Management of solid ameloblastoma of the jaws with liquid nitrogen spray cryosurgery

Marcos Martins Curi, DDS,[a] Luciano Lauria Dib, DDS, PhD,[b] Décio Santos Pinto, DDS, PhD[c]
A. C. CAMARGO HOSPITAL, SÃO PAULO, BRAZIL

Objective. This study evaluated the results of the use of curettage followed by liquid nitrogen spray cryosurgery in a number of solid or multicystic ameloblastomas of the jaws and the postoperative complications related to this treatment modality.
Study design. Thirty-six patients with solid ameloblastoma of the jaws were treated with curettage followed by cryosurgery. The cryotherapy consisted of hand instrumented curettage of the bone lesion followed by three freezing cycles, of 1 minute each, of the remaining bone cavity with liquid nitrogen spray. Postoperative complications were evaluated clinically and radiographically.
Results. Local recurrence occurred in 11 (30.6%) patients. Excepting local recurrence, postoperative complications were frequent but not severe: wound dehiscence (5.5%), paraesthesia (5.5%), infection (5.5%), and pathologic fracture (11.1%).
Conclusion. Management of solid or multicystic ameloblastomas of the jaws with curettage followed by cryosurgery may decrease the local recurrence rate and also to reduce the initial indication of resection with continuity defect. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;84:339-44)**

Ameloblastoma is an odontogenic epithelial tumor that accounts for approximately 10% of odontogenic tumors and 1% of all tumors and cysts of the jaws.[1] Its etiology, clinical behavior, histologic patterns, and treatment modalities have been extensively discussed in the literature.[2-5]

Clinically, ameloblastoma is characterized by slow growth, painless swelling, and expansion of the involved bone, leading to great facial deformity and a delayed diagnosis. This lesion occurs more commonly in the mandible, mainly in molar and angle-ramus regions, and less often in the maxilla. The origin of ameloblastoma is still controversial, but recently the dental lamina has been accepted more than the enamel organ, epithelial rests, basal cells of the surface epithelium, or epithelium of odontogenic cysts.[4] Until the study by Eversole et al.,[6] ameloblastomas were classified according to histologic findings into follicular, plexiform, acanthomatous, granular cell, basal cell, squamous metaplastic, and other rare types. In recent years, the literature has divided clinical ameloblastomas into unicystic, multicystic or solid, peripheral, and malignant subtypes.[7-23]

Unicystic ameloblastoma is defined as a cystic lesion with intramural or intraluminal epithelial proliferation with ameloblastic microscopic features. It occurs most often in the mandible during the third decade of life and seems to have a less aggressive clinical behavior and better prognosis than the solid ameloblastoma. Conservative treatment, such as enucleation and curettage, seems to be effective and sufficient.[7-10] Peripheral ameloblastoma is the soft tissue counterpart of intraosseous ameloblastoma and is a relatively rare lesion. Malignant ameloblastoma is also rare, but the term has been used to define ameloblastoma that leads to metastasis keeping the same histologic features of the primary lesion. Few reports are available about peripheral and malignant ameloblastomas; additional investigations and follow-up are necessary.[17,20,21]

Treatment modalities for ameloblastoma have been divided into conservative and radical therapies.[3-5] Because of its slow growth and tendency to local invasion of bone and soft tissue, high rates of recurrence are common if the tumor is not adequately treated. Metastases are rarely observed. Some authors have treated ameloblastoma with exclusive radiation therapy or in combination with chemotherapy.[22,23] Conservative approach, such as enucleation and curettage, has shown a high recurrence rate of 90% in the mandible and 100% in the maxilla.[2] Radical approach consists of partial and total maxillectomy or resections, with or without continuity defect in the mandible. This type of treatment has decreased the recurrence rate of ameloblastoma but has created severe and serious cosmetic, functional, and reconstructive problems.

