Intense Granulomatous Inflammatory Lesions Associated With Absorbable Internal Fixation Devices Made of Polyglycolide in Ankle Fractures

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Since absorbable internal fracture fixation devices made of polyglycolide have been increasingly used clinically, a peculiar type of complication has emerged. After an initially uneventful course, a local nonbacterial inflammatory reaction appears two to four months after the operation, resulting in a copiously discharging sinus on the skin. A series of 286 patients with unimalleolar or bimalleolar fractures were treated by open reduction and internal fixation using cylindrical rods made of polyglycolide. Among these there occurred 18 nonbacterial inflammatory tissue responses (6.3% of the total) requiring surgical drainage. Six patients had an intense reaction necessitating repeated surgical measures and inpatient management. The hospital stay of these patients averaged 18 days. The mean duration of the discharge from the lesions was 10.8 weeks. Microscopic examination of biopsy specimens showed a nonspecific foreign-body reaction composed mainly of neutrophilic polymorphonuclear leukocytes and foreign-body giant cells phagocytizing the polymer debris left behind by the decomposing implants. On roentgenograms, osteolytic increase of the diameter of the implant channels was observed, but the bony union of the fracture seemed not to be disturbed. Thus the factors increasing the susceptibility of some individuals to this complication remain unknown.

During the last five years, internal fixation devices made of absorbable (biodegradable) synthetic polymers have been used more often in fracture surgery.[1-4,9-11,14,16-19,25] In animal experiments, it was found that implants made of polyglycolide, lactide-glycolide copolymer, or polydioxanone provoke a histologically indisputable foreign-body reaction when placed within bone tissue, despite the degradability of these polymers.[5,6,8,12,13,24] In consideration of these findings, the clinical occurrence of inflammatory tissue responses when these polymers were introduced as fracture fixation devices can hardly be totally unexpected. The reported incidence of macroscopically manifest nonbacterial inflammatory reactions in clinical series has varied from 5.9 to 22.5%.[2,4,10,11,17] The intensity of these tissue responses has ranged from a small solitary discharging sinus of short duration to an intense reaction requiring repeated surgical drainage procedures and several months' convalescence.

The most common types of injury in which absorbable implants have been clinically used are malleolar fractures of the ankle. The purpose of the present study was to analyze the clinical and histopathologic features of severe nonbacterial inflammatory lesions associated with absorbable fracture fixation rods made of polyglycolide when used in the treatment of 286 unimalleolar or bimalleolar ankle fractures.

MATERIALS AND METHODS

From 1985 to 1987, 286 patients with displaced unimalleolar or bimalleolar fractures were treated

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by open reduction and internal fixation using absorbable cylindrical rods of polyglycolide at the author's department and in two other hospitals within its liability district. The rods, measuring 3.2 or 4.5 mm in diameter and 50 or 70 mm in length, were composed of pure polyglycolide with no lactic acid component. According to the information provided by the producer (TTK Laboratories, Tampere, Finland) they were manufactured by partially melting and sintering commercial Dexon, size USP 2, sutures (Davis and Geck, Gosport, United Kingdom) at temperatures of 205°–232° and at elevated pressure into rods in cylindrical molds. The rods were sterilized by γ-radiation at doses of 25 kGy. The surgical technique consisted of drilling of a channel from the tip of the fractured malleolus in the cancellous bone through the reduced fracture surfaces and tapping a polyglycolide rod of the same diameter into the channel.[2] Postoperatively, the ankle was immobilized in a below-the-knee plaster cast for six weeks.

In this series of 286 patients, there were four bacterial wound infections (1.4%). In the remaining patients, the initial postoperative course was clinically uneventful until an inflammatory sinus with sterile discharge emerged on the skin at the operation site in 18 cases (6.3%) two to four months later. Surgical drainage by incision under local anesthesia as a simple office procedure was sufficient to cure the lesion in 12 patients. In six cases with intense reactions, inpatient treatment and repeated drainage and debridement were necessary.

During the debridement procedures, tissue specimens were taken for histopathologic examination. The biopsy specimens were fixed in formaldehyde. Calcified tissue was decalcified in formic acid. Both the soft-tissue specimens and any small fragments of bone were embedded in paraffin. All sections were stained with hematoxylin and eosin and examined by light microscopy. In addition, polarizing microscopy was used to identify birefringent polymer debris in the sections.

The six patients with intense inflammatory lesions were analyzed in detail for the clinical course and the radiographic and histopathologic findings. The patients were followed for at least two years.

