Embolication of benign and malignant bone and soft tissue tumors of the extremities

Seda Börüban, Tanzer Sancak, Yusuf Yıldız, Yener Sağlık

The use of selective arterial embolization for treating bone tumors was first described by Feldman et al. in 1975 (1). In order to reduce bleeding during surgery, it was initially performed preoperatively. Lately, it has been used for controlling pain due to bone metastasis and management of some tumors, which do not respond to classical treatment (2, 3).

Embolication of primary or metastatic bone and soft tissue tumors has a broad range of indications, from curative treatment to palliation. The main indications for embolization are reducing the risk of bleeding during and after surgery of hypervascularized tumors, simplifying the manipulation of tumors, the palliation of pain, bleeding, fever, and hypercalcemia-like symptoms in inoperable tumors, preventing further dissemination of a tumor, and increasing the response to chemotherapy and radiotherapy. Embolization may be a therapeutic alternative to surgery in cases in which surgery is inappropriate or associated with high risk (2, 4, 5–8).

Materials and methods

Diagnostic angiography was performed on 35 patients (14 females, 40%; 21 males, 60%) between the ages of 6 and 70 years (mean, 32 years) with tumors located at their extremities. Diagnoses included aneurysmal bone cyst (ABC) (n = 10), hemangioma (n = 11), arteriovenous malformation (AVM) (n = 2), osteosarcoma (n = 1), giant cell tumor (GCT) (n = 1), soft tissue sarcoma (STS) (n = 4), thyroid follicular or thyroid papillary carcinoma metastasis (n = 4), and renal cell carcinoma (RCC) (n = 2) metastasis. Patients were evaluated between March 2000 and March 2004 in our digital subtraction angiography (DSA) unit upon referral from the orthopedics, general surgery, and oncology clinics. No interventional procedure was scheduled for patients without sufficient arterial blood flow. In all, 17 patients were considered as suitable for embolization and were included in the study.

Curative, selective-superselective DSA-guided intra-arterial embolization was performed on the lesions of 4 patients with ABC, 1 with hemangioma, and 1 with leiomyosarcoma (LMS).

Preoperative intra-arterial embolization, with the purpose of bleeding control, was performed on 11 cases; 2 AVMs, 1 hemangioma, 1 GCT, 1 RCC and 4 thyroid carcinoma metastases, and 2 STSs.

Diagnostic angiography was performed on all the cases before embolization. Based on the tumor dynamics during angiography and embolization, images were obtained at the rate of 2–3 frames/s. Non-ionic contrasting agents (Ultravist® [iopromid] 370 IU 100 per ml, Schering-Germany, and Omnipaque® [iohexol] 350 IU 100 per ml, Nycomed, Ireland) were administered using an Angiomat 6000 (Liebel-Flarsheim Company, USA) automatic injector. After administration of local anes-
Figure 1. a–c. Angiogram (a) showing a thyroid carcinoma metastasis located at the proximal part of the left lower extremity, enhanced with contrast medium administered through the left common iliac artery over the right femoral path. Superselective access to the feeding artery (b) and complete occlusion of the feeding artery (c) can be seen on the internal iliac arteriograms obtained after embolization.

Embolization was carried out following selective or coaxial superselective catheterization. After distal catheterization was achieved using a diagnostic catheter, superselective catheterization was performed, if needed. Polyvinyl alcohol (PVA) particles (embolizing agent) (Polyvinyl Alcohol Embolization Particles, TRUFILL™ 150–1000 μm, Cordis Endovascular Systems, Miami, FL, USA) 150–900 μm in size were used as 1 or 2 flacons, according to the type and size of lesion. A mixture of PVA particles and contrast agent was administered carefully and slowly with an injector under fluoroscopic control, avoiding any back flow. During each step, control angiograms were taken and tumor enhancement was evaluated in order to monitor the sufficiency and reliability of the occlusion (Fig. 1).

In an effort to save as many arteries as possible that feed normal bone tissue, the main feeding arterial branches of the tumor that could be catheterized were embolized separately. As a final step, reduction in tumor enhancement was evaluated using follow-up angiography.

