ETHANOL AS A LOCAL ADJUVANT FOR GIANT CELL TUMOR OF BONE

Kevin B. Jones, M.D.[1], Barry R. DeYoung, M.D.[1,2], Jose A. Morcuende, M.D., Ph.D.[1], Joseph A. Buckwalter, M.D., M.S.[1]

ABSTRACT

Giant cell tumor is an aggressive benign neoplasm of bone. A number of adjuvant agents have been used to supplement intralesional curettage to reduce the otherwise high local recurrence rate. High concentration ethanol is more readily available and less toxic to use than some common alternatives. No report on its use in a group of patients with giant cell tumor is available. Records were retrospectively reviewed for all giant cell tumors treated by intralesional curettage and high concentration ethanol irrigation as the only chemical adjuvant. Twenty-five primary excisional curettages and 12 repeat curettages for giant cell tumors of bone were performed in 31 patients. Patients were followed for a mean of three years and 10 months. There were five recurrences after primary excision procedures, and three after repeat excisions. Only use of a high-speed burr and lower Campanacci staging correlated with reduced recurrence rate, and these were not statistically significant. Most defects were filled with allograft or calcium sulfate. In the 11 patients treated primarily with curettage using a high-speed burr and adjuvant ethanol with minimum two-year follow-up, only one stage 3 lesion in a distal radius recurred. Multiple washes with high concentration ethanol, when used in conjunction with aggressive curettage including high-speed burring, is an effective and safe adjuvant. The necessity of any chemical adjuvant after appropriately aggressive curettage and burring can only be definitively demonstrated with a prospective, randomized, multi-center trial. Until such evidence becomes available, the use of adjuvant ethanol offers a compromise between higher toxicity adjuvants and no chemical adjuvant at all.

[1]Department of Orthopaedics and Rehabilitation
University of Iowa Hospitals and Clinics
Iowa City, Iowa, USA

[2]Department of Pathology
University of Iowa Hospitals and Clinics
Iowa City, Iowa, USA

Correspondence:
Kevin B. Jones, M.D.
Department of Orthopaedics and Rehabilitation
University of Iowa Hospitals and Clinics
200 Hawkins Drive, 01051 John Pappajohn Pavilion
Iowa City, IA 52242
E-mail: kevin-jones@uiowa.edu
Telephone: 319-356-2595
Facsimile: 319-356-8999

INTRODUCTION

Jaffe and colleagues offered the first thorough characterization of giant cell tumor (GCT) of bone in 1940.[1] Since then, large series of bone tumors have found GCTs to represent approximately 20 percent of all benign bone tumors and five percent of all osseous neoplasms.[2]

Giant cell tumor is a locally aggressive but usually benign neoplastic disease of bone. In the appendicular skeleton, it typically arises eccentrically in the metaphysis, but usually extends into the epiphysis, often involving the subchondral bone.

Because of its periarticular location, resection for wide oncologic margins would require complex joint reconstructions and incur significant morbidity with regard to joint function in the long term. Intralesional curettage through a broad cortical window therefore remains the treatment of choice for most GCTs of bone in most treatment centers.

Early reports of curettage alone noted high rates of local recurrence.[3-7] This prompted the use of a variety of local adjuvants, most commonly including phenol and liquid nitrogen cryotherapy. Concomitant to the use of these adjuvants are complexities and complications that some surgeons find undesirable.

For the last few years, three to four 60-second washes with 95 percent ethanol have been used at the University of Iowa as local adjuvant treatment after aggressive curettage of giant cell tumors in the appendicular skeleton. We retrospectively review this experience.

METHODS

With the permission of the Institutional Review Board, electronic pathology records were searched to identify all giant cell tumors of bone treated at the University of Iowa Hospitals and Clinics over the last 20 years. Extant medical records were reviewed. Patients were excluded if the tumor was located in the axial skeleton or if adjuvant ethanol was not used during intralesional curettage. For the included patients, basic demographic data

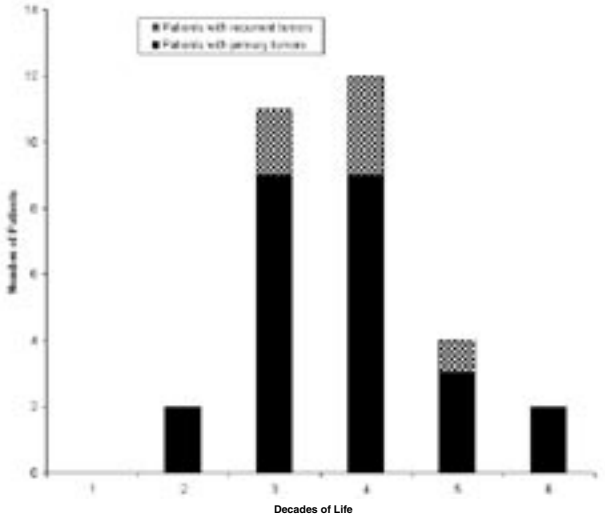

Figure 1. Distribution of ages of presentation among patients with giant cell tumor of bone treated by intralesional excisional curettage, adjuvant ethanol irrigation, and defect filling.