RESULTS

The mean interval between the fracture fixation operation and the first clinical signs of an inflammatory tissue response was 11.2 weeks (Table 1). The reaction appeared as a suddenly emerging painful swelling, approximately 10 mm in diameter, in an already

TABLE 1. Patient Data

Case	*Fracture*	*Volume of Implanted Polymer (mm³)*	*Time from Operation to Inflammatory Lesion (weeks)*	*Highest ESR (mm/hour)*[a]	*Highest CRP (mg/liter)*[b]	*Drainage Procedures*	*Duration of Discharge (weeks)*
1	Bimalleolar	1900	9	56	25	Four incisions	10
2	Lateral malleolar	1100	12	17	10	Two incisions	5
3	Bimalleolar	1900	8	95	53	Needle aspiration, incision	8
4	Bimalleolar	1900	7	75	73	Two incisions	20
5	Lateral malleolar	1100	15	73	23	Debridement, (two skin transplantations)	18
6	Bimalleolar	1500	16	13	29	Needle aspiration, incision	4

[a] Erythrocyte sedimentation rate: normal value less than 11.
[b] Serum C-reactive protein: normal value less than 10.

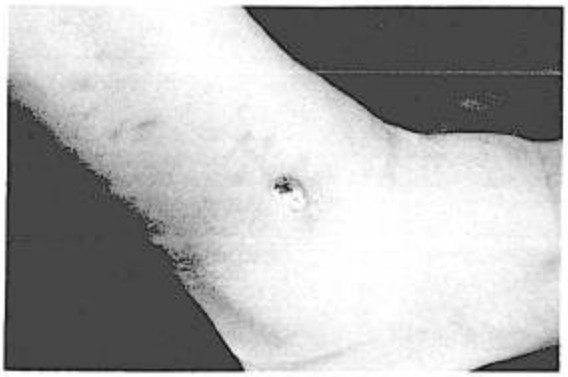


FIG. 1. Lateral side of the ankle of Case 1 seen three months after the initial fracture fixation operation showing the characteristic appearance of a nonbacterial inflammatory sinus yielding polyglycolide debris.

healed operation wound that spontaneously formed a sinus on the skin unless it was surgically drained immediately (Fig. 1). The discharge contained an abundance of polyglycolide debris left behind by the decomposed implant. The bacterial cultures were all negative.

There were no signs of circulatory disorder in the affected extremities of these six patients. Two patients had a solitary fracture of the lateral malleolus; and four, a bimalleolar fracture. In three of the four patients with bimalleolar fractures, the lesion affected both the lateral and medial sides of the ankle. The fourth patient was affected on the lateral side only. The three patients with the largest volumes of implanted material, one 4.5- × 70-mm rod and two 3.2- × 50-mm rods, also had the three shortest intervals between the initial operation and the inflammatory reaction. The highest recorded erythrocyte sedimentation rates and serum concentrations of C-reactive protein in the patients showed a remarkable variation and could be relatively low despite an intense lesion (Table 1).