Cryosurgery has been an alternative treatment modality for ameloblastoma and other locally invasive odontogenic bone lesions.[24-34] Since the first experimental and clinical studies, this therapy has provided excellent results in the maxillofacial region.[24,25,31-34] The aim of cryosurgery is to eliminate the invasive bone lesion without necessarily involving the problems of conventional anatomic radical surgery. Therefore the use of extreme cold temperature to manage ameloblastomas

[a]Assistant Professor, Department of Stomatology.
[b]Chairman, Department of Stomatology.
[c]Department of Stomatology.
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permits treatment of the bone in situ by devitalizing it and maintaining its inorganic matrix.

There are four basic cryosurgery methods for use in the maxillofacial region: probe alone, probe plus water-soluble jelly, liquid nitrogen coil, and liquid nitrogen spray. Each technique has advantages and disadvantages when applied to bone lesions of the jaws. However, probe plus water jelly and liquid nitrogen spray have been the most common freezing methods applied to bone lesions of the jaws. Liquid nitrogen spray is a potent and rapid freezing method that reaches a temperature of –198° C within a few minutes. It can be used to treat large and irregular cavities in the jaws, but care must be taken to avoid necrosis of the surrounding soft tissue. In 1984, Whittaker[35] proposed that the mechanism of tissue necrosis after cryosurgery is a combination of extracellular and intracellular ice crystal formation, resulting in a direct cell injury as well as osmotic and electrolyte disturbances across the cell membrane.

Postoperative complications of cryosurgery in bone, such as sequestrum formation, pathologic fracture, dehiscence, and edema, have been reported.[24,33,34] Pathologic fracture and sequestration after cryosurgery have been prevented with the use of autogenous cancellous bone graft of the bone cavity.[32]

Because of the insufficient information available in the literature concerning the use of cryosurgery in the management of ameloblastomas, the objective of the present study was to evaluate the results of this technique in a number of solid or multicystic ameloblastomas of the jaws and to discuss the complications related to the use of this treatment modality.

MATERIAL AND METHOD

A retrospective study was conducted on 36 patients treated for ameloblastoma of the jaws with curettage associated with liquid nitrogen spray cryosurgery at the Department of Stomatology, A. C. Camargo Hospital, São Paulo, Brazil, over a 20-year period from 1975 to 1995. All cases were reviewed and histologically confirmed to be solid ameloblastomas according to the WHO histological criteria for diagnosis. Radiographic examination included panoramic x-ray and occlusal and periapical films. Computed tomography and ultrasonography examinations were routinely used as complementary examination.

The cryosurgery technique performed in all cases was based on the use of a LINDE E-8 (Union Carbide, Brymill Corporation) cryosurgery equipment. The cryotherapy consisted of hand instrumented curettage of the bone lesion followed by freezing of the remaining bone cavity with liquid nitrogen spray. The surrounding soft tissues were retracted and protected away from the freezing treated area with gauze and flap retractors. The entire bone cavity was then frozen with liquid nitrogen spray until a solid frost could be observed over the entire bone cavity bed. Three freezing cycles of 1 minute each were applied with a slow thawing interval (5 minutes) between cycles. Mucoperiosteal flaps were sutured to obtain primary union and eversion of flap margins. Antibiotics and corticosteroids were frequently prescribed during the postoperative period.

Postoperative follow-up consisted of visits every 3 months during the first year, every 6 months during the second year, and once a year thereafter. The same radiographic examination used preoperatively was performed during each follow-up. Computed tomography was performed only in doubtful cases of recurrence versus bone repair. Postoperative cryosurgery complications were recorded in the patient medical records.

RESULTS

The study group included 36 patients with ameloblastoma of the jaws treated with curettage followed by liquid nitrogen spray cryosurgery. Women (18 patients, 50%) and men (18 patients, 50%) were equally affected. Mean patient age at the time of diagnosis was 31.0 years. Ameloblastoma occurred over a wide age range, with the youngest patient being 12 years old and the oldest 70 years old. The tumor affected 33.4% patients during the third decade of life and 36.1% through the fourth to fifth decades. All 36 patients were submitted to clinical and radiographic follow-up, with a mean observation period of 62 months (5 years), ranging from 14 months to more than 18 years.