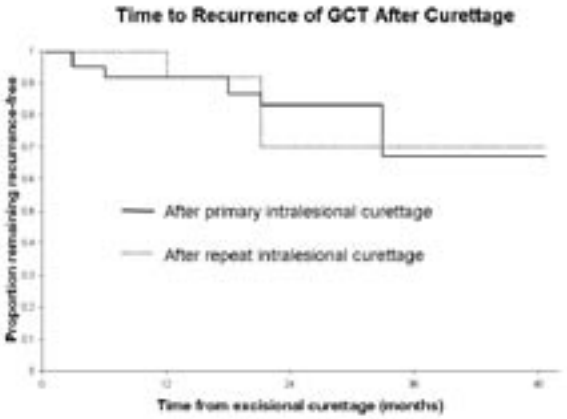

Figure 2. Kaplan-Meier plot of time to recurrence following primary intralesional excisional curettage with adjuvant ethanol for giant cell tumor of bone, and following repeat intralesional excisional curettage with adjuvant ethanol for recurrent giant cell tumor of bone, given a variable length of follow-up.

were recorded in addition to lesion location, Campanacci staging,[8] use of a high-speed burr, defect-filling material selected, perioperative complications, and details of longer-term follow-up such as recurrence and metastasis. Patients were not excluded for follow-up of less than two years, so as not to bias the study group.

With recurrence as the primary outcome, survival curves were independently generated for both primary excisions and recurrence excisions. Fisher's exact test was used to test categorical variables such as use of a high-speed burr, defect-filling agent used, and Campanacci staging for their relationships with rate of recurrence.

RESULTS

The electronic pathology records identified 87 tissue reports containing "giant cell" and "bone" since 1985. Of these, 26 were other bone lesions containing giant cells, such as aneurysmal bone cysts and giant-cell rich osteosarcomas. Sixty-one records showed giant cell tumors of bone, prompting review of additional medical records. With additional medical record information, two were incisional biopsies, one was a lung wedge resection of a benign metastasis from a GCT of bone, 12 were GCTs of the axial skeleton, six were GCT resection specimens from the appendicular skeleton, and 40 were excisional curettage specimens from appendicular skeleton GCTs. The six resections had been performed for three highly aggressive GCTs with widely displaced intra-articular fractures, two typical GCTs in expendable bones, and one highly aggressive, multiply recurrent GCT of the proximal tibia. Of the 40 excisional curettages, three did not use ethanol as an adjuvant.

The final study group included 37 excisional curettages in 31 patients. Twenty-five patients presented primarily and six presented with a recurrent GCT after previous curettage by another surgeon. Among the patients receiving primary excisional curettage, 16 were female and nine male. The average age at surgery was 31.6 years (range 19 to 58 years) (Figure 1). Among patients presenting with recurrent lesions, four were male and two female, with an average age of 32 years, (range 27 to 42 years). Patients were followed for a mean of three years and ten months.

One of the GCTs in the primary group was Campanacci stage 1, 11 were stage 2, and 10 were stage 3. Three others had associated fractures with significant displacement. For 12 of the primary excisions, a high-speed burr was used after curettage prior to ethanol irrigation. For 13 primary excisions, no burr was used. All defects were filled after lesion ablation, one with autograft, nine with allograft, nine with calcium sulfate putty or pellets, three with a mixture of allograft and calcium sulfate, and three with polymethylmethacrylate cement.

Following primary excisional curettage, five GCTs recurred (Figures 2 and 3). One tumor recurred after use of a high-speed burr and acrylic cement in addition to adjuvant ethanol. The other four recurrences followed curettage with ethanol irrigation but without the aid of a high-speed burr. No wound problems or post-operative fractures were noted following primary excisions. Two patients without recurrence had further surgery, one to replace acrylic cement with allograft and another to fill with acrylic cement an area where allograft had poorly incorporated.

Soft-tissue involvement was noted on most of the 12 repeat excisional curettages for recurrence. A high-speed

