Chronic Sclerosing Osteomyelitis Treated With Wide Resection and Vascularized Fibular Autograft: A Case Report

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Abstract

Treatment recommendations for chronic culture-negative sclerosing osteomyelitis in the pediatric population have largely focused on supportive care, given the typical improvement in symptoms that occurs over time.

This case report describes a patient with chronic sclerosing osteomyelitis (CSO) of the humerus who failed a prolonged course of nonoperative management. Definitive treatment consisted of resection of the diseased bone and reconstruction using a vascularized fibular osteocutaneous flap. To our knowledge, this is the first reported case of this technique being utilized specifically for CSO refractory to nonoperative management. At the time of most recent follow-up (35 months), the patient was completely pain-free and off all medication. Physical examination revealed full unrestricted passive and active range of motion. Radiographs at the time of most recent follow-up revealed intact hardware, excellent proximal and distal graft incorporation, and cortical hypertrophy. Vascularized fibular osteocutaneous flap reconstruction following resection is a viable alternative to nonoperative, expectant management for patients with refractory chronic sclerosing osteomyelitis.

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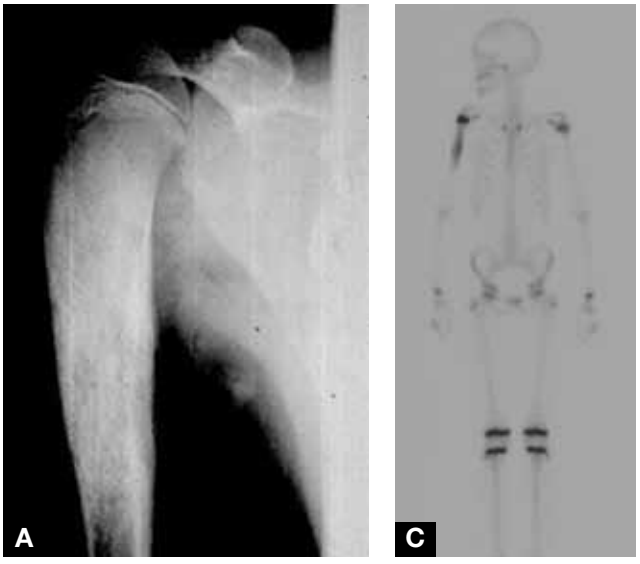
Chronic sclerosing osteomyelitis (CSO) was first described by Garré[1] in 1893 as a nonsuppurative, sclerotic form of osteomyelitis that results in cortical distention and bone thickening. Patients characteristically present with localized pain in the absence of constitutional symptoms, and cultures of the lesion are typically negative.[2-4] A set of related disorders includes chronic recurrent multifocal osteomyelitis (CRMO) and the SAPHO syndrome (characterized by synovitis, acne, pustulosis of the hands and feet, hyperostosis, and osteitis).[5-13] Although the exact etiology of these disorders has not been determined, recent studies have pointed to autoimmune or genetic factors or both.[14-16]

Treatment recommendations for chronic culture-negative osteomyelitis in the pediatric population have largely been supportive, given the typical diminution of symptoms that occurs over time.[2,6,17-20] One popular regimen consists of an initial course of broad-spectrum empiric antibiotics followed by symptomatic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs).[6] This may be supplemented with a short course of oral steroids in severe cases. In 1997, Vienne and Exner[21] described 2 patients treated surgically. One patient underwent intralesional curettage through a bony trough that extended the entire length of the lesion, and the other patient underwent complete resection of the involved bone and reconstruction with bone graft and a plate. The latter treatment provided complete and sustained pain relief. In the past decade, various studies have found increased efficacy with use of bisphosphonates[22,23] and tumor necrosis factor a (TNF-a) inhibitors.[24]

In this case report, we describe a patient with CSO of the humerus who failed to improve after multiple attempts at surgical débridement, several courses of intravenous antibiotics, use of NSAIDs, and use of TNF-a inhibitors. Complete and sustained relief of symptoms occurred only after wide resection of the involved portion of the humeral diaphysis and reconstruction using a vascularized fibular osteocutaneous flap. The authors have obtained the patient's guardian's written informed consent for print and electronic publication of the case report.