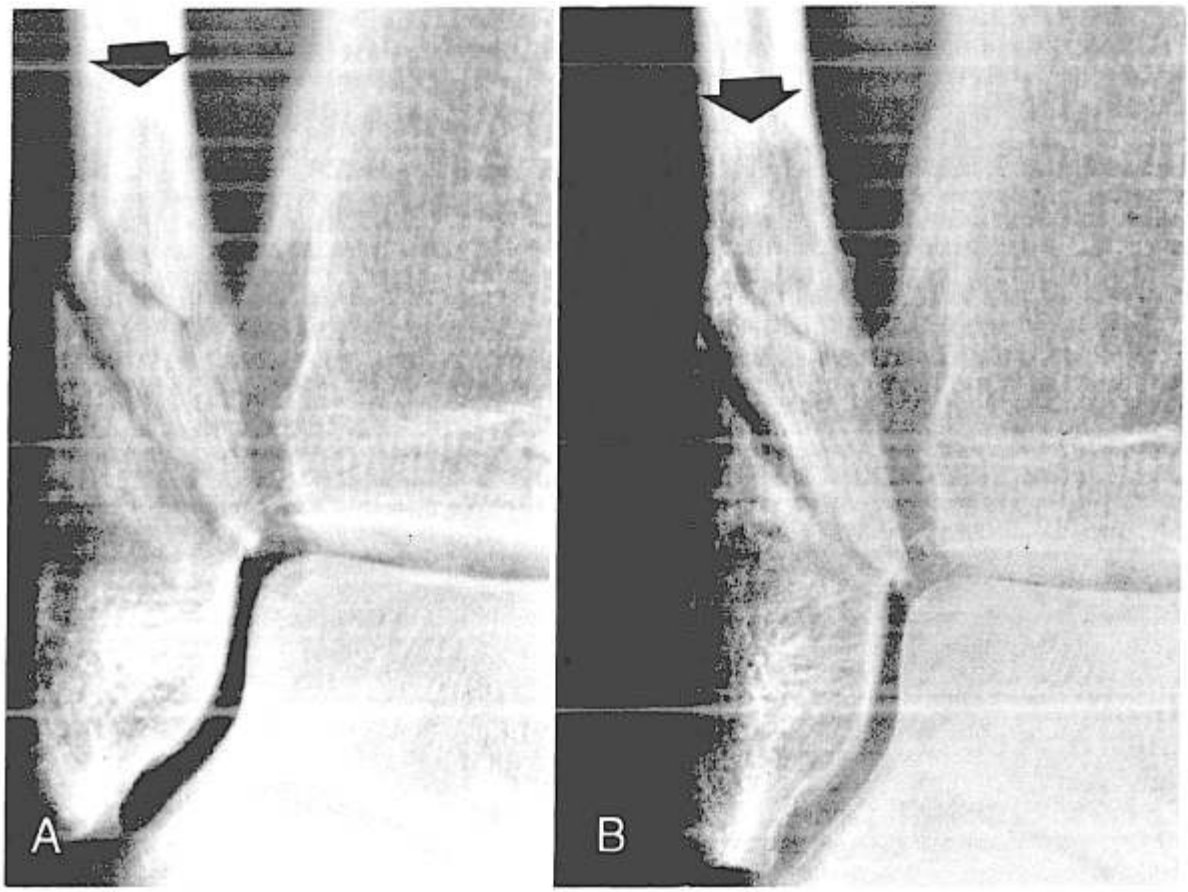
All patients were managed with bed rest with the foot elevated. Physiologic saline solution was used for dressings. The lesions were cleaned with hydrogen peroxide in 3% concentration. Drainage procedures gradually extinguished the lesions but the discharge could continue for as long as 20 weeks (Table 1). In one patient (Case 5), instead of simple drainage, a more extensive debridement had been done in another hospital. Necrosis of the skin over the lateral malleolus ensued that later necessitated two separate skin transplantation procedures. The mean duration of the hospital stay was 18 days.

On serial roentgenograms, a widening of the implant channel could be seen in five of the six patients (Fig. 2). The increase of the diameter of the channels seemed to occur eight weeks after the initial operation. The position of the fragments and the bony union of the fracture appeared to be undisturbed by the inflammatory tissue response. In one patient with osteoporotic bone (Case 3), the fixation had failed six weeks before the clinical manifestation of the inflammatory lesion, eight weeks after the initial operation. The resultant severe incongruity of the ankle joint later necessitated talocrural arthrodesis.

On microscopic examination, the biopsy specimens showed an intense inflammatory response composed of neutrophilic polymorphonuclear leukocytes and small lymphocytes (Fig. 3). Another histopathologic finding common to all the patients was the occurrence of monocyte-macrophages and foreign-body-type giant cells in a granulomatous pattern. Under polarized light, birefringent polymeric debris was identifiable both intracellularly within the phagocytes and intercellularly within the fibroconnective tissue (Fig. 4).

DISCUSSION

Among the complications associated with internal fracture fixation devices, the occurrence of intense, nonbacterial inflammatory tissue responses are undoubtedly unique to the absorbable implants made of synthetic biodegradable polymers. Although polyglycolide has been in worldwide use as absorbable suture for two decades, clinical macro-



FIGS. 2A AND 2B. (A) Anteroposterior roentgenogram of a lateral malleolar fracture (Case 2) obtained immediately after open reduction and internal fixation using a 4.5- × 70-mm polyglycolide rod. The outlines of the implant channel can be seen (arrow). (B) A roentgenogram obtained eight weeks later shows a considerable increase of the diameter of the implant channel (arrow).

scopic inflammatory reactions to the material have been only sporadically reported before the introduction of polyglycolide in the form of fracture fixation implant. In 155 patients who were operated on for abdominal conditions and had their fascia and the subcutaneous tissues closed with polyglycolide sutures, 3.8% developed a local granuloma or sinus.[7] In another study, a mesh of polyglycolide was used to repair rupture of the spleen, which resulted in perisplenic sterile fluid collections visible on computed tomography scans in two of nine patients, both suffering from persistent postoperative fever.[15]

Considering the nature of the tissue reactions, no evidence exists or emerged in this study for an immunologically mediated response against polyglycolide. The histopathologic findings in the present study were characteristic of a nonspecific foreign body reaction and were similar to those described previously in animal experiments.[6,8,12,24] Fragments of the decomposing implants were always present on microscopic examination at the time of the reaction. The degradation of the polymer appears to be too slow to get ahead of the foreign body response.

