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Case Report

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Infected humeral shaft nonunion treatment with the induced membrane technique and a novel fixation construct: a case report

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Abstract

Case: A 51-year-old woman with an infected left humeral shaft recalcitrant nonunion presented 3 years after initial injury. This case report focuses on the staged treatment of a 17-centimeter (cm) humeral shaft nonunion with the induced membrane technique (IMT) using a unique fixation construct of dual locked plating around a humeral nail to provide long-lasting fixation and allow for bone graft consolidation.

Conclusion: Large segmental bone loss of the humerus can be treated with the IMT using nail-plate fixation constructs that allow for early mobilization, increased time for bone graft consolidation before hardware failure, and less frequent follow-up.

Keywords: humeral shaft nonunion, induced membrane technique, septic nonunion, nail-plate construct

1. Introduction

Humeral shaft nonunions occur in up to 15% to 23% of humeral shaft fractures, and the risk of nonunion is increased with nonoperative treatment.[1,2] Associated factors include operative fixation of the acute fracture with a plate, infection, and more than 2 surgical procedures.[3,4] There are multiple treatment options available, and the induced membrane technique (IMT, also known as the Masquelet technique), has been shown to lead to high union rates.[5–7] In the setting of infected nonunions with large segment bone loss treated with IMT, a staged approach to infection eradication, fracture fixation, and subsequent bone grafting is necessary to achieve a good outcome.

2. Statement of Informed Consent

Patient was informed that data concerning the case would be submitted for publication and agreed. The study was deemed exempt from Institutional Review Board and Animal Use Committee Review.

S. Konda is a consultant for Stryker. The remaining authors have no relevant financial or nonfinancial interests to disclose.

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3. Case Report

A 51-year-old woman presented to the emergency department after traveling from her home country (Guyana) with a draining sinus from her left humerus with significant pain and limb dysfunction. She was in a motor vehicle collision 3 years before presentation in Guayana when she sustained a left midshaft humerus fracture and bilateral femoral shaft fractures. She underwent a total of 4 surgeries on her left humerus: the initial humeral fracture open reduction and internal fixation and 3 subsequent bone grafting procedures using autogenous left and right tricortical anterior iliac crest bone graft (ICBG) and autogenous left fibula shaft. The timing and order of these surgeries was unclear because the patient was a poor historian. The nature of the bone grafting procedures was deduced by plain radiographs of the pelvis and tibia which demonstrated bone loss consistent with harvest from these sites as well as healed surgical incisions over these bone graft harvest sites. Her last surgery for her humerus was 11 months before presentation.

On examination of the left upper extremity, there were 2 prior longitudinal incisions, one anterolateral and one directly posterior extending from the proximal to distal humerus. A draining sinus was noted over the middle aspect of the posterior incision. She had an apex-anterior deformity with 3 centimeter (cm) shortening of the upper arm compared with the contralateral side and painful gross motion at the fracture site (see **Video 1, Supplemental Digital Content**, http://links.lww.com/OTAI/A90). Her left hand was resting in a "claw" position with 4/5 interossei strength and decreased sensation in the ulnar nerve distribution. Her wrist range of motion (ROM) was extension 80 degrees and flexion 80 degrees, with 60-degree wrist pronation and supination. Initial passive ROM of the shoulder and elbow was assessed when the patient was under anesthesia. Her shoulder ROM was forward elevation to 160 degrees, external rotation to 45 degrees, and internal rotation to L5. Her elbow ROM was extension to 45 degrees and flexion to 90 degrees.