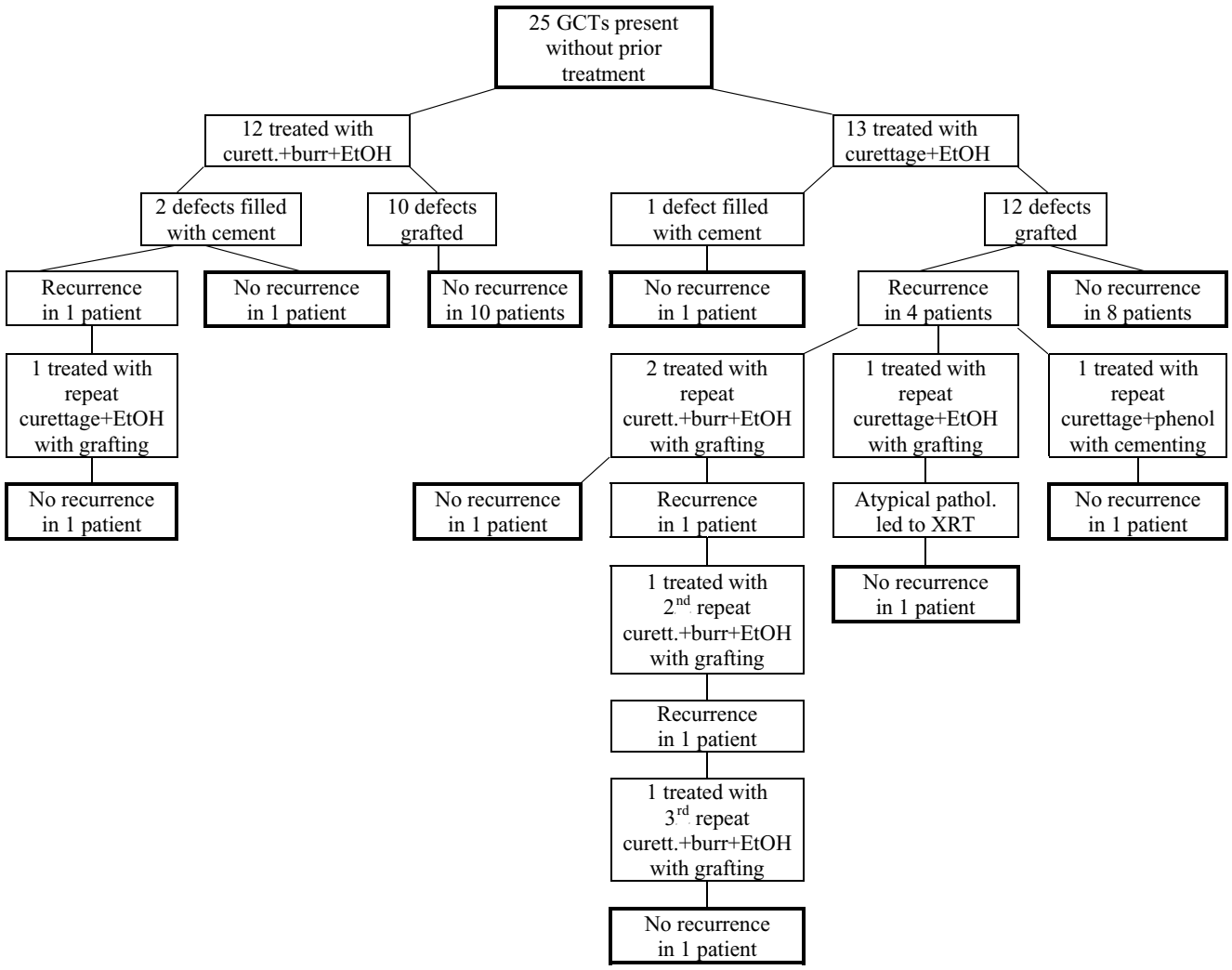

Figure 3. Treatment course and outcome at latest follow-up of patients with giant cell tumor of bone treated primarily with intralesional excisional curettage and adjuvant ethanol irrigation.

burr was used during nine of these repeat excisions, with the other three utilizing curettage alone prior to adjuvant ethanol. Defects were filled with allograft in two cases, calcium sulfate in two cases, a mix of allograft and calcium sulfate in four cases, and polymethylmethacrylate in four cases. One of the patients had moderate atypia noted histologically in his recurrent tumor. He was treated with adjuvant external beam irradiation after a brief delay for early graft incorporation (Figure 5).

Three recurrences followed these 12 repeat excisional curettages (Figures 2, 3, and 4), two in a single patient (Figure 6). The other re-recurrence was also associated with benign pulmonary metastases. These metastases were wedge-resected and the recurrent bone lesion was widely resected prior to endoprosthetic reconstruction.

Two patients without recurrences had noteworthy complications after repeat excisional curettage. One patient sustained an intra-articular fracture around the cemented defect, which was treated conservatively, but led to significant osteoarthritis 12 years later. Another patient had persistent wound drainage, which was treated with graft removal, antibiotics, and delayed re-grafting. Whether this represented a low-grade infection or the wound drainage occasionally associated with calcium sulfate filling of non-contained bone defects[9] was never concluded, but all cultures were negative.

Fisher's exact test noted statistically insignificant trends toward use of a high-speed burr associating with lower recurrence rate ($p = 0.16$), and higher Campanacci stage associating with a higher recurrence rate ($p = 0.32$) for primary excisions. Defect filling material did not appreciably correlate with recurrence rate.