Ameloblastoma occurred in the mandible in 34 cases (94.4%) and in the maxilla in 2 cases (5.6%). Of the total number of mandibular ameloblastomas, 30 cases (83.3%) were located in the posterior area (bicuspid to condyle) and 4 (11.1%) were located in the anterior area (cuspid to cuspid). The two cases found in the maxilla occurred in the posterior region.

Local recurrences occurred in 11 (30.6%) patients, with the earliest recurrence occurring within 14 months and the latest within 10 years after initial treatment. All recurrences were located in the mandible. Of these 11 patients, 9 were retreated with curettage followed by cryosurgery, and 2 were retreated by resection with continuity defect. Three (8.3%) patients retreated by curettage followed by cryosurgery had a second recurrence and underwent resection with continuity defect. Data about the treatment of ameloblastomas in the study are summarized in Table I.

Postoperative complications were divided into minor and severe. Local recurrence was the most severe postoperative complication and occurred in 11 patients (30.6%). Pathologic fracture was also a severe postop-

Table I. Treatment of ameloblastomas in 36 patients

Patient	*Age/Sex*	*Site*	*Treatment*	*Recurrence*	*Complications*	*Follow-Up (months)*
01	48/F	Posterior mandible	Curettage/Cryosurgery	Yes	Fracture	220
02	15/M	Maxilla	Curettage/Cryosurgery	No	Dehiscence	151
03	33/F	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	39
04	22/M	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	158
05	24/F	Posterior mandible	Resection/Cryosurgery	No	—	101
06	23/F	Posterior mandible	Curettage/Cryosurgery	Yes	Dehiscence	81
07	12/M	Posterior mandible	Resection/Cryosurgery	Yes	Dehiscence	84
08	21/F	Posterior mandible	Resection/Cryosurgery	Yes	—	133
09	18/M	Anterior mandible	Curettage/Cryosurgery	Yes	Dehiscence	81
10	31/M	Posterior mandible	Curettage/Cryosurgery	No	Fracture	100
11	27/M	Posterior mandible	Resection/Cryosurgery	No	—	16
12	27/M	Posterior mandible	Curettage/Cryosurgery	Yes	Infection	82
13	21/F	Posterior mandible	Curettage/Cryosurgery	Yes	Dehiscence	95
14	35/F	Posterior mandible	Curettage/Cryosurgery	Yes	—	84
15	26/F	Posterior mandible	Resection/Cryosurgery	No	—	43
16	22/M	Posterior mandible	Curettage/Cryosurgery	Yes	—	68
17	27/F	Posterior mandible	Curettage/Cryosurgery	Yes	—	76
18	35/F	Posterior mandible	Curettage/Cryosurgery	Yes	Dehiscence	43
19	40/M	Posterior mandible	Curettage/Cryosurgery	No	—	25
20	48/M	Posterior mandible	Curettage/Cryosurgery	No	Fracture	20
21	36/M	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	58
22	31/F	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	61
23	70/M	Anterior mandible	Curettage/Cryosurgery	No	—	15
24	50/F	Posterior mandible	Curettage/Cryosurgery	No	Infection	45
25	65/M	Posterior mandible	Curettage/Cryosurgery	No	Fracture	43
26	27/M	Posterior mandible	Curettage/Cryosurgery	No	Paraesthesia	47
27	34/F	Posterior mandible	Curettage/Cryosurgery	No	—	38
28	17/M	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	41
29	23/M	Posterior mandible	Curettage/Cryosurgery	No	—	36
30	40/F	Maxilla	Curettage/Cryosurgery	No	—	30
31	32/F	Posterior mandible	Curettage/Cryosurgery	No	—	20
32	16/M	Anterior mandible	Curettage/Cryosurgery	No	Dehiscence	24
33	19/M	Posterior mandible	Curettage/Cryosurgery	No	Dehiscence	21
34	33/F	Posterior mandible	Curettage/Cryosurgery	No	—	21
35	34/M	Anterior mandible	Curettage/Cryosurgery	No	—	15
36	25/F	Posterior mandible	Curettage/Cryosurgery	No	Paresthesia	20

erative complication and occurred in four patients (11.1%) 6, 8, 16, and 24 weeks after cryosurgery. Wound dehiscence was the most common minor postoperative complication and occurred in 13 (36.1%) patients. It frequently developed during the first 10 days after cryosurgery. Because of wound dehiscence, two (5.5%) patients had infection of the bone cavity. Paraesthesia of the inferior alveolar nerve was observed in two patients (5.5%).