Initial radiographs of the left humerus demonstrated a midshaft atrophic nonunion with segmental bone loss and 2 plates with hardware failure (Figs. 1A and B). Baseline infection laboratory test results were elevated: erythrocyte sedimentation rate (ESR) 145 millimeters per hour (mm/h; normal 0–20 mm/h), c-reactive protein

(CRP) 4.7 milligrams per deciliter (mg/dL; normal 0.7–1.0 mg/dL), and white blood cell (WBC) count 7.1 thousand cells per microliter (K/μL; normal 4.8–10.8 K/μl) with 62.5% neutrophils. Initial Short Musculoskeletal Functional Assessment (SMFA) score was 90.76 out of 100 points, indicating significant loss of function as a score of 0 indicates no functional impairments.[8]

Her initial surgical procedure included removal of all humeral hardware, thorough irrigation and sharp excisional debridement of necrotic soft tissue and bone, and placement of antibiotic spacer around a guidewire and application of uniplanar elbow-bridging external fixator (Fig. 1, see **Video 1, Supplemental Digital Content**, http://links.lww.com/OTAI/A90). An external fixator was used to provide increased stability of the arm and minimize fracture motion which would improve the ability to eradicate the infection.

The prior midline posterior incision was used to excise the sinus tract over the distal third of the humerus. A triceps splitting approach was used to access the humeral shaft.[9] Care was taken to identify and protect the radial nerve and the ulnar nerve. After debridement, the defect was measured to be 17 cm in length. Intraoperative aerobic, anaerobic, fungal, and acid-fast bacillus cultures were sent to the microbiology laboratory. An antibiotic spacer using 140 mg packet of cement mixed with 2 g vancomycin and 3.6 g tobramcyin placed over a 2.5 mm guidewire was implanted into the defect. The external fixator was applied with two 5.0 mm Schantz pins placed anterolaterally in the proximal humerus and two 4.0 mm Schantz pins placed posterolaterally in the proximal ulna and statically locked with the elbow in 90 degrees of flexion.

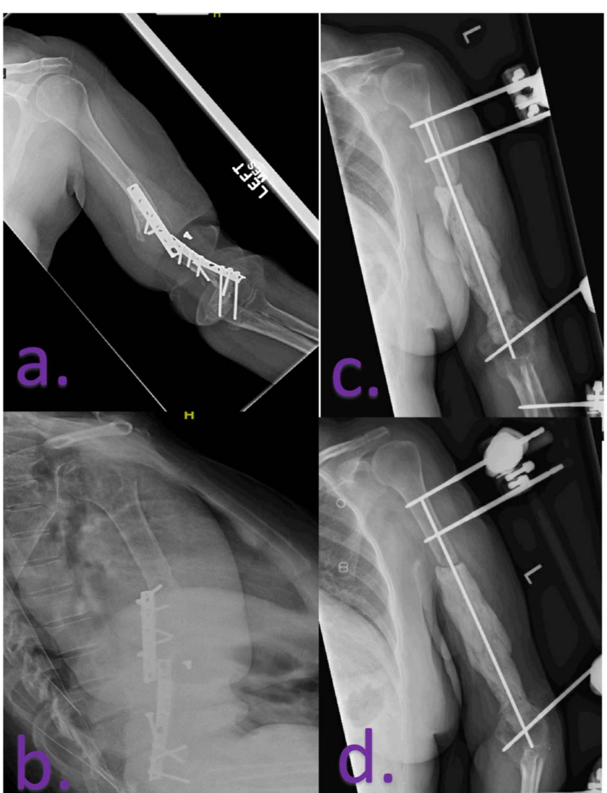

Figure 1. Initial and first stage IMT radiographs. Initial AP (A) and transthoracic lateral (B) of the left humerus demonstrating atrophic nonunion with hardware failure. Six weeks postoperative first stage IMT: AP (C) and lateral (D) plain radiographs of the left humerus with external fixator and antibiotic cement spacer over a guide wire. AP, anteroposterior; IMT, induced membrane technique.