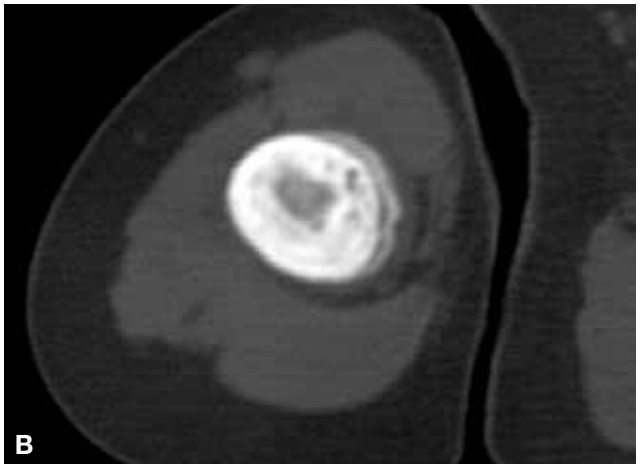


Figure 1. (A) Anteroposterior radiograph of humerus at initial presentation. Heterogeneous sclerosis along proximal to mid humeral shaft with thickening of bone and immature but benign-appearing periosteal new bone medially. (B) Axial computed tomography shows near obliteration of medullary canal by sclerotic lesion, and circumferential cortical thickening. (C) Bone scan shows intense increased radiotracer uptake in proximal third of humeral diaphysis, most prominent medially, corresponding to periostitis seen radiographically.

Case Report

An otherwise healthy 11-year-old boy presented to our clinic with the chief complaint of right arm pain, most notable at night. Anteroposterior (AP) and lateral radiographs were obtained at initial presentation (Figure 1), as were magnetic resonance imaging (MRI), computed tomography (CT), and technetium-99m whole-body bone scans. The radiographs showed heterogeneous medullary and cortical sclerosis along the proximal to mid humeral shaft, with mild bone expansion. Immature unilaminar periosteal new bone could be seen medially. Axial CT images better defined near obliteration of the medullary canal by the sclerotic lesion and showed circumferential cortical thickening as well as the periosteal new bone seen radiographically. MRI showed intense marrow edema beginning at the unfused proximal humeral physis and extending 14 cm distally to the distal diaphysis. Inflammatory periostitis was present circumferentially. No discrete soft-tissue mass could be seen. The bone scan showed intense increased radiotracer uptake in the proximal third of the humeral diaphysis, most prominent medially, corresponding to the periostitis seen radiographically.

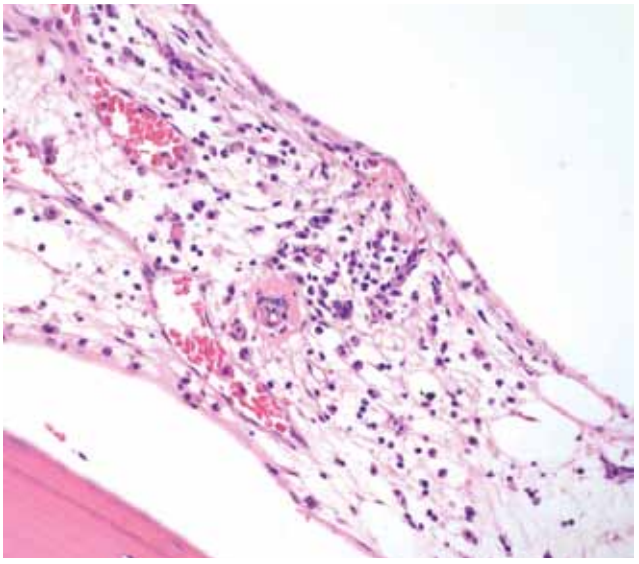


Figure 2. Histologic sections reveal thickened trabeculae of medullary bone containing fibrous marrow. Abundant plasma cells comprise more than 50% of cellular element (hematoxylin-eosin, original magnification ×400).

