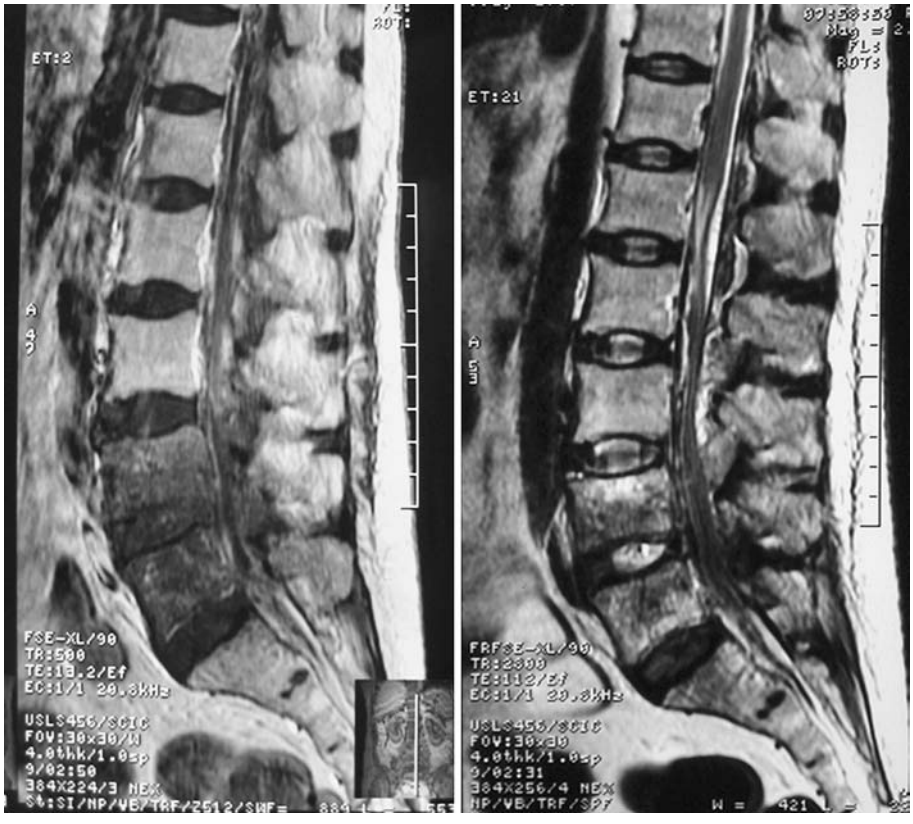

Fig. 2 MRI images show hypointensity of L4 and L5 vertebral bodies on T1-weighted image (*left*) and patches of hyperintensity on T2-weighted image (*right*), suggestive of inflammatory changes

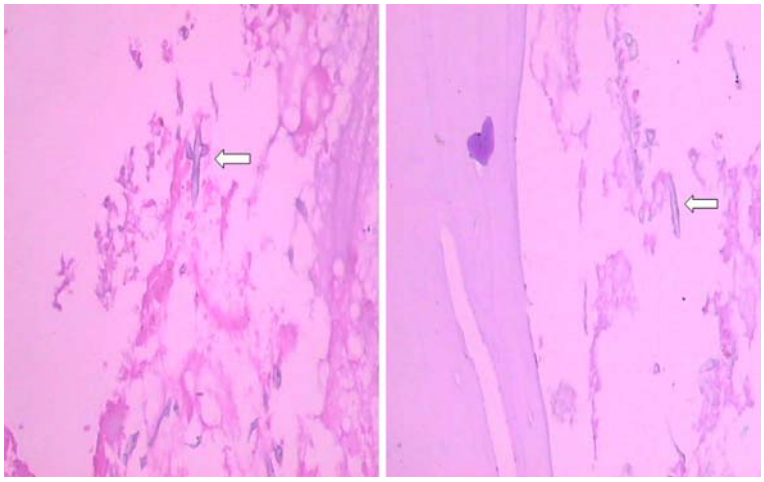

Fig. 3 Histological sections from the biopsy tissue show typical mucoraceous hypha with irregular branches arising from the parent hypha at right angles (*left image, arrow*; staining, HE; original magnification 100×). Mucoraceous hyphae could also be seen around the bone biopsy specimen (*right image, arrow*; staining, PAS; original magnification 100×)