Intraoperative cultures ultimately grew methicillin-resistant staphylococcus aureus (MRSA), and the patient received a total of 6 weeks of intravenous vancomycin followed by a 2-week antibiotic holiday in which the antibiotics were held to look for signs of recurrent infection before return to the operating room. Laboratory test values at this time were CRP 2.9 mg/dL (normal 0.7–1 mg/dL), ESR 129 mm/h (0–20 mm/h), vitamin D 17.2 ng/mL (normal 30–100 ng/mL), and calcium 8.3 mg/dL (normal 8.4–10.2 mg/dL). Vitamin D3 supplementation with 50,000 units weekly for 3 months and calcium supplementation with 1200 mg daily were initiated. Although her infection laboratory test results were elevated, her clinical examination demonstrated no erythema or abnormal swelling, her pin sites were clean and dry, and her pain was well controlled which was consistent with infection eradication and/or suppression. The decision was made to proceed with the second stage of her IMT procedure and perform intraoperative evaluation and culture for persistent infection.

For the second stage of IMT, the external fixator was removed first and pin sites were irrigated and debrided. Next, a posterior approach to the humerus was used to expose the antibiotic spacer. Dissection was carried posteriorly to the triceps muscle, and medial and lateral paratricipital flaps were developed, and the ulnar nerve and radial nerve were identified and protected. The triceps muscle was then split, and the induced membrane was incised directly posteriorly and then elevated with the surrounding triceps musculature posteriorly and brachialis muscle anteriorly. Care was taken to preserve the induced membrane. The antibiotic spacer and intramedullary wire were removed. Gross inspection of the wound revealed no purulence or active sign of infection. Cultures of the surrounding bone and soft tissue were performed, as well as debridement and irrigation of the wound and intramedullary canal of the humerus. Next, initial fixation of the humeral shaft nonunion was performed with a long humeral nail which was inserted through a 4-cm anterolateral approach to the proximal humerus.[10] The nail was locked proximally with 2 proximal locking bolts. Distally, there was no bone available to lock the nail to the condylar fragment using the anterior-posterior holes, and the medial-lateral holes were saved for linking to the plates. Dual 14-hole medial and lateral distal humeral locking plates were then used to fix the condylar fragment to the proximal humeral shaft fragment. Both the radial and ulnar nerves are protected as the medial and lateral plates are applied to the fracture. Distally, the plates were linked to the nail with 3.5-mm locking screws inserted from the plate through the medial-lateral distal interlocking holes in the nail. Proximally, the deltoid insertion was split, the axillary nerve was identified and protected, and the deltoid was elevated both medially and laterally (approximately 50% of the insertion) to allow for proximal fixation of the medial and lateral plates.

To fill the 17-cm bone void, bilateral posterior ICBG with 30 cubic centimeters (cc) additional demineralized bone matrix (DBM) and 30 cc of allograft cancellous bone chips were used (see **Video 1**, **Supplemental Digital Content**, http://links.lww.com/OTAI/A90). No antibiotics were added to the bone graft. The induced membrane, which was adherent to the triceps muscle and brachialis muscle, remained intact and enveloped the bone graft. The triceps split was repaired, the wound was closed primarily, and the patient was allowed full active range of motion of the shoulder elbow immediately in the postoperative periods. She was given a 2-pound weight restriction for 3 months postoperatively.

Cultures obtained during the second stage were ultimately negative for infection. Three-month and 6-month postoperative plain radiographs demonstrated maintenance of the fixation construct with interval consolidation of bone graft at the nonunion