Laboratory workup results were normal white blood cell count ($8.5\times10^3/mm^3$), normal differential (46% neutrophils), slightly elevated erythrocyte sedimentation rate (ESR, 18 mm/h; normal, <15 mm/h), and normal C-reactive protein level (0.2 mg/dL; normal, <0.8 mg/dL). Skin purified protein derivative (PPD) test was negative for tuberculosis. Radiologic and laboratory findings were considered to be most consistent with a diagnosis of chronic osteomyelitis or Langerhans cell granulomatosis. Ribbing disease and Ewing sarcoma were considered less likely.

The pathologic specimen obtained from open biopsy is shown in Figure 2. The histologic sections revealed an abnormal medullary canal characterized by thickened trabeculae of lamellar and woven bone. Normal marrow had been replaced by loose, fibrous tissue populated by abundant plasma cells, which comprised more than 50% of the cellular element. Bland-appearing lymphocytes were also present. The cells were normal in appearance, with no nuclear atypia or features suggestive of malignancy. All the cultures obtained from the initial biopsy were negative for organism growth. In addition, workup was negative for atypical organisms, including *Mycobacterium, Nocardia, Bartonella,* and *Coccidioides*.

The patient was taken to the operating room for creation of a 5.5-cm trough in the diaphysis—a procedure similar to our preferred method of surgical treatment for Ribbing