DISCUSSION

Ameloblastoma is a benign odontogenic tumor and represents 1% of all the cysts and tumors of the jaws.[1] Despite its benign histologic appearance, ameloblastoma is a locally aggressive and invasive tumor with great propensity for recurrence if not adequately treated. In large studies, ameloblastomas located in the mandible and maxilla account for 80% and 20% of all cases reported, respectively.[2] Usually, this tumor is diagnosed during the fourth decade of life with no sex or race preference. Our study shows that ameloblastoma affected the mandible more than the maxilla, without sex preference, and occurred in patients with a mean age of 31.0 years at the time of diagnosis, in agreement with other studies.[2,12,15]

After an ameloblastoma is diagnosed histologically, a decision must be made about the treatment modality. Over the last decades, many types of treatment have been indicated, including conservative surgery (curettage), radical excision, radiotherapy, chemotherapy, and a combination of some of these.[2-5,15,22,23] Conservative methods have failed to control local recurrences, and radical approaches have resulted in serious functional and cosmetic maxillofacial impairment.

The currently recommended surgical management of ameloblastomas is radical therapy for solid or multiloc-

ular ameloblastomas situated in the posterior region of the mandible.[5] Radical treatment is defined as the procedure in which the ameloblastoma is resected, with a safety margin of 1 to 2 cm of "normal bone," with or without a continuity defect. Several reports agree with this concept.[4,15] In 1974, Sehdev et al.[2] analyzed 72 patients with ameloblastoma of the mandible and 20 patients with ameloblastoma of the maxilla. They concluded that the conservative approach (curettage) led to 90% recurrence of mandibular ameloblastomas and 100% recurrence of maxillary ameloblastomas. In the same study, treatment of mandibular recurrences with subsequent resection successfully controlled 80% of cases initially submitted to conservative treatment. In 1965, Shatkin and Hoffmeister[36] reported 20 cases of ameloblastoma and observed that 86% of mandibular lesions recurred after curettage compared to a 14% recurrence rate after en bloc resection. In 1985, Müller and Slootweg[11] reported 186 surgical procedures performed in 84 patients. They found a 52% rate of recurrence in patients with primary ameloblastoma treated conservatively and a 25% rate of recurrence in patients with primary tumors treated by the radical approach. In 1980, Gardner and Pecak[3] discussed the treatment of ameloblastomas based on pathologic and anatomic considerations. They agreed that solid or multilocular ameloblastomas located in the posterior region of the mandible should be treated with radical surgery. However, they did not find sufficient information in the literature with regard to the use of cryosurgery in the treatment of ameloblastoma.

Cryotherapy is not a new treatment modality for bone lesions and may play an important role in the treatment of benign locally invasive bone lesions of the jaws. It is now 30 years since the initial experimental and clinical studies were reported.[37] In 1966, Gage et al.[37] reported the histologic bone effects after cryotherapy in dog femora. In 1969, Marcove and Miller[24] treated 50 patients with primary and metastatic bone tumors by cryosurgery and recommended this method for locally destructive bone processes. In 1971, Emmings et al[26] published the first case of acanthomatous ameloblastoma treated by curettage followed by cryosurgery. In 1977, Marciani et al.[27] managed two cases of ameloblastoma (one intraosseous and the other peripheral) with curettage followed by cryosurgery and did not observe signs of recurrence. Several experimental and clinical studies were reported by Bradley et al.[25,33] and Fisher et al.[34] about the mechanism, techniques, and bone responses after cryosurgery in the maxillofacial region.