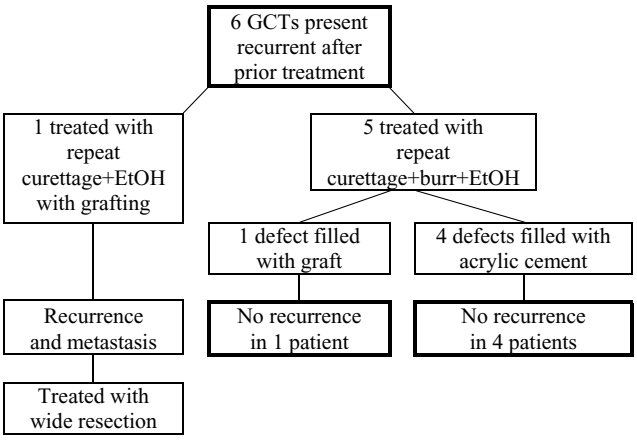

Figure 4. Treatment course and outcome at latest follow-up of patients with recurrent giant cell tumor of bone treated with repeat intralesional excisional curettage and adjuvant ethanol irrigation.

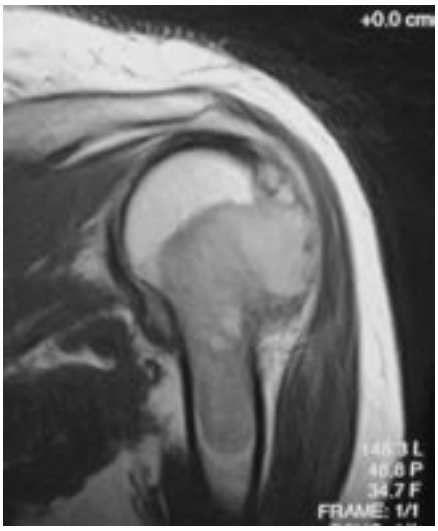

Figure 5A

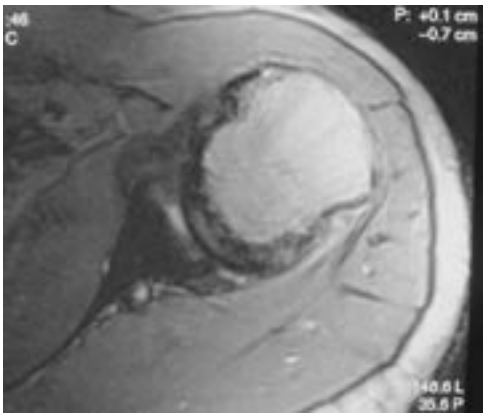

Figure 5B

Figure 5. Magnetic resonance images (A and B) demonstrating the presentation of a Campanacci stage 3 giant cell tumor of the proximal humerus in a 32-year-old male. Four months after curettage, ethanol irrigation, and grafting, this lesion recurred. Histopathology from excisional curettage of the recurrence was atypical, prompting postoperative external-beam radiation therapy.

DISCUSSION

Early reports of intralesional curettage for GCTs of bone noted recurrence rates ranging greater than 50 percent.[4-7] As recurrence can make joint-preserving strategies much more difficult, such frequent recurrence is to be avoided if possible.

A number of different techniques (Table 1) and chemical agents have been used as adjuvants to intralesional curettage of benign aggressive bone tumors such as GCT. These have included the use of a high speed burr, painting or irrigating with phenol,[3,6,10-16] cryotherapy with liquid nitrogen,[17-19] irrigation with hydrogen peroxide,[20] irrigation with aqueous zinc chloride,[21] thermal cautery with a carbon dioxide laser,[22] defect filling with polymethylmethacrylate (for its heating properties),[3,11,12,23-26] and the use of defect-filling agents that elute methotrexate[27] or adriamycin.[28]

Most surgeons agree that aggressive curettage through a sufficiently wide cortical window for visibility is of paramount importance. Typically, a high-speed burr is used to extend the intralesional margins after removal of the gross tumor. Some authors argue that these more aggressive excision techniques are sufficient to achieve an acceptably low frequency of recurrence, ranging from 0 to 19 percent.[29-33] These authors argue that benefits attributed to chemical adjuvants may stem from their association with more recent curettage and burr techniques.

Of chemical techniques, adjuvant phenolization and cryotherapy have surfaced as the most popular. Phenol, which has been shown to be cytotoxic to GCT cells in vitro,[34] has been associated with favorable results ranging from six to 18 percent recurrence rates in recent series.[10,11,14,15] While some data exist to confirm low systemic toxicity from the use of phenol as a local adjuvant,[35] it is a caustic substance and must be handled carefully with respect to the patient's adjacent tissues and operating suite personnel. Cryotherapy with liquid nitrogen also results in reportedly low recurrence rates, but has associated risks of fracture and skin necrosis.[17,18]

We are unaware of any previous reports of the use of ethanol irrigation as an adjuvant to intralesional curettage for GCT of bone. High concentration ethanol is readily available in most surgical suites and relatively safe to use. The cytotoxicity from ethanol does not likely extend deeply into surrounding bone, but its adverse effects on adjacent tissues are also minimal.