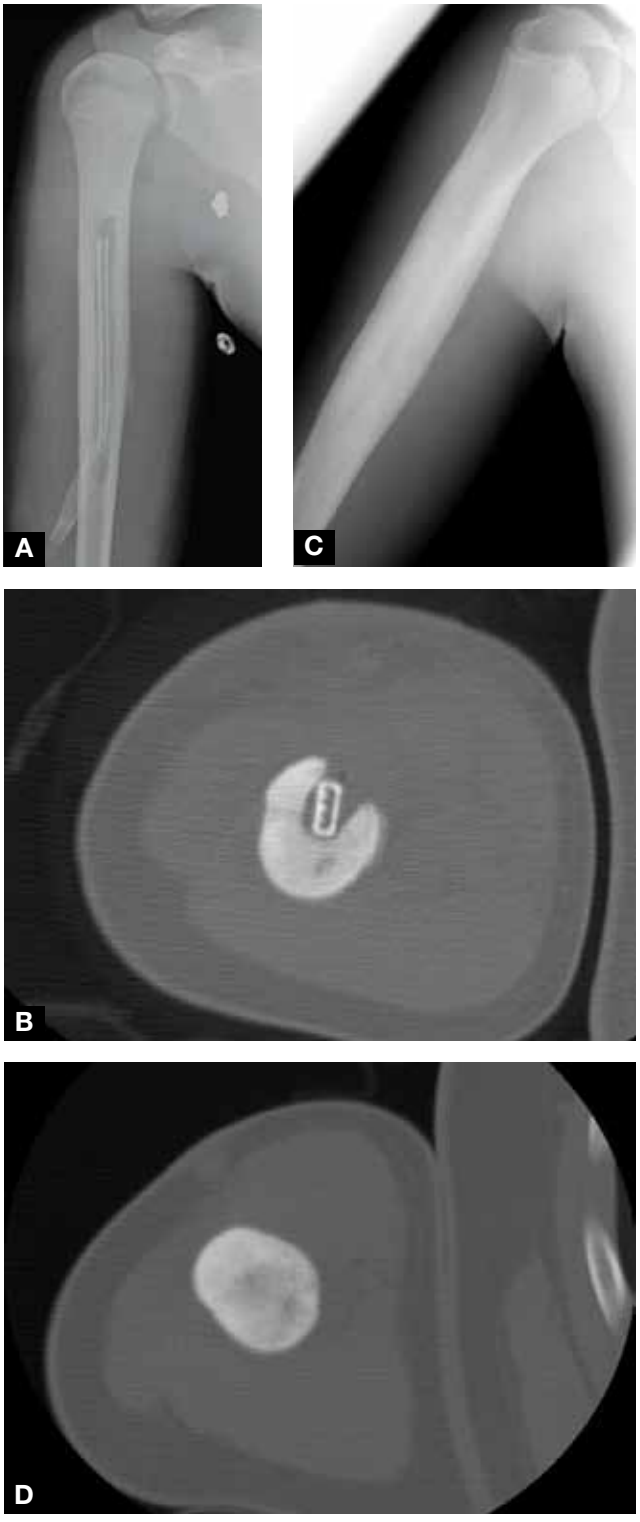


Figure 3. Radiograph (A) and computed tomography (B) immediately after creation of surgical trough. Radiograph (C) and computed tomography (D) show recurrence of medullary sclerosis 3 months after trough procedure. Obliteration of medullary canal recurred after each of 3 surgical débridements.

disease.[25,26] During this procedure, multiple cultures were obtained, including aerobic, anaerobic, acid-fast bacillus, and fungal; none of these revealed an offending organism.

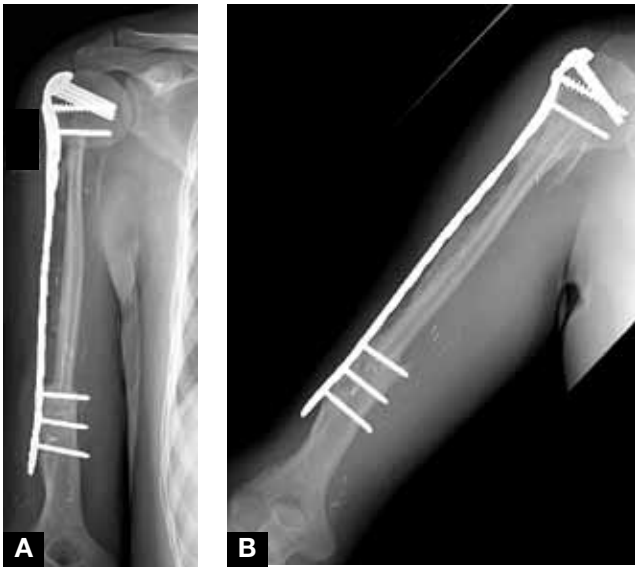


Figure 4. Anteroposterior radiographs of humerus (A) immediately after resection and autografting and (B) 35 months later (interface of fibula and humerus is confluent; mature incorporation of posterior iliac crest autograft placed along length of tibia graft led to apparent thickening of bone compared with initial postoperative radiograph; hardware is stable).

Pediatric Infectious Disease Service recommendations included empirical treatment for osteomyelitis with 5 weeks of intravenous ceftriaxone followed by 3 weeks of oral cephalexin. Symptoms temporarily improved on this regimen, but 4 months after initial treatment the pain recurred, necessitating readministration of NSAIDs and eventually narcotics. Pain resurgence was coincident with disease progression and obliteration of the previous surgical trough. Two more surgeries were performed, 9 and 29 months after the index débridement. At the time of each procedure, a trough was created from normal metaphysis proximally through the sclerotic diaphysis to normal metaphysis distally (confirmed by intraoperative frozen section). The second trough was 9 cm, and the third was 12 cm, as the diaphyseal sclerosis not only recurred but extended proximally and distally. Both cases were followed by a short course of intravenous antibiotics.