Angiograms of all the patients obtained before and after preoperative embolization were compared. Devascularization rates were assessed, evaluating the relative contrast agent reduction. In addition, the time interval between embolization and surgery was considered. Bleeding grade was estimated subjectively by the surgical team and objectively by bleeding records obtained intra-operatively. In patients that underwent preoperative embolization for metastatic bone lesions and subsequent surgery within 3 days, embolization was considered clinically successful if intra-operative blood loss was ≤1,500 ml, and ≤3,000 ml if surgery was after 3 days (9). The follow-up of each case that underwent curative or palliative embolization was evaluated based on subjective symptoms and clinical findings, in addition to X-ray, computed tomography (CT), and magnetic resonance imaging (MRI).

Results

Diagnoses, findings, and results of all cases are summarized in the Table.

Metastatic bone lesions originated from 4 thyroid papillary or follicular carcinomas and one RCC; 4 of the bone lesions were located at the lower and one was at the upper extremity, and 2 patients had an accompanying pathologic fracture. Diagnostic angiography performed prior to embolization revealed that tumors at the lower extremities were fed by the common, superficial, and deep femoral arteries, and the iliac artery, and those located at the upper extremities were fed by the posterior circumflex artery. Accessible feeding branches were embolized with superselective catheterization. Mean devascularization rate in follow-up angiographies after embolization was 89% (range, 80%–100%). One patient who was operated on the same day of embolization had intra-operative blood loss of 200 ml. The other 4 cases had surgery between 4 and 8 days (mean, 4 days) after embolization and had blood loss of 100–2,500 ml (mean, 1,360 ml), intraoperatively and early postoperatively.

Of the 2 cases that were diagnosed as AVM, one had lesions located at the right forearm and other on her right labium. The labial AVM had multiple feeding branches originating from the internal iliac artery, the pudendal artery, the common and deep femoral arteries, and the superficial circumflex artery. Superselective catheterization and embolization were performed on the internal-external pudendal artery and the deep femoral artery, including aberrant branches. Ninety percent devascularization was obtained in the labial tumor case. Intraoperative blood loss was 2,000 ml in the patient who had surgery 3 days after embolization. The AVM localized at the right forearm...
was fed by multiple millimetric sized branches originating from the radial, ulnar, and interosseous arteries. The mass could only be partially embolized (70%) by superselective catheterization. The patient was operated on the same day. There was minimal blood loss pre- and post-operatively.

Excisional biopsy was attempted in one patient with LMS, but excessive bleeding occurred. To prevent intraoperative bleeding from the highly hypervascularized mass, embolization was carried out 1 day prior to surgery. Devascularization of 80% was achieved after superselective catheterization and embolization of the feeding branches that arose from the internal iliac and common femoral arteries. Intraoperative blood loss was 1,500 ml.

The patient with right axillary malignant fibrous histiocytoma underwent 4 operations, and received radiotherapy and chemotherapy beforehand; however, there was still uncontrolled bleeding from the ulcerated mass lesion. Unlike the other cases, embolization was performed in this patient in order to stop bleeding and maintain homeostasis. Blood flow to the mass completely disappeared following the procedure. No recurrent bleeding occurred during 2 years of follow-up (Fig. 2).

One patient with GCT at the left proximal fibula had surgery in another hospital, but the tumor recurred. With the help of superselective embolization performed preoperatively, blood flow

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<th>Diagnosis</th>
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<th>IBL</th>
<th>Follow-up method</th>
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DR: devascularization rate, OD: operation day, IBL: intraoperative blood loss, M-: reduction in mass size, M+: increase in mass size, M0: stable mass size, P-: relief in pain, P+: increase in pain, PF: plain films, CT: computed tomography, MRI: magnetic resonance imaging.
to the mass was reduced by 80%. No bleeding occurred during the surgery that was performed 3 days after the embolization.

Preoperative embolization achieved 100% devascularization in a patient with a sacral hemangioma. Intraoperative blood loss was 2,000 ml 3 days after the embolization.

Among the curative embolization cases, 3 were diagnosed as ABC. One ABC patient’s symptoms abated after the procedure; therefore, surgery was postponed. ABC was present on the distal femur in 2 cases, on the distal fibula in one case, and on the scapula in another case. Two cases had epiphyseal presentation and one had a pathologic fracture. None of these cases had undergone prior surgery. Embolizations were carried out to the scapular lesion 2 times every 2 months, and the others had a single embolization. Devascularization rates of the lesions were assessed using follow-up angiographies taken before and after embolization. Cases were followed-up on the 3rd, 6th, and 12th post procedure months using X-ray, CT, and MRI.