Overall, the recurrence rate after the use of adjuvant ethanol is not widely different from the use of other adjuvants for GCT of bone. This series does reiterate the argument for the use of a high-speed burr, regard-

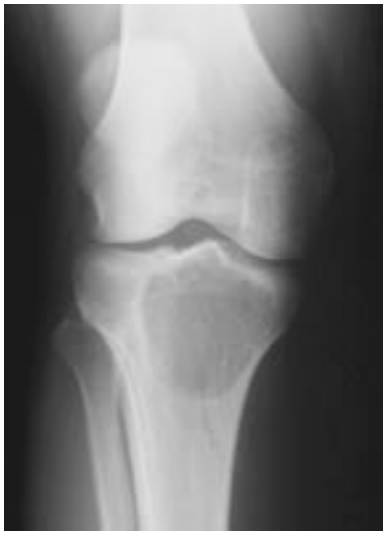

Figure 6A

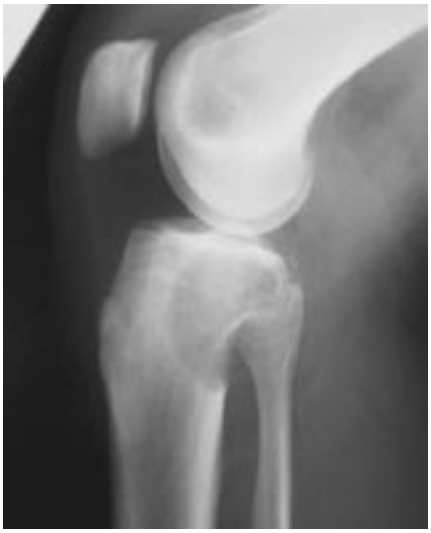

Figure 6B

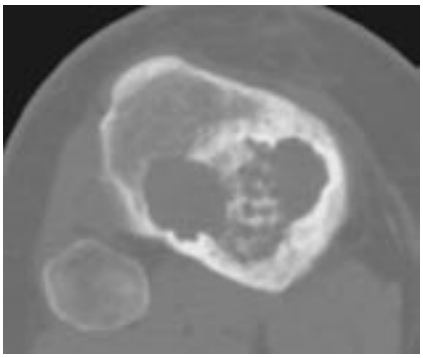

Figure 6C

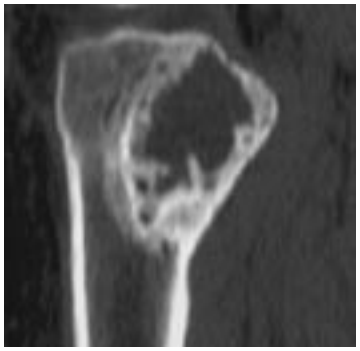

Figure 6D

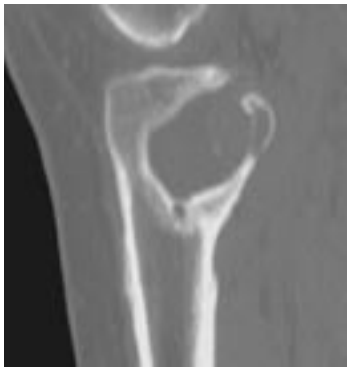

Figure 6E

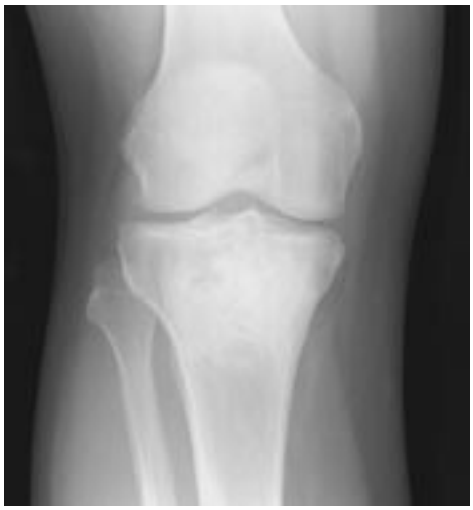

Figure 6F

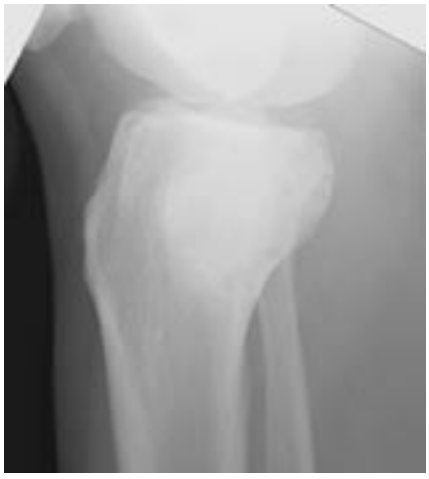

Figure 6G

Figure 6. Images representing the clinical course of a 22-year-old male who presented with this Campanacci stage 3 giant cell tumor of bone (A and B). After curettage, ethanol irrigation, and grafting, it recurred (C). After repeat curettage, high-speed burring, ethanol irrigation, and grafting, it recurred two more times (D and E, respectively). Plain radiographs obtained 15 months after a fourth intralesional excisional curettage with high-speed burring, ethanol irrigation, and calcium sulfate grafting show no recurrence (F and G).

