BENIGN BONE TUMORS AND TUMOR-LIKE BONE LESIONS: TREATMENT UPDATE AND NEW TRENDS

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ABSTRACT

The treatment of benign bone tumors (BBT) and tumor-like bone lesions (TBL) has observed the introduction of new drugs, such as intravenous bisphosphonates, which have ossified bone lesions caused by fibrous dysplasia. Aneurismal bone cyst has been treated with sclerosing agents by percutaneous injection, yielding good results. Adjuvants allow joint salvage, maintenance of movements and function, with low rates of recurrence. Among them, the most used ones are bone cement (PMMA), phenol, nitrogen-based cryotherapy, hydrogen peroxide, ethanol and radiotherapy. New methods of treatment include thermal ablation with radiofrequency and laser, mainly utilized for treating osteoid osteoma. Arthroscopy allows resection of benign intra-joint lesions and assists the surgery of subchondral tumors. A great advance is the utilization of synthetic bone substitutes, which are a mixture of osteoinductive growth factors and osteoconductive ceramics, and have presented comparable results to autogenous bone grafts. There is a recent trend for closed treatments, with percutaneous injection of demineralized bone matrix (DBM) and calcium sulfate. Autogenous cancellous bone graft remains as the gold standard. Vascularized fibula graft, on the other hand, incorporates faster in the treatment of large destructive lesions. Also, allogenic cortical support allows structural augmentation for aggressive tumors. Freeze-dried allografts are used to fill contained defects and as expanders of autografts. Joint endoprosthesis may be used in large destructive lesions of the distal femur, hip and shoulder.

Keywords – *Bone diseases; Bone neoplasms/surgery; Bone neoplasms /therapy; Bone neoplasms /chemotherapy; Bone neoplasms/radiotherapy*

INTRODUCTION

Benign primary bone tumors are relatively rare, which creates some difficulty for diagnosis and treatment. Tumor-like bone lesions are non-neoplastic lesions that simulate tumors. An awareness of them is important since they can be confused with bone tumors and receive excessive or inadequate treatment.

Benign bone tumors and tumor-like bone lesions occur most frequently between the ages of five to 25 years and in the areas of greatest bone growth, with about 60% of cases in the knee region. For this reason, they can cause osteoarticular deformities, fractures, limb length discrepancies, gait disturbances, sometimes with disabling sequelae.

Treatment of these lesions has undergone recent and ongoing innovations such as the use of new drugs, new types of adjuvants, synthetic bone graft substitutes, and advanced arthroscopy and radio frequency techniques.

The objective of this study was to describe the most current and emerging trends in the treatment of benign bone tumors (BBT) and tumor-like bone lesions (TLBL).

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We declare no conflict of interest in this article

TREATMENT

Medications

Some benign tumors can be treated with different types of medications. The knowledge and treatment of fibrous dysplasia have evolved much over the past ten years. Frequent recurrences after their traditional treatment of curettage and bone grafting are explained by what is now known about its genetic nature. Recently, the disease has been treated with intravenous bisphosphonate that inhibits the bone resorption mediated by osteoclasts. Initial results in fibrous dysplasia have shown a decrease in pain, the prevention of fractures, and partial radiographic resolution of lesions. Pamidronate is the most commonly used third-generation bisphosphonate and is administered by monthly intravenous infusion over a period of two to four hours. It has also been used in Paget's disease and metastatic bone disease with good results. Zoledronic acid and other bisphosphonates have anti-tumor activity and can reduce the bone tumor burden, prevent metastasis and inhibit the progression of bone lesions[1].

For the treatment of simple bone cysts, methylprednisolone acetate is the most commonly used medication for infiltration, with good results[1].

The use of fibrosing agents for the treatment of aneurysmal bone cyst (ABC) presents controversial results. Treatment with zein-alcohol solution showed high rates of local and systemic complications and has been abandoned[2]. Sclerotherapy with polidocanol was safer and more effective, with published long follow-up results[3].

Adjuvants

The use of adjuvants aims to eradicate microscopic disease by thermal and chemical means. The current trend is the preservation of the joint with intralesional surgery and use of adjuvants in the treatment of benign bone lesions[4,5]. Wide excision has lower recurrence rates but worse functional outcomes.

Treatment of giant cell tumor (GCT) with intralesional excision, cauterization and the use of phenol over bone cement (polymethylmethacrylate, PMMA) as an adjuvant has shown excellent functional results and low rates of relapse and secondary osteoarthritis[4].

Bone cement provides immediate structural stability, but there is no evidence of a tumoricidal effect from thermal necrosis of tumor cells. Phenol is a non-selective cytotoxic agent that acts on other tissues and is systemically toxic. It is used locally in the cavity and produces superficial cell death over 1 to 2mm[6].