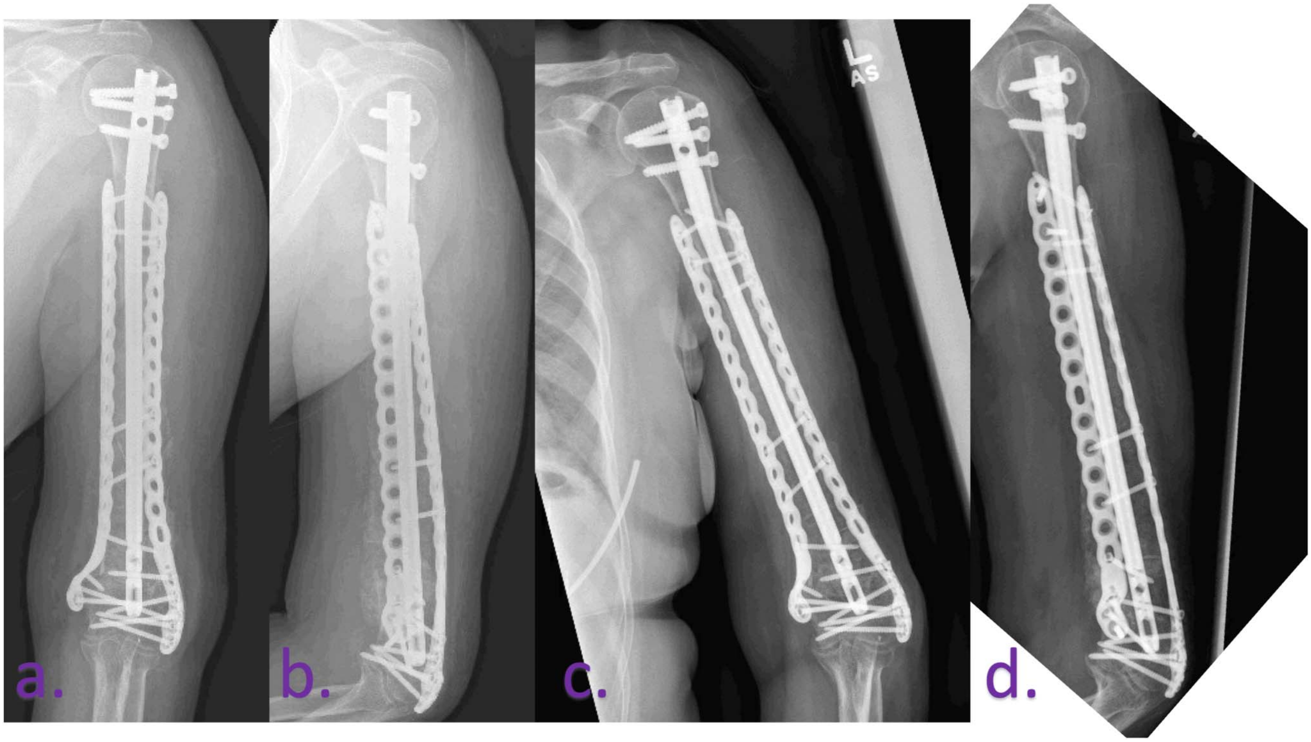

Figure 2. Postoperative radiographs after second stage Masquelet. Six weeks postoperative second stage Masquelet AP (A) and lateral (B) plain radiographs. Three months postoperative second stage Masquelet AP (C) and lateral (D) plain radiographs.

site (Fig. 2). Her SMFA scores were 46.2 and 16.3 at 3 and 6 months respectively, and ESR and CRP were within normal limits. Her range of motion at 6 months postoperatively demonstrated active shoulder forward elevation to 120 degrees, external rotation to 50 degrees, internal rotation to L3, elbow extension to 10 degrees, and elbow flexion 90 degrees (Fig. 3, see **Video 1, Supplemental Digital Content**, http://links.lww.com/OTAI/A90).

At 9 months postoperatively from the second stage IMT procedure, the patient reported mild persistent pain about the left arm and CT scan of the humerus demonstrated incomplete healing at the nonunion site (Fig. 4). Infection laboratory test results were obtained which were within normal limits. She returned to the operating room 11 months after her second stage IMT for repeat bone grafting of the left humerus nonunion using right tibial intramedullary bone graft harvested with a reamer-irrigator-aspirator (RIA) system. Her tibia was used for the RIA because she had bilateral femoral shaft intramedullary nails in place from prior injury. Intraoperatively, cortical healing was noted 50% circumferentially over the entire length of the 17 cm defect, but the posterior cortex had a fibrous union which was excised, and the defect was grafted with 30cc of tibial autograft and 30cc of DBM. Repeat bone and soft tissue cultures were performed intraoperatively which were negative for infection. Her left humerus progressed to union on subsequent radiographs obtained at 5 months and 1 year postoperatively (Figs. 5A–D). Her SMFA score at 1 year after her initial surgery and 3 months after her repeat bone grafting was 15.76.