In the patient with a scapular lesion, the first month follow-up X-ray and CT showed an increase in lesion size, but there was a regression of pain after the second curative embolization. The case with a lesion on the right distal fibula demonstrated a decrease in size and the formation of sclerosis during 2 years of follow-up, which was considered as an almost full response (Figs. 3–5). The embolization of the other lesion was initially planned as preoperative, but after the reduction of pain symptoms, surgery was postponed and the patient was followed-up. The 4th month follow-up X-rays revealed minimal remission of periosteal reaction. This case had surgery at the end of 4th month.

The patient with a hemangioma previously underwent vessel ligation, but was scheduled for embolization because of an increase in mass size. The third post-embolization month follow-up MRI revealed some reduction in mass size.

One of the lesions located on a femur demonstrated a decrease in size and the formation of sclerosis during 2 years of follow-up, which was considered as an almost full response (Figs. 3–5). The embolization of the other lesion was initially planned as preoperative, but after the reduction of pain symptoms, surgery was postponed and the patient was followed-up. The 4th month follow-up X-rays revealed minimal remission of periosteal reaction. This case had surgery at the end of 4th month.

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One case of LMS previously underwent surgery; however, progression of the lesion was determined during chemotherapy treatment. The case was then scheduled for embolization. After embolization, 80% devascularization was obtained. Follow-up MRI 1 month post procedure revealed no difference in mass size, but metastasis was evident in cranial CT.

Apart from preoperative embolization, when we considered all curative and palliative embolization cases together, there were 6 cases; 4 males and 2 females between the ages of 6 and 47 years (mean, 26.3 years). Among them, 3 had a reduction in mass size or pain symptoms during their time in our hospital’s follow-up program. Follow-up duration ranged from 1 to 24 months (mean, 8.5 months), according to our hospital records. Two patients underwent surgery after the 3-month post embolization follow-up revealed that the mass size had increased. In one patient the lesion was stable; however, a newly developed cranial metastasis was detected.

Discussion

The main purpose of embolization is to achieve thrombus formation and occlusion by administrating embolizing materials through a selective catheter placed in an arterial or venous vessel. Embolizing agents must be nontoxic, sterile, radiopaque, and easy to prepare or to obtain (2, 10). Currently, embolizing agents of primary use are gelfoam, PVA particles, metallic coils, pure alcohol, microfibrillar collagen, sodium tetradenia sulfate, and tissue glues (10).

Embolization aims to maintain ischemia and necrosis in the center of the tumor, by occluding small distal branches inside the tumor. Thus, a tumor will shrink, borders between the tumor and the surrounding tissue will become clear, and operational excision and manipulation will be easier. Moreover, devascularization of a tumor provides improved bleeding control (3, 11–13).

Vascular mapping of and the hemodynamic status of the tumor, as well as the anatomic region must be determined using selective angiography before embolization. Feeding arteries of the tumor and collaterals, the tumor’s relationship with adjacent vascular processes, and possible AVFs inside the tumor must be evaluated carefully. Ar-
teries feeding the tumor must be catheterized superselectively and the procedure must be undertaken with the most suitable embolizing agent, so as to protect the hemodynamics of normal bone tissues as much as possible (9, 12).

In large and unresectable tumors, reducing the amount of live tissue, destroying the tumor tissue, or at least inhibiting tumor growth will diminish the treatment dose before radiotherapy and chemotherapy. Embolization can be used to support treatment in these situations (9).

Embolization is also palliatively useful for reducing the severity of symptoms related to tumors. Occlusion of the vessels will decrease the volume of a tumor; thus, compression on the periosteum will be reversed and that will provide pain relief. The pain-free period can be variable and re-embolization may be necessary in some cases. In the literature, reported pain-free periods are between 2 and 8 months (9, 14). According to Varma et al.’s study, in all 5 of their cases (100%) of bone metastasis originating from hypernephroma, pain symptoms were reduced and life quality improved (14). Wallace et al. reported that 3 patients out of 4 (75%) with bone metastasis had diminished pain symptoms after embolization for a period of 4–9 months (15). Barton et al. reported that pain is reduced in the first 12 hours after embolization and the pain-free period lasts about 2–8 months (9). In our study, patients with bone metastasis were scheduled to undergo embolization for preoperative bleeding control rather than palliation; however, significant pain relief was experienced in 3 out of 6 patients that had curative embolization for their primary bone tumors.