Cryotherapy with liquid nitrogen is curative treatment for benign aggressive and low-grade malignant bone tumors[7]. It is also useful for the local control and symptomatic relief of metastatic bone disease. Bone necrosis produced from the cavity makes cryosurgery, which is intralesional by definition, as effective as a wide excision. The surgical technique consists of exposure, curettage and margin expansion with a rotary drill, cryosurgery, bone cement reconstruction, internal fixation, and subchondral bone graft. Osteosynthesis and protection from impact for six months are important in preventing a pathological fracture because bone regeneration occurs slowly[7].

Cryosurgery can produce cell necrosis up to 2 cm from the bone surface and, in this respect, is more effective than cement and phenol. To reduce the complication rate of cryosurgery with direct instillation of liquid nitrogen in an open system, new techniques were developed to allow for the control of temperature and freezing time and so that the whole cavity, independent of geometric shape and irregularities, is evenly treated. Pressurized liquid nitrogen and argon gas spray is used[6,8].

Hydrogen peroxide (H2O2) is used clinically as a chemical adjuvant to the removal of residual tumor cells in intralesional curettage surgery for GCT. It causes the lysis and death of tumor cells and has shown low rates of recurrence when associated with bone cement[9]. Ethyl alcohol has been used in osteoid osteoma by injection into the nidus guided by computed tomography (CT) [5,10].

Radiation therapy is very effective in stopping the progression of or achieving full and permanent resolution of benign mesenchymal diseases, but there is a small risk of malignant lesion[11]. It provides good results in hemangioma of the vertebral body and the sacrum. In GCT and ABC, it may be

indicated for lesions that are difficult to access, recurrences in the spine and pelvis, or for patients that are medically unfit for surgery. In primary or metastatic tumors of the sacrum, radiotherapy alone or combined with surgery and radiosurgery are indicated[12].

Radiofrequency

Radiofrequency ablation uses long wave electromagnetic radiation to produce thermal coagulation.

A comparative study between CT-guided percutaneous ablation and open surgical treatment for osteoid osteoma suggests that the methods are essentially equivalent[13]. The percutaneous radiofrequency method is preferred because it does not require hospitalization, is not associated with complications, and allows rapid recovery. It is indicated for lesions that are not closely adjacent to the neurovascular structures in the appendicular skeleton and pelvis. It is contraindicated in the hand and spine. Needle biopsy is performed during the same surgery. Two large series of patients treated at the Massachusetts General Hospital (MGH) and the Istituti Ortopedici Rizzoli have been published[14,15].

The technique has more recently been used for the treatment of chondroblastoma[16], pain in bone metastases, and recurrence of chordoma[15].

Thermal laser therapy guided by CT has also been successful. The laser energy transmitted by the fiber optic cable produces heat and cell necrosis[5,15].

Arthroscopy

Arthroscopic biopsy and surgical treatment are recommended for selected intra-articular lesions, such as pigmented villonodular synovitis, synovial chondromatosis, arborescent lipoma, synovial angioma, intra-articular synovial lipoma, and osteochondroma[17-19].

Even minimally invasive procedures such as arthroscopy may have adverse consequences in the presence of an unsuspected neoplasia. Before arthroscopy, non-invasive tests should be performed, including magnetic resonance imaging when indicated, to rule out tumor. Unwarranted arthroscopy can contaminate the joint, hamper limb salvage surgery, and even lead to amputation[17].

Additionally, arthroscopy is a useful adjunct during open surgical treatment of patients with certain juxta-articular benign bone tumors such as GCT and chondroblastoma. Arthroscopic curettage has technical limitations and there are limitations in the tumor biology, and is not the standard procedure thus far. Curettage should be made through the cortical bone window with the assistance of arthroscopy to visualize the joint surfaces and observe joint integrity while pursuing open subchondral curettage and filling with graft or cement without damaging the articular cartilage[17,20].

Juxta-articular osteoid osteoma at the knee and the hip, involving the acetabulum and the femoral neck, can be resected with the aid of arthroscopy and CT, with minimal morbidity, excellent relief of symptoms, and rapid functional recovery[20,21].

Arthroscopy has been performed for resection of intra- and periarticular exostoses in the hip and knee that were causing pain, restrictions of movement, subluxation, and early joint damage. The risk of iatrogenic injury and necrosis of the femoral head is smaller because there is no need for hip dislocation to access the exostosis[18,19].

Endoscopic curettage without bone grafting can be used in cases of extra-articular benign bone tumors without extension into soft tissues. The tumor cavity is large enough for endoscopy[22].