At her most recent visit 3 years from her initial left humerus second stage IMT and 2 years from repeat bone grafting, humerus radiographs demonstrate a healed nonunion without hardware loosening or failure (Figs. 5E–H). She no longer has any heavy lifting restrictions and has returned to work as a home health aide and is able to perform all work-related duties without restrictions and perform all activities of daily living. (see **Video 1, Supplemental Digital Content**, http://links.lww.com/OTAI/A90). Her shoulder ROM is active shoulder forward elevation to 140 degrees, external rotation to 60 degrees, internal rotation to L1, elbow extension to 10 degrees, and elbow flexion 90 degrees. Her ulnar nerve sensory deficit has resolved, and she has 5-/5 interossei strength. Her SMFA score at final follow-up was 7.61 out of 100, a significant improvement from initial presentation. She is overall extremely happy with her outcome.

4. Discussion

There are many options for bone grafting in the setting of humeral shaft nonunions, including autograft, allograft, and DBM. Augmenting bone graft is possible with the use of bone morphogenic proteins.[11] Various autografts are available for use; however, each carries an inherent set of morbidity because of graft harvest. Structural autograft in the form of tricortical iliac crest (anterior or posterior) and fibular strut (vascularized or non-vascularized) can be used in segmental defects to provide additional structural support to the overall fixation construct. These also provide osteoinductive, osteoconductive, and osteogenic properties. Similar structural allografts can be used with no harvest site morbidity; however, these provide mostly osteoconductive properties and generally lack osteoinductive properties and have no osteogenic potential. DBM is a form of allograft that has osteoinductive and osteogenic potential.[11]

The IMT is a 2 stage method used to create a bioactive membrane in which bone graft can be placed to augment bony union.[5,12] In the first stage, all devitalized bone and soft tissue is thoroughly debrided, the remaining fracture with the bony defect are stabilized and a polymethylmethacrylate (PMMA) spacer is placed into the bony defect. Between the first and second stages, a bioactive membrane is formed around the