Symptoms completely resolved for 5 months after the second procedure and for 11 months after the third procedure. Cultures at the time of both procedures were negative for all growth. Histopathology was identical to that of the first biopsy. ESR remained slightly elevated during this time (range, 18-40 mm/h). Radiography and CT after these procedures showed persistent reconstitution of the diaphyseal sclerosis (Figure 3). After all 3 trough procedures, the pain ceased initially but recurred as the disease process appeared to fill in the troughs and create a solid sclerotic diaphysis. The pain became continuous, especially at night, and ultimately unresponsive to treatment with NSAIDs and opioid analgesics.

Treatment with acupuncture and transcutaneous electrical nerve stimulation (TENS) failed to relieve the symptoms. The patient had now undergone creation of 3 surgical trough decompressions from normal bone proximally to normal bone distally with 4, 5, and 11 months of pain relief but not long-lasting relief. At this point, the patient was referred to another institution for treatment with a TNF-a inhibitor (etanercept). Therapy was begun approximately 4 years after the patient's initial presentation to our clinic. Pain improved after initiation of this medical therapy, though 4 months later the pain returned and gradually worsened.

After failure of all previous courses of treatment, the patient was offered wide resection of the diseased portion of the humerus and reconstruction using a vascularized fibular autograft. At time of surgery, the patient was 17 years old and skeletally mature.

Surgical Procedure

The patient was placed in the lateral decubitus position, and the entire right side of the body was prepared and draped. Preoperative antistaphylococcal antibiotics were administered. Two teams worked simultaneously: Dr. Eckardt's team performed the wide resection of the right humerus diaphysis, and Dr. Jones's team harvested the vascularized fibular autograft and performed the vascular anastomoses. The resection was performed proximally just distal to the level of the surgical neck and distally just proximal to the level of the epicondylar flare. Total resection length was 17 cm. An intraoperative frozen section was obtained of the distal and proximal marrow margins to ensure that the resection was adequate.

Posterior iliac crest autograft was harvested to supplement the proximal and distal graft–host junction. The fibular autograft was fixed provisionally by intussusceptting the graft into the residual proximal and distal bone. A right-sided proximal tibial locking plate (Synthes) was used to obtain additional fixation proximally and distally. Under microscopic visualization, the peroneal artery was anastomosed end-to-side to the brachial artery, and one of the venae comitantes was anastomosed to one of the brachial veins using 9-0 nylon suture by the microvascular team (Dr. Jones). After the anastomoses, there was excellent blood flow with bleeding from the periosteal surface of the fibula and bleeding from the skin edges of the monitoring skin flap.

The wound was closed over a drain placed laterally adjacent to the fibular autograft, and a long-leg splint was applied to the right lower extremity. The patient was discharged 7 days after surgery with a gunslinger-type upper extremity brace, which was maintained for 3 months after the reconstruction. Within 2 weeks of surgery, the patient reported that his preoperative symptoms had completely resolved. Afterward, the patient was followed quarterly.

At time of most recent follow-up (35 months), the patient was completely pain-free and not taking any pain medication. Physical examination revealed full/unrestricted passive and active range of motion and 4+/5 strength. Radiographs (Figure 4) showed intact hardware, excellent proximal and distal graft incorporation, and cortical hypertrophy.

Discussion

The diagnosis of CSO or one of its variants should be made only after a thorough workup and exclusion of more aggressive, potentially life-threatening conditions (eg, Ewing sarcoma).[27] CSO can also be confused with Langerhans cell granulomatosis or conventional bacterial osteomyelitis. According to Schultz and colleagues,[6] the diagnosis may be made on the basis of prolonged disease course (typically, >3 months), evidence of chronic inflammation on biopsy, and lack of organism growth.