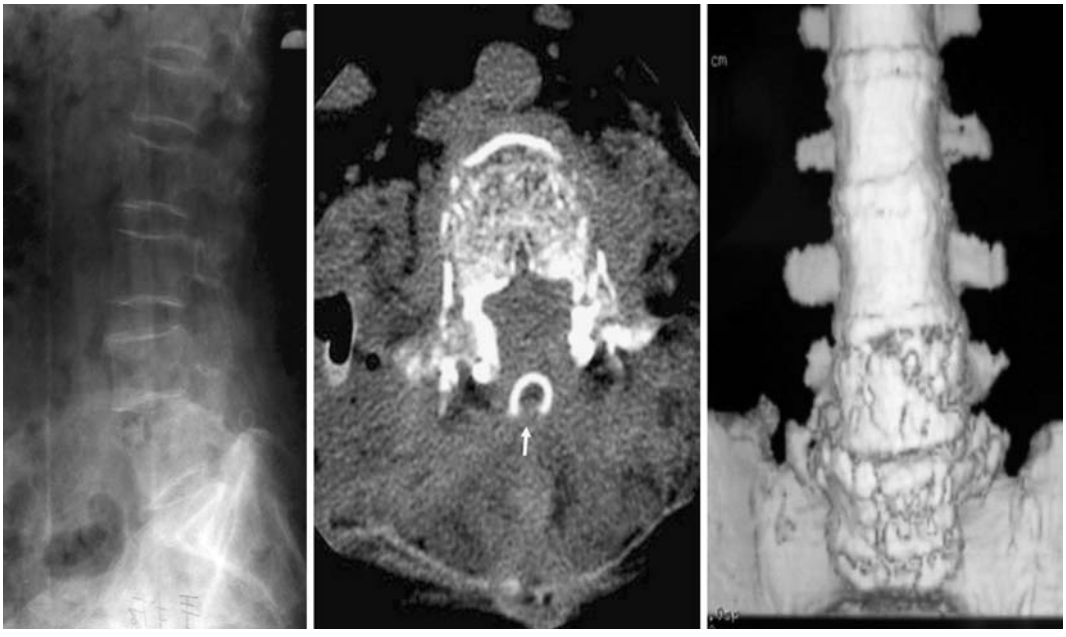

Fig. 4 One and half months after the first surgical debridement and drainage, L4 vertebral body shows grade I spondylolisthesis and prominent bony destruction both on plain radiograph (*left*) and CT image (*middle*). Swelling of the surrounding soft tissue can also be seen (*middle*, *arrow* points to the drainage tube). The range of bony destruction is well delineated by the 3D-reconstructed CT image (*right*)

The AmB therapy was discontinued when the cumulative dosage of 890 mg of AmB and 3,120 mg ABCD was administered intravenously. The patient was given itraconazole (200 mg bid, Janssen Pharmaceutical Ltd) for antifungal maintenance therapy. Four months after the second debridement, the drainage stopped completely and the draining wound tract healed. Oral itraconazole was continued for 8 months after the draining wound tract healed. The maintenance therapy was stopped because of adverse effect in the intestinal tract. At the most recent follow-up visit, 1 year after the wound healed, the patient did well without any signs of recurrence of the infection. She was free of pain and the ESR was 20 mm/h. A lumbar plain radiography showed the cessation of the destructive changes of the bone and the presence of fusion at the fourth and fifth lumbar vertebrae (Fig. 6). However, small abscesses could still be found in the CT scanning images and there was no improvement in the neurological functions.