Cryotherapy as a mode of treatment for ameloblastoma and other locally aggressive bone lesions has been advocated by several authors. Webb and Brockbank[29] described a giant cell lesion and a keratocyst treated by curettage and enucleation followed by cryosurgery, respectively. In 1983, Bradley[25] reported 25 odontogenic and nonodontogenic bone lesions treated successfully by curettage or enucleation followed by cryosurgery. In contrast, Jensen et al.[30] published 25 odontogenic keratocysts treated by enucleation alone or enucleation combined with cryotherapy and found no difference in recurrence rate between the two methods. Pogrel[31] described the use of cryotherapy in 37 locally aggressive bone lesions (25 keratocysts, 8 ameloblastomas, 2 giant cell lesions, and 2 myxomas of the mandible). No signs of recurrence were observed during a mean follow-up period of 75 months.

The cryotherapy mechanism consists of eliminating abnormal cells within bone by freezing and devitalizing bone segments after the macroscopic tumor has been removed without the need for radical resection or bone grafting. The bone segments treated in situ keeps the inorganic matrix, which acts as a perfect autogenous graft. The effects of cryosurgery on bone tissues were divided into three overlapping stages: a necrotic phase, an osteogenic phase, and a remodeling phase. The initial phase takes place a few days after treatment and results in cell loss and bone tissue necrosis. The osteogenic phase occurs over several weeks during which new subperiosteal woven bone is formed, replacing the necrotic bone. The final phase takes many months and consists of remodeling the formed woven bone and replacing it with vital lamellar bone.

Four basic cryosurgery methods are used in the maxillofacial region: probe alone, probe plus water-soluble jelly, liquid nitrogen coil, and liquid nitrogen spray. Infrared thermography has been used to evaluate the freezing bone area of each cryotherapy method.[25,38] Liquid nitrogen coil has the capacity to freeze long segments of bone and to preserve the integrity of the outer cortex. However, this technique is slow and requires an extensive soft tissue dissection to adapt the tube to the bone in clinical situation as the angle of the mandible. Probe alone is a useful method for localized area of soft tissue but not the bone because of its superficial infiltration in this tissue. It is time-consuming and difficult to ensure the cryosurgery effect on bone tissue. Probe plus water-soluble jelly is a useful technique for use in irregular bony cavities because the jelly freezes rapidly and improves the adaptation of the probe to the bone, increasing its effectiveness. Care must be taken to ensure that the jelly does not flow with gravity away from the treatment zone. Liquid nitrogen spray is a potent method capable of freezing large volumes of bone rapidly and to treat irregular cavities independently of gravity.

Our study represents one of the largest series in the

literature with regard to the management of ameloblastoma with curettage combined with liquid nitrogen spray cryosurgery. Of 36 cases initially treated by curettage followed by cryosurgery, 11 (30.6%) had local recurrence. Local recurrences showed peculiar clinical and radiographic aspects in these patients. The lesions were small and well-circumscribed, unilocular, radiolucent images located in the reformed superior cortical bone of the mandible, which became sufficiently thick to support radical surgery because there was enough time for mandibular bone healing before local recurrences occurred. These lesions recurred at least 14 months after the initial treatment. Three (8.3%) patients developed a second recurrence after they had been retreated with curettage followed by cryosurgery. This study shows that management of ameloblastomas with liquid nitrogen spray cryosurgery decreased the local recurrence rate and also reduced the initial indication of segmental mandibular resection. At the time of initial treatment, all 36 patients were chosen for segmental resection because of the initial tumor size. However, only five patients underwent resection with continuity defect because of local recurrence at the end of the study. There was improvement in patient quality of life and a decreased tumor morbidity; 31 of 36 patients are free of disease and without cosmetic or functional impairment resulting from a mandibular continuity defect.