In cases involving bone metastasis, the goals of embolization are to control bleeding, to simplify surgical excision, to inhibit tumor growth, and to...
relieve pain by reducing the tumoral mass. Embolization success with metastatic lesions depends on the type and behavior of the primary tumor. In thyroid carcinoma, treatment combinations of vascular occlusion, radioactive iodine therapy, and chemotherapy produce satisfactory results, whereas in cases of bronchogenic carcinoma metastasis embolization is useless, despite subsequent surgery (9, 16, 17).

The method used in more than 95% of hypervascularized bone metastases is intralesional resection. Preoperative embolization must be considered in these patients. Nevertheless, in rare cases that are scheduled for broad and radical excision embolization is unacceptable because the hypervascularized site that tends to cause bleeding is already being resected. Additionally, as small and accessible lesions are expected to bleed less, they are well tolerated by transfusions, and therefore embolization is unnecessary (9).

According to the literature, bone metastases that present in 30%–45% of thyroid and renal carcinomas are the most common tumors for which embolization is performed, as they are hypervascularized at the rate of 65%–70% (9).

While 10-year life expectancy in differentiated thyroid carcinoma is 90%–95%, it decreases to 7%–20% with the presentation of a bone metastasis. In consideration of the treatment of metastatic thyroid carcinomas, quality of life is the main goal. The aim of palliative treatment is to achieve a mild response by offering the least discomfort to the patient with the minimum possible medical risk. Alternative treatment methods, such as chemotherapy and radiotherapy, in addition to the primary protocols of surgery and radioactive iodine treatment are not able to provide a desirable response in a short period of time. When combined with embolization, radioactive iodine treatment provides a more sufficient drop in blood thyroglobulin levels compared to radioactive iodine treatment alone (16, 17).

According to the literature, patients with metastatic thyroid carcinoma experience rapid pain relief and a reduction of neurological symptoms after embolization (17). As mentioned before, that situation is related to a decrease in tumor size and thus, decompression of the periosteum, which has a dense innervation (9).

In RCC metastases, embolization performed preoperatively or palliatively is most often targeting spinal neurological symptoms (13, 18, 19). Nevertheless, Stepanek et al. provided a pain-free period in a patient with severe knee pain arising from a RCC metastasis at the distal end of the femur using palliative embolization during 5 months until he passed away (20).

Sun and Lang’s experiences with 16 patients reveal that when tumor enhancement is reduced >70% according to post embolization follow-up angiographies, expected bleeding reduces significantly (18). According to Barton et al., preoperative embolization is considered successful if tumor enhancement falls below 25% in follow-up angiographies, 1500 ml blood loss occurs in cases undergoing surgery within 3 days, and ≤ 3,000 ml blood loss in cases operated 3 days after embolization (9).

Ideally, surgery must be performed within 3 days of embolization in order to avoid revascularization (9). There was no significant difference in blood loss between patients whose time intervals between embolization (with PVA) and surgery were 24 and 36 hours in the series of Sun and Lang. Sun and Lang prolonged this period up to 96 hours (18). We achieved 89% (80%–100%) devascularization in 5 patients with metastatic bone tumors after embolization. Our patients, on average, underwent surgery within 4 days (0–8 days). Mean blood loss was 1,360 ml (100–2,500 ml). Our results were consistent with respect to Barton et al.’s success criteria (9).

Embolization is performed in primary bone tumors, as well as metastatic lesions, in an ever-increasing number. GCT is a local aggressive lesion of bone and a highly vascularized tumor. Surgery is the preferred treatment method; however, local recurrence can be seen after curettage and grafting. Severe bleeding may occur during surgery, as it is a highly vascularized tumor. Radiotherapy is contraindicated because of its potential for malignant transformation (21). It is often located in the distal femur, proximal tibia, and distal radius. Spinal involvement is rare and the most common spinal presentation is on the sacrum. Total excision of such localized tumors is difficult and the risk of local recurrence is high. Embolization is an alternative treatment method for non-resectable tumors (21–24).

The GCT case with a lesion in the proximal fibula in our study had previously undergone surgery, but recurrence had developed. Preoperative embolization resulted in 80% devascularization and surgery was performed without bleeding, although in our case the tumor was located at a suitable site for surgery, and in case of bleeding, compression could be practical. Nonetheless, in locations like the sacrum and shoulder, in which these procedures are difficult to perform, preoperative embolization can decrease the risk of bleeding and thus facilitate surgical excision.