Discussion

Mucorales osteomyelitis is a rare clinical entity, only a fewl cases of documented limb mucorales osteomyelitis were found in literature [8–12]. The occurrence of vertebral mucorales osteomyelitis is extremely rare. Buruma

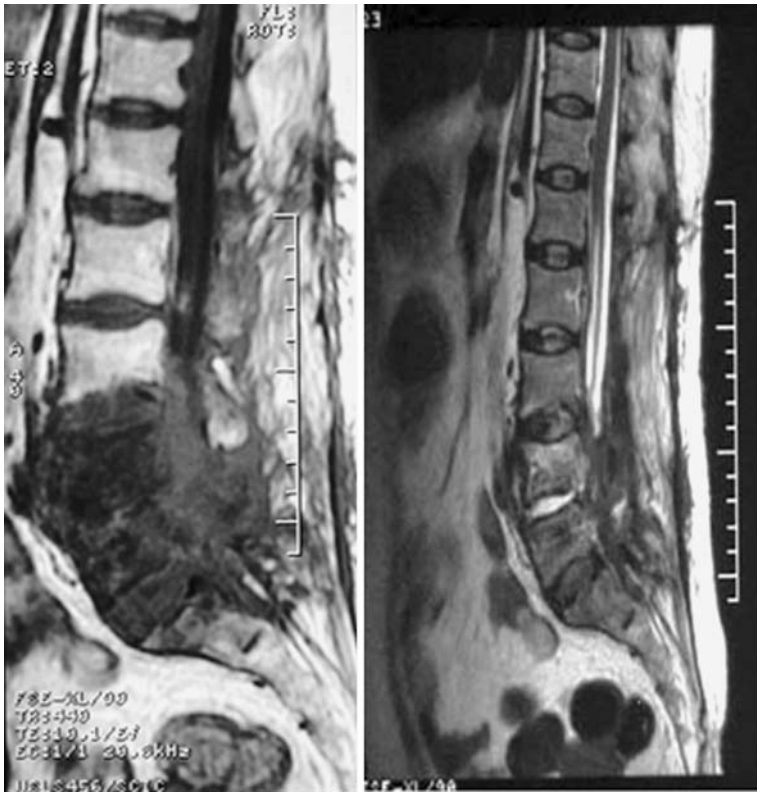

Fig. 5 MRI images one and half months after the first debridement. T1-weighted sagittal image (*left*) shows hypointensity of L4 and L5 vertebral bodies with involvement of posterior elements. T2-weighted image shows heterogenous density similar to the preoperative image (*right*)

et al. [7] reported about a patient with a history of pain in the neck, followed by a slow progressive loss of muscle strength in both the arms and finally resulted in teraplegia,; medical history included laryngectomy with partial hypopharyngectomy preceded by radiotherapy because of carcinoma. The patient died as a consequence of massive pulmonary embolism and the autopsy showed the cause of the neurological deficit to be vertebral osteomyelitis and epidural abscess due to mucormycosis. The present case was, however, not immunocompromised, the diagnosis was made at a relatively early stage, and she was treated appropriately with a good outcome.

Lumbar disc puncture of L4–5 disc space was believed to be the cause of introducing the fungi into the present patient. Mucorales has been reported as a source of nosocomial infection from adhesive tape, intravenous catheters and intramuscular infection [13–16]. The final diagnosis of mucormycosis is usually difficult to make before ischemia and necrosis are well advanced. The routine laboratory tests, X-ray, CT and MRI are all nonspecific. A definitive diagnosis requires either histological identification or growth of the organism on culture. Mucormycosis is characterized histologically by broad, irregularly shaped, nonseptate hyphae with right-angle branching. Staining techniques include hematoxylin eosin and periodic acid-Schiff. Speciation requires culture of the fungus and the advice of a mycologist [17]. Two characteristics helped in raising clinical suspicion in the present patient. First, the patient did not respond to the usual antibacterial therapy. Second, the mucorales preferentially invade vascular walls and cause ischemia and subsequent infarction, which lead to the production of black necrosis pus [18], as in the case of the present patient.