CSO, conventional osteomyelitis, Langerhans cell granulomatosis, and Ribbing disease look similar on imaging. All show sclerosis on plain radiograph and increased tracer activity on bone scan. Medullary and adjacent soft-tissue edema are usually seen with all of these on MRI. Ewing sarcoma, on the other hand, generally shows a prominent circumferential soft-tissue mass surrounding the diaphysis on CT and MRI, and edema on MRI is lacking. Analysis of the pattern of periostitis may also be useful. The periosteal new bone seen with Ewing sarcoma is multilayered and interrupted, as opposed to the unilaminal and continuous periosteal new bone seen in our patient's case. Patient age can help in discriminating between Ribbing disease and the other entities, as patients with Ribbing disease are generally middle-aged.

There are few reports of surgical management of CSO. In 1933, Wishner[28] reported that open biopsy and partial excision of the diseased portion of bone were effective treatment in 5 cases. Collert and Isacson[4] in 1982 described the outcomes of 8 patients with CSO treated with open biopsy and intralesional curettage. Lack of prolonged or sustained symptomatic improvement among all the patients in the series led those authors to conclude that there was "no effective [surgical] treatment" for this disease. Later, in 1997, Vienne and Exner[21] advocated creating a trough in the bone to open the medullary canal to relieve symptoms. One patient had complete pain relief but was followed for only 2 months. That outcome is similar to our patient's—the surgical trough gave good pain relief for a short time. Our decision to create a surgical trough was based on our successful use of a trough in treating diaphyseal sclerosis, or Ribbing disease.[26] The conditions are similar in that the medullary canal is obliterated and is filled radiographically with cortical bone. The histopathology, however, is different; chronic inflammatory cells are not seen in Ribbing disease. The second distal femur case described by Vienne and Exner[21] was completely resected and reconstructed using a mixture of autograft and allograft with plate fixation. This treatment provided complete pain relief for 6 years. Complete and sustained pain relief appears

to require resection of the entire area of involved bone.

Historically, symptoms in this condition are typically self-limited and managed with NSAIDs and occasionally oral steroids.[2,6,17-20] Use of bisphosphonates and TNF-a inhibitors has improved symptomatic control among patients with chronic culture-negative osteomyelitis, further popularizing use of nonoperative management regimens. Wagner and colleagues[24] described using etanercept to treat 2 patients with SAPHO syndrome who previously failed therapy with other disease-modifying antirheumatic drugs. Both patients demonstrated sustained symptomatic improvement over a 9-month period. Similarly, Simm and colleagues[23] reported decreased pain after a single infusion of pamidronate (1 mg/kg/dose) in 4 of 5 patients diagnosed with CRMO. Miettunen and colleagues[22] reported a similar improvement in symptoms among 9 patients with CRMO and concluded that pamidronate is an effective second-line therapy for refractory CRMO.

Despite the results obtained in these and other studies, our patient failed to respond to these second-line agents, and a novel therapeutic approach was necessary. Performing additional subtotal resections by creating a surgical trough did not seem like a feasible long-term solution. In the absence of additional treatment guidelines, we opted to treat this patient with wide resection of the diseased portion of the humerus, as we would have done for localized primary sarcoma of bone.

After resection, various reconstructive options were available. Use of vascularized tissue provides an improved biological substrate for healing and has the potential for remodeling and growth, particularly in the pediatric population. Excellent results have been demonstrated with use of vascularized osteocutaneous flaps for difficult traumatic and oncologic conditions. Yajima and colleagues[29] described use of vascularized fibular autograft for reconstruction after resection of methicillin-resistant staphylococcal infection in 20 patients. Eighteen of the 20 cases were considered successful, and only 1 patient had a recurrence of infection. Chang and Weber[30] reported successful use of vascularized fibular autograft for reconstruction of 14 segmental defects after either primary bone sarcoma resection or allograft nonunion. Mean time to incorporation was 8.6 months, and all patients except 1 had successful bony union. Similar cases have demonstrated equivalent efficacy.[31-37]