TABLE 1
Recurrence rates reported after curettage of giant cell tumors of bone

Author	Year	Tumor Characteristics	Adjuvant Treatments	Number of Patients	Recurrence Rate
Capanna et al.[3]	1990		none	280	45%
Shih et al.[33]	1998		none*	22	0%
Richardson et al.[32]	1998		none	16	0%
Blackley et al.[29]	1999		none	59	12%
Durr et al.[10]	1999		none	7	43%
Saglik et al.[41]	1999		none	21	33%
Trieb et al.[16]	2001		none	14	21%
Turcotte et al.[40]	2002		none	~50	17%
Khan et al.[30]	2004	distal radius only	none	23	17%
Prosser et al.[31]	2005	stage 1 &2	none	61	7%
		stage 3	none	52	29%
		recurrent	none	29	34%
Capanna et al.[3]	1990		PMMA	187	19%
O'Donnell et al.[12]	1994		PMMA	49	24%
Bini et al.[23]	1995		PMMA	38	8%
Saglik et al.[41]	1999		PMMA	6	0%
Wada et al.[42]	2002		PMMA	15	7%
Turcotte et al.[40]	2002		PMMA	62	19%
McDonald et al.[5]	1986		phenol	80	34%
Capanna et al.[3]	1990		phenol	147	19%
Durr et al.[10]	1999		phenol	11	9%
Trieb et al.[16]	2001		phenol	12	25%
Turcotte et al.[40]	2002		phenol	37	19%
Su et al.[15]	2004		phenol	56	18%
Capanna et al.[3]	1990		cryotherapy	20	19%
Sheth et al.[19]	1995	distal radius only	cryotherapy	12	25%
Malawer et al.[17]	1999	primary	cryotherapy	86	2.3%
		recurrent	cryotherapy	16	37.5%
Turcotte et al.[40]	2002		cryotherapy	10	0%
Zhen et al.[21]	2004		Zinc Chloride	92	13%
Capanna et al.[3]	1990		phenol+PMMA	33	3%
Ghert et al.[43]	2002		phenol+PMMA	47	13%
Lackman et al.[11]	2005	stage 2 & 3 only	phenol+PMMA	63	6%
O'Donnell et al.[12]	1994		phenol+PMMA	11	27%
Saiz et al. [14]	2004		phenol+PMMA	40	13%
Ward and Li[20]	2002		H_2O_2+phenol+ electrocautery+ PMMA (in half)	24	8%

PMMA = polymethylmethacrylate cement.
* "none" may include the use of a high speed burr, which some authors consider an adjuvant.

less of the chemical adjuvant selected. While numbers were too small to reach statistical significance, of the 12 primary intralesional curettages that utilized a high-speed burr and adjuvant ethanol, only one led to lesion recurrence. Only one of the 12 patients was followed for less than two years.

A number of factors must be considered in comparing different series of GCT patients for rates of recurrence. While histologic grading (other than malignancy) is not predictive of recurrence in GCT of bone,[36] Campanacci staging is considered to be important, as stage 3 lesions, or those that have breached the cortex and involved the adjacent soft tissues, have a higher recurrence rate in series that distinguish them from lower stage lesions.[31] Unfortunately, not all series distinguish them. Many others have skewed numbers due to the institutional practice of treating most stage 3 GCTs with wide resection rather than intralesional curettage. Our series had more recurrences after stage 3 primary lesions (three of 10) than after stage 2 lesions (two of 11), but the difference did not reach statistical significance.

Others have noted preoperative fractures as a major risk for recurrence.[37] Three patients in the study group had preoperative fractures with significant displacement but none had a recurrence of their tumor.

Location can also play a role in prognosis, with the distal radius being a location notorious for more rampant soft tissue involvement and frequent recurrence.[12,19,30,38,39] Only one of the four distal radius GCTs in this series recurred. However, notably, it was the only recurrence after use of a high-speed burr and adjuvant ethanol.

Treatment of recurrent lesions with repeat intralesional curettage is debated by some practitioners who believe that GCT recurrence merits wide excision. Rates of re-recurrence after repeat intralesional curettage range between 30 and 40 percent among the varied techniques reported.[5,17,19,31,40] The three re-recurrences of 12 repeat intralesional curettages represent a respectable local control rate with the use of ethanol as an adjuvant. The contribution of the use of acrylic cement as the filling material more frequently in these repeat surgeries is difficult to isolate given the small numbers.