The liquid polymer debris mixed with inflammatory fluid that was sequestered within the bone before discharging out through the sinuses probably contributed to the widening of the implant channels on roentgenograms. This osteolysis bore some resemblance to the roentgenographic appearance of the aggres-

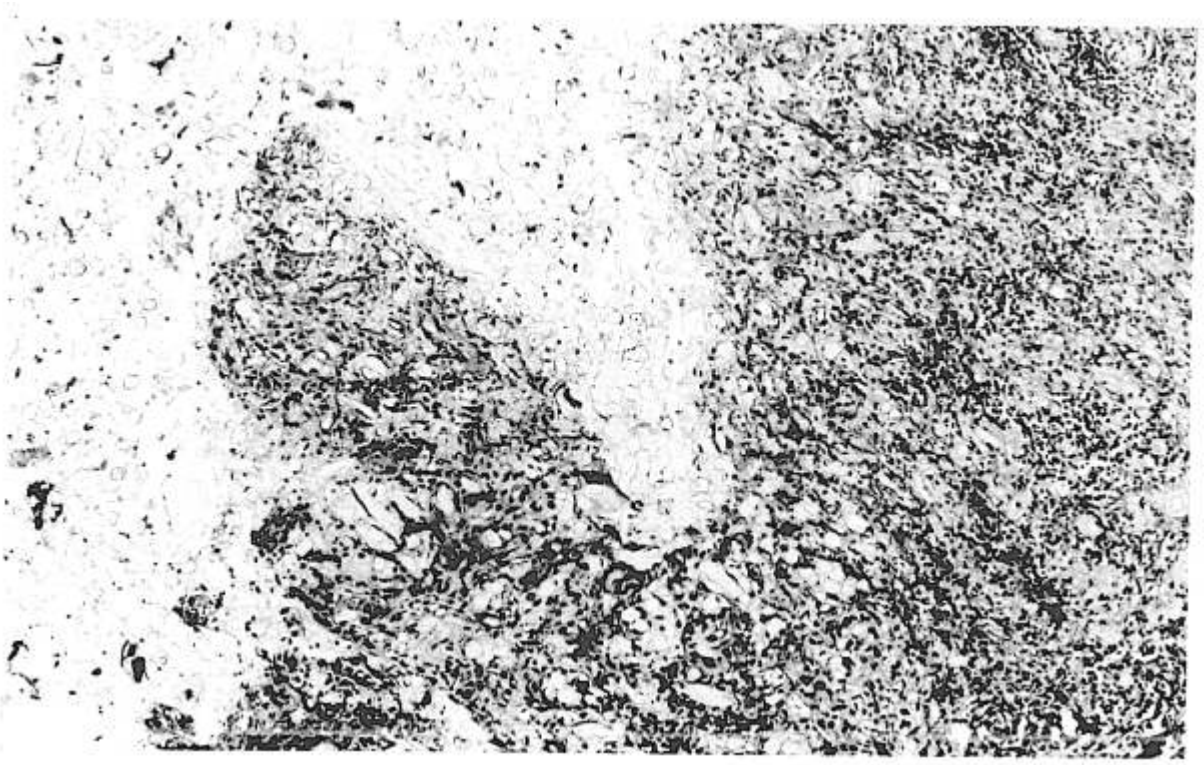


FIG. 3. A polarized light photomicrogram of a tissue specimen from Case 2. An intense inflammatory response composed of neutrophilic polymorphonuclear leukocytes and small lymphocytes surrounds the degrading implant material seen to the left. (Stain, hematoxylin and eosin; original magnification, ×80.)

sive granulomatous lesions sometimes associated with cemented total hip arthroplasty.[20]

The incidence of clinically manifest inflammatory reactions to absorbable fracture fixation devices varies in different anatomic regions. The incidence seems to be high, up to 22.5%, in the distal radius and in the elbow joint,[11] whereas the recorded reaction rates in malleolar fractures have been lower, 6–8%.[2,4,10]

The more intense inflammatory responses amounted to one third of all the reactions encountered in the present study. Analogous to this variation in intensity among the macroscopically manifest reactions there probably also occur foreign-body responses of subclinical intensity that never exceed the threshold for subjective symptoms and objective pathologic clinical signs. The causes of such a great interindividual variations remain obscure, but may reflect possible differences in the transport potential of the tissues within the concept of the bone–body fluid continuum.[22] These inflammatory reactions occur in all age groups, however, and do not seem to be linked to arterial or venous insufficiency of the extremity. Against the background of the great human interindividual variation in the intensity of the tissue response, it may deserve mentioning that in a few experimental studies on rabbits, contrary to other studies, no histologic signs of an inflammatory response could be seen after intraosseous implantation of pieces of polyglycolide or lactide-glycolide copolymer.[21,23]