Mucormycosis is notoriously difficult to treat [13]. AmB accompanied by surgical debridement has proved to be the only effective therapy, but mortality remains high [8–12, 19]. Before effective antifungal therapy was available, a mortality rate of 50% was reported [10]. However, long-term high dose AmB administration is associated with nephrotoxicity. Because of the rising level of creatinine, this patient could not tolerate further after 890 mg of conventional AmB was administered for over 46 days. ABCD is a kind of lipid-base AmB with lower nephrotoxicity [20], which offers an option when long-term therapy is required.

The purpose of surgical debridement was to explore and decompress the neural elements, and to drain abscess in order to decrease the fungal load and to prevent hematogenous dissemination. In the mean time, continuous closed drainage and irrigation could deliver AmB locally. Furthermore, the debridement could also provide the tissues for cultivation and pathohistology. The repeated partial debridements, which were more common in appendicular mucormycosis osteomyelitis, usually were unsuccessful and resulted in amputation at last [8, 9].

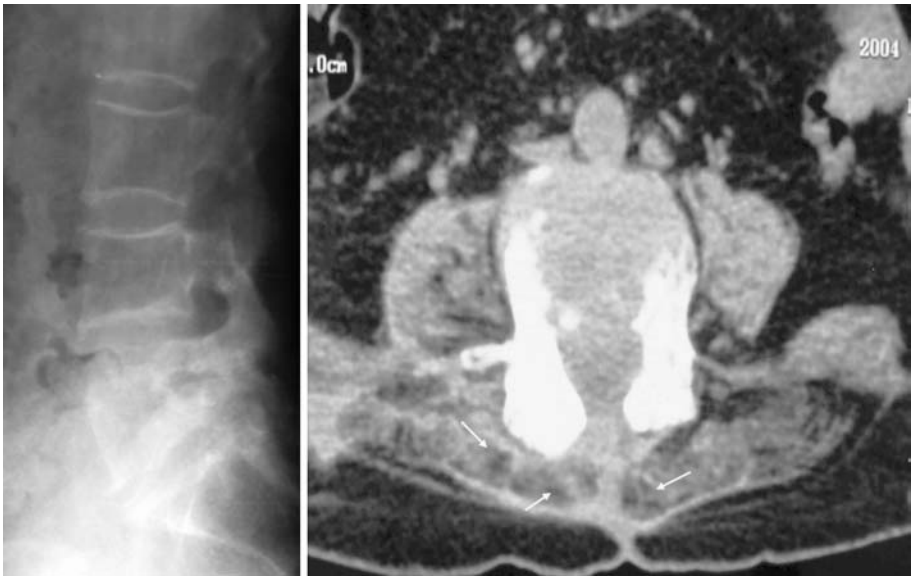

Fig. 6 Twelve months after the patient's drainage wound healed. Plain lateral radiograph shows disappearance of L4–5 intervertebral disc space and fusion of the two vertebrae (*left*). Vertebral destruction halted and shows signs of healing (*right*). Paraspinal soft tissue swelling greatly decreased; however, small fibrotic abscesses can be seen inside the paraspinal muscles or are located subcutaneously (*arrows*)

In the present case, the repeated surgical debridements were unable to clear all involved tissue of the deep-seated infection, due to the great extent of the area affected, which is characteristic of the mucorales infection.

Although the infection was finally quiescent, which was confirmed by the cessation of destructive bony changes and the presence of fusion and a decline in the ESR, the granulation tissue or small fibrotic abscesses inside the paraspinal muscles still harbor the mucorales that could reactivate the infection. Frequent clinical and radiological follow-up examinations were required. In the present patient, itraconazole was administered for maintenance therapy to prevent the recurrence of the infection based on the literature report [21]; however, we could not conclude when to stop the maintenance therapy.

Conclusion

The successful control of mucormycosis in the present case involved three fundamental components: early recognition, systemic and local antifungal treatment and surgical debridement. Other factors, such as general nutritional status, should also be taken into consideration.

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