Several complications have been reported after cryosurgery therapy of bone lesions of the jaw.[24,33,34] Infection, sequestration, and pathologic fracture can appear because of a failure of adequate soft tissue cover. In the present study, postoperative complications following cryotherapy were frequent but not severe. The most common complication was wound dehiscence, with total or partial exposure of the treated bone cavity that was managed with daily irrigation with 0.12% chlorexidine or antiseptic solutions (ioditine and peroxide solutions); the mean time required for soft tissue recovery was 15 days. Extended antibiotic therapy was not necessary in these cases. Experiments in vitro and in vivo have shown that bone submitted to cryosurgery undergoes a reduction in mechanical strength, which is more critical around 8 weeks after treatment.[34] Simultaneous bone grafting has been used with the objective of reducing the risk of complications and preserving the alveolar ridge height and width.[32] None of these patients were submitted to immediate bone grafts. Four patients developed pathologic fractures during the sixth, eighth, sixteenth, and twenty-fourth week after cryosurgery. At the time of fracture diagnosis, patients were asymptomatic with stable occlusion. All fractures occurred in the angle and body regions of the mandible without bone segment displacement. All patients were managed conservatively with closed reduction and indirect skeletal fixation. Intermaxillary fixation was performed with Erich bars in combination with an acrylic resin splint. Bone healing occurred uneventfully in all cases. Two of four patients developed pathologic fractures during this period of time (sixth and eighth); however, two other patients developed late spontaneous pathologic fractures after cryosurgery (sixteenth and twenty-fourth). The most likely explanation for the late fractures was the major bone loss as a result of the original lesion size, which involved the mandibular bone from the condyle to the symphysis area. In a recent study, Salmassy and Pogrel[32] concluded that for locally aggressive lesions larger than 4.0 cm, simultaneous cancellous bone grafting following cryosurgery would decrease the risk of complications of this technique.

Table II. Recurrence rate of ameloblastomas in various studies

Study	*Number of cases*	*Treatment modality*	*Recurrence rate (%)*
Shatkin & Hoffmeister[36]	20	Bloc resection	14
		Curettage	86
Sehdev et al.[2]	32 Mandible	Curettage	90
	11 Maxilla	Curettage	100
	23 Mandible	Segmental Resection	22
Tsaknis & Nelson[13]	24 Maxilla	Curettage and excision	50
Müller & Slootweg[11]	25	Curettage	52
	20	Resection	15
Ueno et al.[12]	51 Mandible	Curettage, enucleation	60
		Resection	8,6
Pinsolle et al.[15]	41 Mandible	Curettage and resection	41

Cryosurgery has been defined as a conservative treatment for solid ameloblastoma. We agree that this lesion should be treated radically with a safety margin of "normal bone." Cryosurgery has the capacity to devitalize the bone to a depth of 1 to 2 cm.[25] Curettage associated with cryosurgery has the capacity to be a radical treatment for ameloblastoma while retaining its conservative nature from an anatomic point of view. Data have also shown that primary mandibular ameloblastomas treated by resection (with or without continuity defect) are not fully free from recurrence.[2] In our study, 11 (30.6%) patients developed local recurrences after curettage followed by cryosurgery, and three (8.3%) developed a second recurrence after they had been retreated by the same therapy. The results are encouraging when compared to other treatment modalities reported by the institutions shown in Table II. The present procedure has the ability to reduce the local recurrence rate of ameloblastomas when compared with conservative treatments and result in fewer sequelae when compared with radical surgery.

The use of liquid nitrogen spray cryosurgery for the treatment of ameloblastoma appears to decrease the recurrence rate. The tendency of ameloblastoma to recur over a 10-year period is well known, and no definitive conclusions can be drawn from short-term follow-up reports. However, many advances in cryosurgery techniques have been used by oral surgeons in recent years, possibly resulting in more predictable operative procedures with relatively limited patient morbidity. Cryosurgery treatment for ameloblastomas is indicated only if an adequate and long follow-up is possible. Results of the present study appear encouraging for the management of ameloblastoma of the jaw by a more conservative first surgical procedure even, if a second or a third surgery becomes necessary.

Dr. Leda Buazar Saba provided histologic diagnosis of all cases and Drs. Ricardo Salgado Souza and Karina de Cássia Braga Ribeiro computed and performed data analysis.

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Reprint requests:
Marcos M. Curi, DDS
Departmento de Estomatologia
Hospital A. C. Camargo
Rua Prof. Antônio Prudente, 211, Liberdade
São Paulo Brazil 01509-900