Because of the nonspecificity of the inflammatory foreign-body responses and because no risk factors could be identified, it is likely that it is impossible to prevent the reactions from occurring or to predict an increased risk in an individual patient. The nonspecific nature of the reaction is further reflected by the observation that rods made of lactide-glycolide copolymer, too, have evoked identical

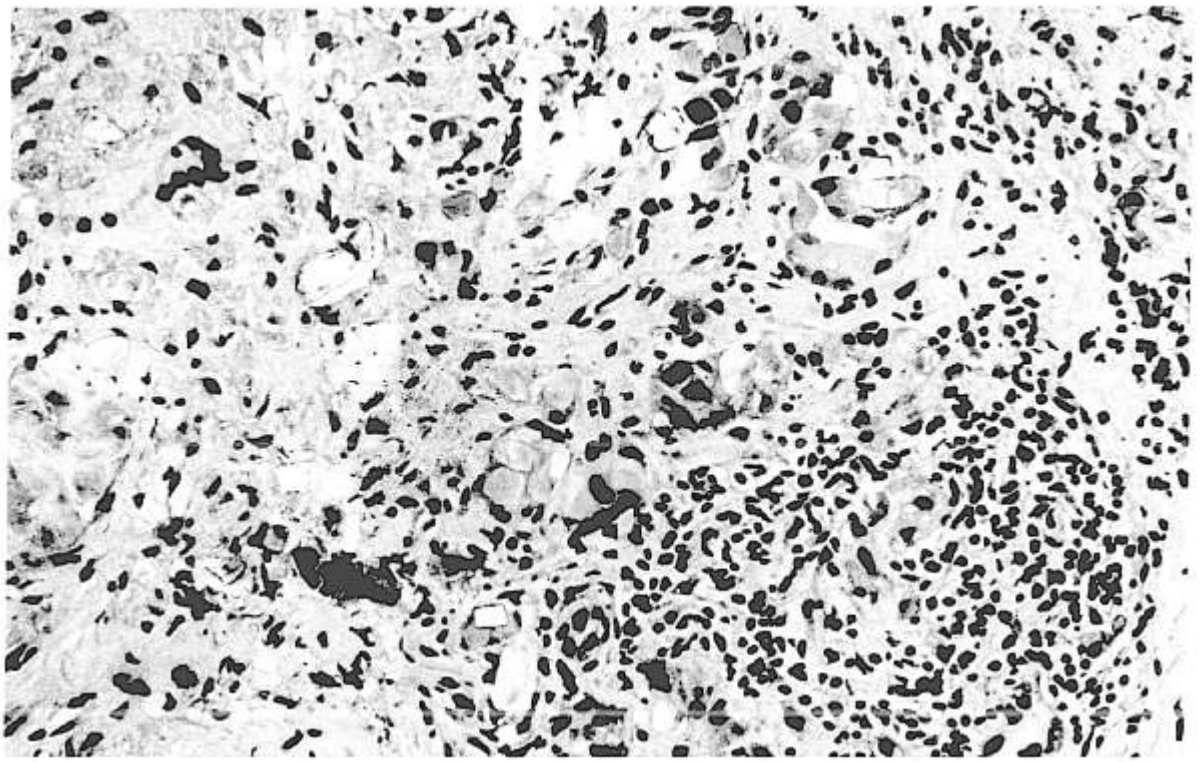


FIG. 4. A polarized light photomicrogram of a tissue specimen from Case 5 showing foreign-body giant cells with phagocytized intracellular polymer debris. (Stain, hematoxylin and eosin; original magnification, ×250.)

tissue responses in clinical use.[4] The intensity of a reaction might possibly be diminished by early surgical drainage of any local fluid accumulations seen in these patients, but this cannot be commented on from the present study. Nevertheless, too extensive debridement procedures may, in turn, result in additional iatrogenic tissue damage. The granulomatous inflammatory lesion sometimes associated with present-day absorbable fracture fixation devices is a risk that has to be taken into consideration when these implants are used. The advantage of avoiding all hardware removal operations should not encourage a rush of unnecessary surgery, but the indications for open reduction and internal fixation of a fracture with absorbable implants should be at least as strict as with metallic implants.

NOTE: The implants referred to in this study contained a green aromatic quinone dye. Since 1989, beige uncolored implants have been in use, and the frequency of the inflammatory lesions has decreased.

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