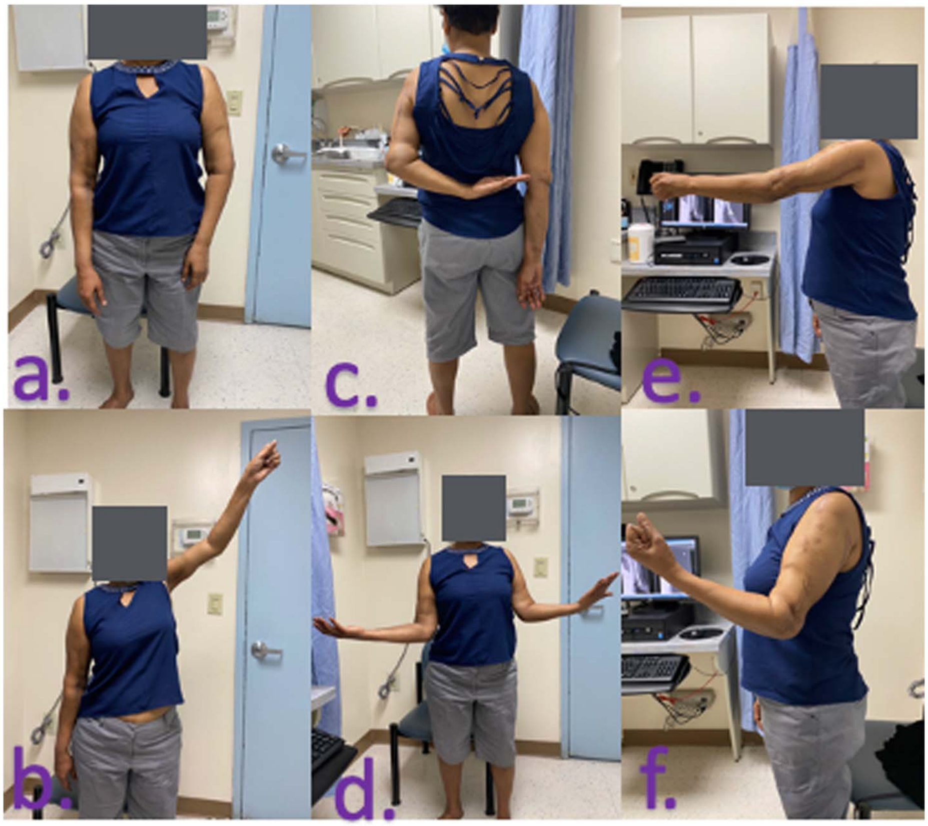

Figure 3. Range of motion 6 months postoperative second stage Masquelet. A, Position of arm at rest. B, Active shoulder abduction. C, Active shoulder external rotation. D, Active shoulder internal rotation. E, Active elbow extension. F, Active elbow flexion.

PMMA spacer that becomes highly vascularized and secretes a combination of growth factors important for bone healing including bone morphogenic protein-2, transforming growth factor-β1, and vascular endothelial growth factor.[13] In the second stage, performed 4–8 weeks later to capitalize on peak growth factor levels, the membrane is incised, the spacer