Although use of vascularized tissue transfer is widespread for other conditions, to our knowledge we are the first to report using vascularized fibular autograft specifically for CSO refractory to surgical decompression and nonoperative medical management. In our patient's case, complete symptomatic improvement and excellent functional results were obtained with wide resection of the diseased bone in CSO of Garré.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

References

1. Garré C. Über besondere Formen und Folgezustände der akuten infektiösen Osteomyelitis [in German]. *Beitr Klin Chir.* 1893;10:257-265.
2. Mollan RA, Craig BF, Biggart JD. Chronic sclerosing osteomyelitis. An unusual case. *J Bone Joint Surg Br*. 1984;66(4):583-585.
3. Blockey NJ. Chronic osteomyelitis. An unusual variant. *J Bone Joint Surg Br*. 1983;65(2):120-123.
4. Collert S, Isacson J. Chronic sclerosing osteomyelitis (Garré). *Clin Orthop*. 1982;(164):136-140.
5. Beretta-Piccoli BC, Sauvain MJ, Gal I, et al. Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome in childhood: a report of ten cases and review of the literature. *Eur J Pediatr*. 2000;159(8):594-601.
6. Schultz C, Holterhus PM, Seidel A, et al. Chronic recurrent multifocal osteomyelitis in children. *Pediatr Infect Dis J*. 1999;18(11):1008-1013.
7. Demharter J, Bohndorf K, Michl W, Vogt H. Chronic recurrent multifocal osteomyelitis: a radiological and clinical investigation of five cases. *Skeletal Radiol*. 1997;26(10):579-588.
8. Giedion A, Holthusen W, Masel LF, Vischer D. Subacute and chronic "symmetrical" osteomyelitis [in multiple languages]. *Ann Radiol (Paris)*. 1972;15(3):329-342.
9. Jani L, Remagen W. Primary chronic osteomyelitis. *Int Orthop*. 1983;7(2):79-83.
10. Jurik AG. Chronic recurrent multifocal osteomyelitis. *Semin Musculoskelet Radiol*. 2004;8(3):243-253.
11. Jurriaans E, Singh NP, Finlay K, Friedman L. Imaging of chronic recurrent multifocal osteomyelitis. *Radiol Clin North Am*. 2001;39(2):305-327.
12. Kopits SE, Debuskey M. Primary chronic sclerosing osteomyelitis. *Johns Hopkins Med J*. 1977;140(5):241-247.
13. Letts M, Davidson D, Birdi N, Joseph M. The SAPHO syndrome in children: a rare cause of hyperostosis and osteitis. *J Pediatr Orthop*. 1999;19(3):297-300.
14. El-Shanti HI, Ferguson PJ. Chronic recurrent multifocal osteomyelitis: a concise review and genetic update. *Clin Orthop*. 2007;(462):11-19.
15. Ferguson PJ, Bing X, Vasef MA, et al. A missense mutation in pstpip2 is associated with the murine autoinflammatory disorder chronic multifocal osteomyelitis. *Bone*. 2006;38(1):41-47.
16. Golla A, Jansson A, Ramser J, et al. Chronic recurrent multifocal osteomyelitis (CRMO): evidence for a susceptibility gene located on chromosome 18q21.3-18q22. *Eur J Hum Genet*. 2002;10(3):217-221.
17. Catalano-Pons C, Comte A, Wipff J, et al. Clinical outcome in children with chronic recurrent multifocal osteomyelitis. *Rheumatology (Oxford)*. 2008;47(9):1397-1399.
18. Girschick HJ, Raab P, Surbaum S, et al. Chronic non-bacterial osteomyelitis in children. *Ann Rheum Dis*. 2005;64(2):279-285.
19. Girschick HJ, Zimmer C, Klaus G, Darge K, Dick A, Morbach H. Chronic recurrent multifocal osteomyelitis: what is it and how should it be treated? *Nat Clin Pract Rheumatol*. 2007;3(12):733-738.