In conclusion, we feel that high concentration ethanol is an effective and safe adjuvant for the treatment of GCT when used in conjunction with aggressive curettage including high-speed burring. Whether any chemical adjuvant is necessary after performance of an appropriately aggressive curettage can probably only be answered definitively with a prospective, randomized comparison including many centers. Until such evidence becomes available, we feel that the use of ethanol is a safe compromise between higher-toxicity adjuvants and no adjuvant at all.

REFERENCES

1. **Jaffe HL, Lichtenstein L, and Portis RB.** Giant cell tumor of bone: its pathologic appearance, grading, supposed variants, and treatment. *Arch Pathol* 30: 993-1031, 1940.
2. **Dahlin DC.** Caldwell Lecture. Giant cell tumor of bone: highlights of 407 cases. *Am J Roentgenol* 144(5): 955-60, 1985.
3. **Capanna R, Fabbri N, and Bettelli G.** Curettage of giant cell tumor of bone. The effect of surgical technique and adjuvants on local recurrence rate. *Chir Organi Mov* 75(1 Suppl): 206, 1990.
4. **Goldenberg RR, Campbell CJ, and Bonfiglio M.** Giant-cell tumor of bone. An analysis of two hundred and eighteen cases. *J Bone Joint Surg Am* 52(4): 619-64, 1970.
5. **McDonald DJ, Sim FH, McLeod RA, and Dahlin DC.** Giant-cell tumor of bone. *J Bone Joint Surg Am* 68(2): 235-42, 1986.
6. **Oda Y, Miura H, Tsuneyoshi M, and Iwamoto Y.** Giant cell tumor of bone: oncological and functional results of long-term follow-up. *Jpn J Clin Oncol* 28(5): 323-8, 1998.
7. **Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, and Li SM.** Giant-cell tumor of bone: analysis of two hundred and eight cases in Chinese patients. *J Bone Joint Surg Am* 64(5): 755-61, 1982.
8. **Campanacci M, Capanna R, Fabbri N, and Bettelli G.** Curettage of giant cell tumor of bone. Reconstruction with subchondral grafts and cement. *Chir Organi Mov* 75(1 Suppl): 212-3, 1990.
9. **Lee GH, Khoury JG, Bell JE, and Buckwalter JA.** Adverse reactions to OsteoSet bone graft substitute, the incidence in a consecutive series. *Iowa Orthop J* 22: 35-8, 2002.
10. **Durr HR, Maier M, Jansson V, Baur A, and Refior HJ.** Phenol as an adjuvant for local control in the treatment of giant cell tumour of the bone. *Eur J Surg Oncol* 25(6): 610-8, 1999.
11. **Lackman RD, Hosalkar HS, Ogilvie CM, Torbert JT, and Fox EJ.** Intralesional curettage for grades II and III giant cell tumors of bone. *Clin Orthop Relat Res* 438: 123-7, 2005.
12. **O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, and Mankin HJ.** Recurrence of giant-cell tumors of the long bones after curettage and packing with cement. *J Bone Joint Surg Am* 76(12): 1827-33, 1994.
13. **Picci P, Manfrini M, Zucchi V, Gherlinzoni F, Rock M, Bertoni F, and Neff JR.** Giant-cell tumor of bone in skeletally immature patients. *J Bone Joint Surg Am* 65(4): 486-90, 1983.
14. **Saiz P, Virkus W, Piasecki P, Templeton A, Shott S, and Gitelis S.** Results of giant cell tumor of bone treated with intralesional excision. *Clin Orthop Relat Res* (424): 221-6, 2004.
15. **Su YP, Chen WM, and Chen TH.** Giant-cell tumors of bone: an analysis of 87 cases. *Int Orthop* 28(4): 239-43, 2004.
16. **Trieb K, Bitzan P, Lang S, Dominkus M, and Kotz R.** Recurrence of curetted and bone-grafted giant-cell tumours with and without adjuvant phenol therapy. *Eur J Surg Oncol* 27(2): 200-2, 2001.
17. **Malawer MM, Bickels J, Meller I, Buch RG, Henshaw RM, and Kollender Y.** Cryosurgery in the treatment of giant cell tumor. A long-term followup study. *Clin Orthop Relat Res* (359): 176-88, 1999.
18. **Marcove RC, Weis LD, Vaghaiwalla MR, Pearson R, and Huvos AG.** Cryosurgery in the treatment of giant cell tumors of bone. A report of 52 consecutive cases. *Cancer* 41(3): 957-69, 1978.