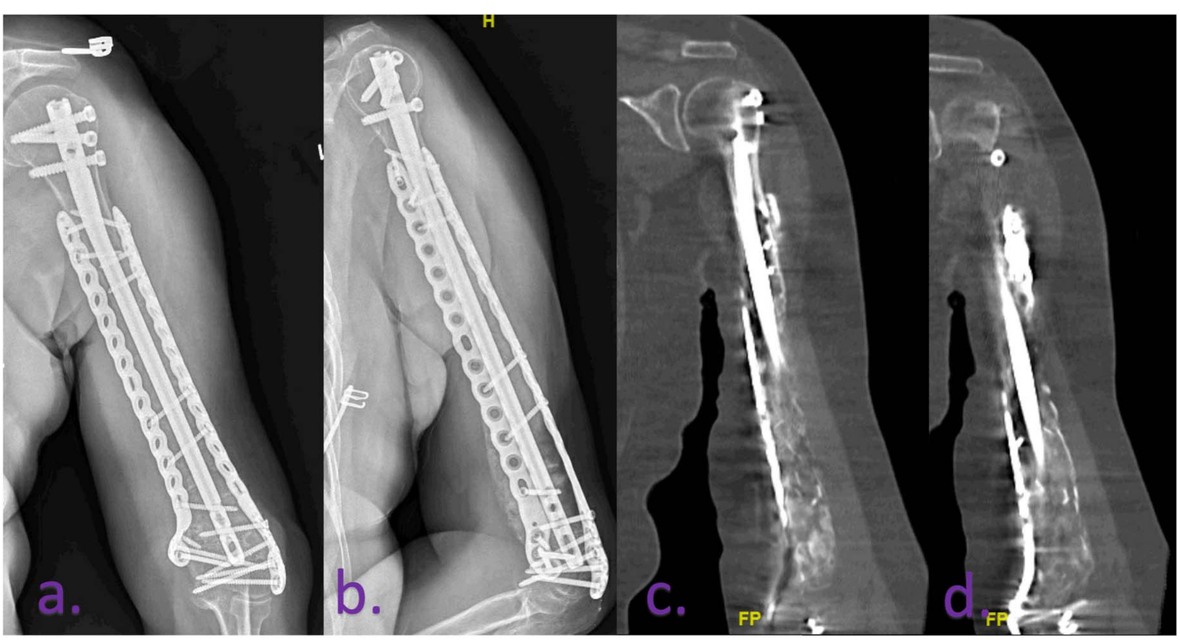

Figure 4. Radiographs and CT at 9 months after second stage Masquelet demonstrating persistent nonunion. Nine months postoperative second stage Masquelet AP (A) and lateral (B) plain radiographs demonstrate persistent nonunion. Nine months postoperative second stage Masquelet coronal CT cuts (C and D) demonstrating persistent nonunion.