20. Huber AM, Lam PY, Duffy CM, et al. Chronic recurrent multifocal osteomyelitis: clinical outcomes after more than five years of follow-up. *J Pediatr*. 2002;141(2):198-203.
21. Vienne P, Exner GU. Garré sclerosing osteomyelitis [in German]. *Orthopade*. 1997;26(10):902-907.
22. Miettunen PM, Wei X, Kaura D, Reslan WA, Aguirre AN, Kellner JD. Dramatic pain relief and resolution of bone inflammation following pamidronate in 9 pediatric patients with persistent chronic recurrent multifocal osteomyelitis (CRMO). *Pediatr Rheumatol Online J*. 2009 Jan 12;7:2.
23. Simm PJ, Allen RC, Zacharin MR. Bisphosphonate treatment in chronic recurrent multifocal osteomyelitis. *J Pediatr*. 2008;152(4):571-575.
24. Wagner AD, Andresen J, Jendro MC, Hülsemann JL, Zeidler H. Sustained response to tumor necrosis factor alpha-blocking agents in two patients with SAPHO syndrome. *Arthritis Rheum*. 2002;46(7):1965-1968.
25. Eckardt JJ, Wirganowicz PZ, Mar T. An aggressive surgical approach to the management of chronic osteomyelitis. *Clin Orthop*. 1994;(298):229-239.
26. Seeger LL, Hewel KC, Yao L, et al. Ribbing disease (multiple diaphyseal sclerosis): imaging and differential diagnosis. *AJR Am J Roentgenol*. 1996;167(3):689-694.
27. Cabanela ME, Sim FH, Beabout JW, Dahlin DC. Osteomyelitis appearing as neoplasms. A diagnostic problem. *Arch Surg*. 1974;109(1):68-72.
28. Wishner JG. Chronic sclerosing osteomyelitis (Garré). *J Bone Joint Surg*. 1933;15:723-732.
29. Yajima H, Kobata Y, Shigematsu K, et al. Vascularized fibular grafting in the treatment of methicillin-resistant *Staphylococcus aureus* osteomyelitis and infected nonunion. *J Reconstr Microsurg*. 2004;20(1):13-20.
30. Chang DW, Weber KL. Use of a vascularized fibula bone flap and intercalary allograft for diaphyseal reconstruction after resection of primary extremity bone sarcomas. *Plast Reconstr Surg*. 2005;116(7):1918-1925.
31. Barnea Y, Amir A, Shlomo D, et al. Free fibula flap elbow-joint hemiarthroplasty reconstruction for chronic osteomyelitis of the distal humerus. *J Reconstr Microsurg*. 2006;22(3):167-171.
32. Chhabra AB, Golish SR, Pannunzio ME, Butler TE Jr, Bolano LE, Pederson WC. Treatment of chronic nonunions of the humerus with free vascularized fibula transfer: a report of thirteen cases. *J Reconstr Microsurg*. 2009;25(2):117-124.
33. Chew WY, Low CK, Tan SK. Long-term results of free vascularized fibular graft. A clinical and radiographic evaluation. *Clin Orthop*. 1995;(311):258-261.
34. de Boer HH, Wood MB, Hermans J. Reconstruction of large skeletal defects by vascularized fibula transfer. Factors that influenced the outcome of union in 62 cases. *Int Orthop*. 1990;14(2):121-128.
35. Jupiter JB, Kour AK. Reconstruction of the humerus by soft tissue distraction and vascularized fibula transfer. *J Hand Surg Am*. 1991;16(5):940-943.
36. Mattar Júnior J, Azze RJ, Ferreira MC, Starck R, Canedo AC. Vascularized fibular graft for management of severe osteomyelitis of the upper extremity. *Microsurgery*. 1994;15(1):22-27.
37. Yajima H, Tamai S, Mizumoto S, Inada Y. Vascularized fibular grafts in the treatment of osteomyelitis and infected nonunion. *Clin Orthop*. 1993;(293):256-264.