Synthetic bone substitutes

The ideal synthetic bone graft should provide osteoinductive growth, undifferentiated primitive mesenchymal cells (stem cells), osteoconductive material to create a structural framework, a favorable environment for good cell function and the formation of new bone with complete integration into the host[23, 24].

Demineralized bone matrix (DBM)[25], bone morphogenetic protein (BMP), and growth factors (fibroblast, platelet, insulin and other) are osteoinductive[23]. Injections of autologous bone marrow with multipotent stem cells promote osteogenesis.

Calcium phosphate is the primary ceramic that is osteoconductive to reconstruction, as are hydroxyapatite (HA), tricalcium phosphate (TCP), the combination of these two (HA-TCP)[26,27], and calcium sulfate (gypsum)[23,24,28,29].

Composite grafts are made of materials that include a combined osteoconductive matrix,with osteogenic cells, or with osteoinductive growth factors[23,24,28,29,30]. They are widely used in

craniofacial reconstruction, benign bone tumors, as bone graft expanders or graft substitutes in stabilized fractures and nonunions. Their results are comparable to autogenous bone graft and without morbidity. They are certain to surpass the well-established autogenous "gold standard"[23,30].

There is currently a trend towards closed, minimally invasive treatment of benign lesions such as non-ossifying fibroma, aneurysmal and simple bone cysts, with percutaneous injection without open curettage with demineralized bone matrix (DBM) associated with calcium sulfate[30] or bone marrow aspirate from the iliac crest, which provides stem cells[1,31]. Injectable calcium phosphate and hydroxyapatite have been used in fractures and benign tumors, functioning as cement and creating mechanical strength[24].

Bone grafts

The autogenous cancellous bone graft is considered the gold standard. It has the basic components for integration and healing: osteoinductive growth factors, an osteoconductive matrix, osteogenic stem cells from bone marrow[23]. The disadvantages would be surgical morbidity at the donor site and few donor sites in the skeletal system, with a limited amount of graft.

Vascularized fibular grafts are incorporated more rapidly than non-vascularized grafts and show superior results in the treatment of aggressive benign bone tumors[32].

Surgery with osteochondral autograft transfer can be performed to treat benign tumors juxtaposed to articular cartilage and with erosion of the same. The graft is usually removed from the lateral condyle of the femur[33].

The allograft is less desirable for its risk of immune rejection, potential for disease transmission, infection, and its inferiority in incorporating biologically. It has osteoconductive properties, but limited osteoinductive potential[23]. Demineralization increases its biological performance and better processing reduces the risk of transmitting infection. Frozen allograft is more often used for osteoarticular reconstruction in large resections, and lyophilized allografts to fill contained defects, and for enhancing the autogenous bone graft[24].

In the treatment of BBT and TLBL with large bone defects, the reconstructive technique that uses allogeneic cortical support provides for increased resistance, easy fixation, cystic defect remodeling, fracture healing, and prevention of deformity. However, remodeling occurs slowly and may not be complete. It may be associated with adjuvants such as alcohol and phenol, allogeneic cancellous bone graft and osteosynthesis, if necessary (usually in the femur)[34].

Embolization

Selective arterial embolization may be used preoperatively as an adjuvant to reduce surgical bleeding, or as a definitive single treatment when surgery is contraindicated[1,31,35].

Although surgery is the main treatment for many benign, malignant, and metastatic sacral tumors, embolization is a valuable primary or adjuvant therapy. Patients with benign lesions, including ABC and GCT, respond to embolization with resolution of symptoms and ossification of the lesions[36].

Surgery

Distal femoral resection and reconstruction with an unconventional endoprosthesis is a safe and reliable technique that provides good function and local tumor control in most patients. Gastrocnemius muscle flaps are used in the reconstruction of soft tissue. It is indicated for malignant and benign aggressive tumors such as the GCT and the rate of limb salvage reaches 96%[37].

Endoprostheses are also useful in the reconstruction of large defects in the proximal femur and humerus. Other techniques that may be used for joint reconstruction are alloprosthetic composites and solid osteoarticular allografts associated with osteosynthesis[24]. Autogenous or allogeneic bone grafting is also indicated when performing arthrodesis.

The most common treatment for aneurysmal bone cyst and other benign tumors such as chondroblastoma, enchondroma, osteoblastoma, and chondromyxoid fibroma is marginal extracapsular excision using a high-speed drill and filling the cavity with autogenous bone graft or allograft. Adjuvants such as phenol, liquid nitrogen, and bone cement can be used in aggressive and recurrent lesions, reducing recurrence rates[1,5,31,35]. Wide excision has a lower risk of relapse and may be more appropriate in expendable bones and eccentric lesions in long bones.

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