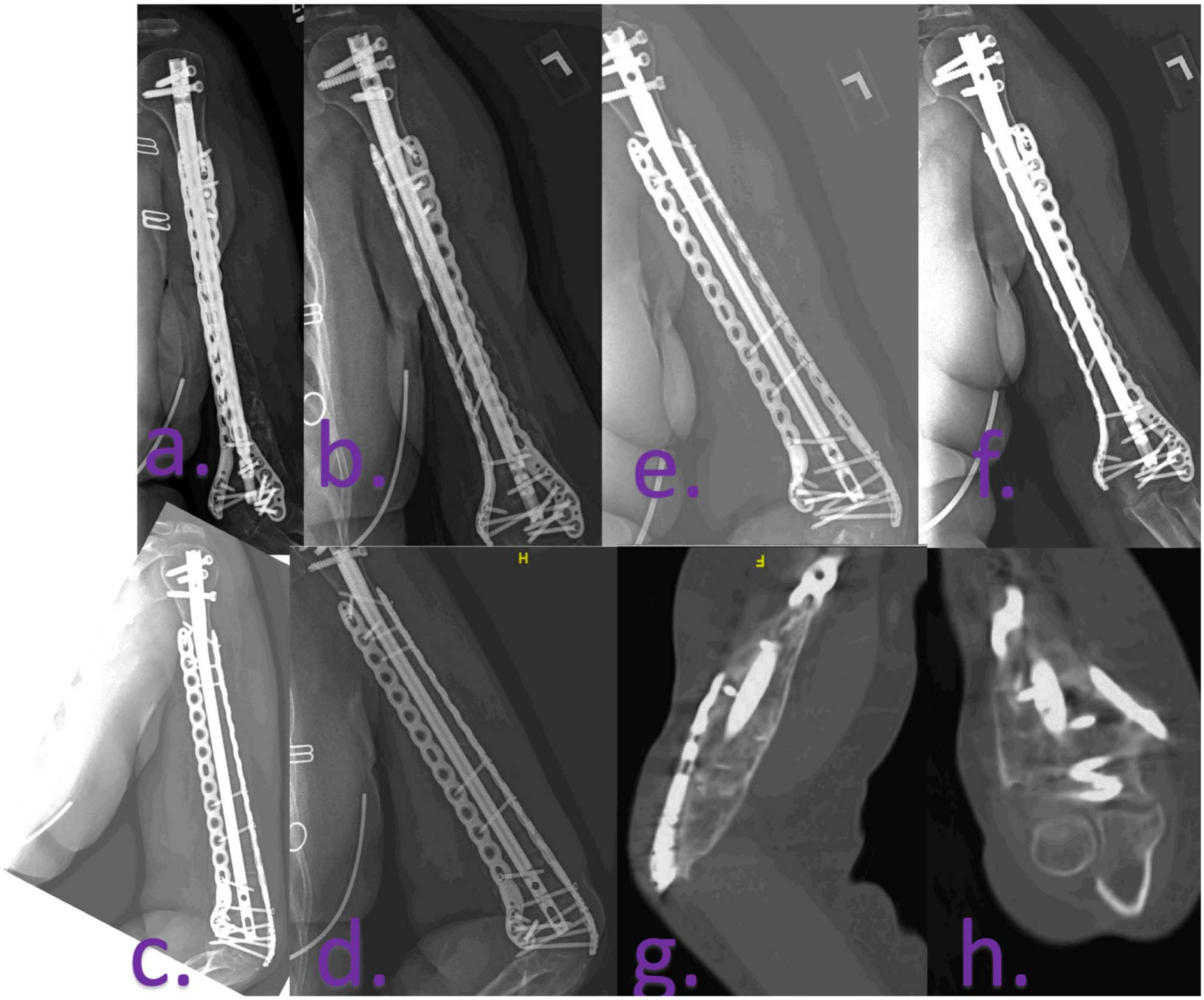

Figure 5. Postoperative radiographs after repeat bone grafting. Five months postoperative repeat bone grafting AP (A) and lateral (B) plain radiographs. 1 year postoperative repeat bone grafting AP (C) and lateral (D) plain radiographs. 2 years postoperative repeat bone grafting AP (E) and lateral (F) plain radiographs. Two years postoperative repeat bone grafting CT cuts (G and H).

removed, and the defect filled with bone graft.[5] The IMT has demonstrated successful results for defects ranging from 5 to 24 cm and in both upper and lower extremity defects for septic and aseptic nonunions.[6,7,14–19] In this case, the patient did not return for a second bone grafting procedure until 8 weeks after her first stage IMT to fully eradicate her infection. This is on the tail end of what has been described as the optimal bone grafting window and may have had an effect on the healing potential of her bone graft because she did require a secondary bone graft procedure to achieve union.

A recent systematic review reported a 90% union rate and 91% infection clearance in 427 patients over 17 studies.[6] However, this review highlighted the significant heterogeneity in techniques for the first and second stages. Furthermore, patients undergoing the IMT for infection had a higher rate of complications, and 18% of cases required reintervention because of persistent infection or nonunion.

Rat models have shown that while the induced membrane does not possess antimicrobial properties to overcome an infected nonunion on its own, the addition of local antibiotics during the first stage leads to new bone formation.[20] Local antibiotics used in adjunct to extensive debridement are advisable during the first stage of an IMT procedure for an infected nonunion.[20,21] Double plate fixation with autogenous ICBG is also recommended as a salvage procedure for humeral shaft nonunion after failed prior interventions.[22]

The fixation construct used in this patient is novel and was chosen for a few reasons. First, the use of an intramedullary nail linked with dual locking plates allowed for construct longevity. Up to 20% of patients with large segment bone defects will require repeat bone-grafting procedures which was taken into consideration on this patient.[6] With this construct, a second bone-grafting procedure could be performed without adjusting or replacing any hardware because it was believed that the construct was still very stable. Second, the dual plating allows for containment of the bone graft, similar to a cage. Finally, the use of an intramedullary nail reduced the volume of bone graft necessary to fill the 17 cm defect.

The use of a nail-dual plate approach to large segmental bone defects can be considered a "hands-off" approach to repair of large segment bone defects because there is less postoperative monitoring required given the rigidity of the construct. Unlike many other techniques for filling osseous defects that require both close patient follow-up and patient compliance with bone transport protocols (eg, external fixator bone transport, lengthening intramedullary nails), the use of nail-plate constructs allow for rigid, stable, and continuous fixation over a long period of time which is necessary for bone graft to consolidate without the need for repetitive weekly or monthly follow-up. This "hands-off" approach can be particularly useful in patients where social determinants of health (lower socioeconomic status, poor health literacy, mental health issues) can lead to infrequent follow-up.

Successful treatment of infected humeral nonunions with large segment bone defects can be performed using the IMT if a staged approach to infection eradication, fracture fixation, and bone grafting is performed. This technique with the intramedullary nailing linked to dual humeral locking plates allows for construct longevity allowing for multiple bone grafting procedures to be performed without need for frequent follow-up.

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