19. **Sheth DS, Healey JH, Sobel M, Lane JM, and Marcove RC.** Giant cell tumor of the distal radius. *J Hand Surg [Am]* 20(3): 432-40, 1995.
20. **Ward WG Sr., and Li G III.** Customized treatment algorithm for giant cell tumor of bone: report of a series. *Clin Orthop Relat Res* (397): 259-70, 2002.
21. **Zhen W, Yaotian H, Songjian L, Ge L, and Qingliang W.** Giant-cell tumour of bone. The long-term results of treatment by curettage and bone graft. *J Bone Joint Surg Br* 86(2): 212-6, 2004.
22. **Kenan S, Kirby EJ, Buchalter J, and Lewis MM.** The potential role of the laser in marginal sterilization of giant cell tumor following curettage. *Bull Hosp Jt Dis Orthop Inst* 48(1): 93-101, 1988.
23. **Bini SA, Gill K, and Johnston JO.** Giant cell tumor of bone. Curettage and cement reconstruction. *Clin Orthop Relat Res* (321): 245-50, 1995.
24. **Liu HS, and Wang JW.** Treatment of giant cell tumor of bone: a comparison of local curettage and wide resection. *Changgeng Yi Xue Za Zhi* 21(1): 37-43, 1998.
25. **Persson BM, Ekelund L, Lovdahl R, and Gunterberg B.** Favourable results of acrylic cementation for giant cell tumors. *Acta Orthop Scand* 55(2): 209-14, 1984.
26. **Rock M.** Curettage of giant cell tumor of bone. Factors influencing local recurrences and metastasis. *Chir Organi Mov* 75(1 Suppl): 204-5, 1990.
27. **Kirchen ME, Menendez LR, Lee JH, and Marshall GJ.** Methotrexate eluted from bone cement: effect on giant cell tumor of bone in vitro. *Clin Orthop Relat Res* (328): 294-303, 1996.
28. **Zhang Y, Hou C, and Chen A.** [A preliminary clinical observation of giant cell tumor of bone treated by adriamycin-loaded chitosan drug delivery system]. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 12(5): 280-2, 1998.
29. **Blackley HR, Wunder JS, Davis AM, White LM, Kandel R, and Bell RS.** Treatment of giant-cell tumors of long bones with curettage and bone-grafting. *J Bone Joint Surg Am* 81(6): 811-20, 1999.
30. **Khan MT, Gray JM, Carter SR, Grimer RJ, and Tillman RM.** Management of the giant-cell tumours of the distal radius. *Ann R Coll Surg Engl* 86(1): 18-24, 2004.
31. **Prosser GH, Baloch KG, Tillman RM, Carter SR, and Grimer RJ.** Does curettage without adjuvant therapy provide low recurrence rates in giant-cell tumors of bone? *Clin Orthop Relat Res* (435): 211-8, 2005.
32. **Richardson MJ, and Dickinson IC.** Giant cell tumor of bone. *Bull Hosp Jt Dis* 57(1): 6-10, 1998.
33. **Shih HN, Hsu RW, and Sim FH.** Excision curettage and allografting of giant cell tumor. *World J Surg* 22(5): 432-7, 1998.
34. **Quint U, Vanhofer U, Harstrick A, and Muller RT.** Cytotoxicity of phenol to musculoskeletal tumours. *J Bone Joint Surg Br* 78(6): 984-5, 1996.
35. **Quint U, Muller RT, and Muller G.** Characteristics of phenol. Instillation in intralesional tumor excision of chondroblastoma, osteoclastoma and enchondroma. *Arch Orthop Trauma Surg* 117(1-2): 43-6, 1998.
36. **Sanerkin NG.** Malignancy, aggressiveness, and recurrence in giant cell tumor of bone. *Cancer* 46(7): 1641-9, 1980.
37. **Dreinhofer KE, Rydholm A, Bauer HC, and Kreicbergs A.** Giant-cell tumours with fracture at diagnosis. Curettage and acrylic cementing in ten cases. *J Bone Joint Surg Br* 77(2): 189-93, 1995.
38. **Cheng CY, Shih HN, Hsu KY, and Hsu RW.** Treatment of giant cell tumor of the distal radius. *Clin Orthop Relat Res* (383): 221-8, 2001.
39. **Harness NG, and Mankin HJ.** Giant-cell tumor of the distal forearm. *J Hand Surg [Am]* 29(2): 188-93, 2004.
40. **Turcotte RE, Wunder JS, Isler MH, Bell RS, Schachar N, Masri BA, Moreau G, and Davis AM.** Giant cell tumor of long bone: a Canadian Sarcoma Group study. *Clin Orthop Relat Res* (397): 248-58, 2002.
41. **Saglik Y, Yildiz Y, Karakas A, Ogut H, and Erekul S.** Giant cell tumor of bone. *Bull Hosp Jt Dis* 58(2): 98-104, 1999.
42. **Wada T, Kaya M, Nagoya S, Kawaguchi S, Isu K, Yamashita T, Yamawaki S, and Ishii S.** Complications associated with bone cementing for the treatment of giant cell tumors of bone. *J Orthop Sci* 7(2): 194-8, 2002.
43. **Ghert MA, Rizzo M, Harrelson JM, and Scully SP.** Giant-cell tumor of the appendicular skeleton. *Clin Orthop Relat Res* (400): 201-10, 2002.