The treatment protocol for AVM depends on the location, size, and type (capillary, venous, arteriovenous) of lesion. The quantity and size of feeding branches should be evaluated angiographically and suitability of the lesion for selective catheterization has to be considered. It is crucial to recognize the size of feeding branches in order to avoid reflux of the embolizing material. Existence of a nidus that separates the arterial and venous components should be evaluated in AVMs. Embolization would be ineffective due to newly developed collaterals if the nidus were not completely occluded (3).

Extended AVMs may not be embolized in a single session. Vascular malformations consist of connected or non-connected compartments. Each compartment possesses one or more feeding arteries. All the feeding arteries of each compartment or major branches should be detected and thrombosed selectively. Only when occlusion of all the compartments is achieved can one consider complete embolization of the lesion. Impermanent embolizing materials like gelatin sponge are not preferred as recanalization occurs within a few weeks. A permanent embolizing agent, such as PVA, can be used for embolization of the nidus. Silicon polymer and isobutyl-2-cyanoacrylate are also suitable for the procedure. When mixed with lipiodol, isobutyl-2-cyanoacrylate polymerization decelerates, which permits occlusion of the distal branches as well. Pure venous AVMs can be directly embolized percutaneously. Absolute alcohol, sclerosing agents, and Ethibloc can be used for this purpose (2, 3, 25–28). In the present study, the 2 AVM cases in which the lesions were located in the forearm and labium each had a tumor that contained multiple feeding
branches of different sizes. Devascularization was obtained at the rate of 70% and 90% after arterial embolization using PVA. Blood loss was <2,000 ml during surgery.

Various additional treatments have been tested for decreasing the risk of recurrence in ABC. Phenol or cryotherapy can be used to sterilize the cavity wall after curettage; however, this can cause damage to the neighboring neurovascular processes. Other complications of this therapy are fracture, flap necrosis, osteonecrosis, and growth retardation in pediatric patients. Loading the bone cavity with bone cement may cause similar problems (29–31).

In arteriography, it can be seen that ABCs have one or more feeding arteries. Tumoral devascularization can be achieved using selective arterial embolization by blocking those feeding branches. If surgery is performed right before the collateral development, intraoperative blood loss can be decreased and a sufficient curettage can be performed. By the way, embolization may shorten the repair period by decelerating the destructive process. It has been shown that embolization can reduce tumor size, relieve pain, and cause new bone development in some cases. Beyond symptomatic relief, selective arterial embolization alone can maintain a radiologically confirmed cure in some patients. Of all recurrent ABCs, 90% appear within 2 years of treatment (29–31).

We performed curative embolization in 4 ABC cases. A dramatic response was achieved in one patient. Reduction in mass size and sclerosis on follow-up were apparent marks of full response to the treatment. In another case, pain relief was obtained, even if the mass size remained unchanged. In 2 patients lesion size increased within a short period (3 months), which demonstrated that our procedure was not successful in those cases.

Hemangiomas are benign tumors that consist of an abnormal proliferation of blood vessels in various organs and tissues. They have 4 histological types: capillary, cavernous, venous form, and arteriovenous malformation. With angiography they can either be seen as a highly vascularized lesion containing irregular, enlarged arterial formations, and arteriovenous shunts, or as thin, regular capillary enhancements. Dilated vascular compartments can be seen in bone hemangiomas. In some cases, tumor-like dense enhancement may cause confusion in differential diagnosis (3). Treatment of hemangiomas located at the extremities is rarely necessary, only when they produce symptoms like pain or swelling does their treatment become essential. Steroids and radiotherapy can be used for lesions that are not easily accessible by surgery (32, 33). Lesions must be removed completely in order to achieve a curative surgical result (34). Intra-arterial embolization is an alternative method to maintain symptomatic relief, to reduce intraoperative blood loss in patients scheduled for surgery, and to prevent recurrence (35–37). Lesions with low blood flow may not benefit from this procedure. In such cases, sclerosing agents can be used. In the literature sclerosing agents produced results similar to surgery (38–40). In the present study, intraarterial embolization was performed on 2 hemangioma cases, one of which was osseous, the other intramuscular. Despite sufficient devascularization of the osseous hemangioma, intraoperative blood loss was at the upper limit of our evaluation criteria. A curative procedure was performed for the intra-muscular hemangioma. Even though there was a minimal reduction in tumor size, the patient remained in our follow-up program for only 3 months, which was a very short and insufficient time to evaluate the efficiency of the method and recurrence risk.

Data on the embolization of STS is not as widespread as on bone tumors, but the procedures are usually performed for preoperative purposes (41). It can be used as an adjuvant or palliative intervention for large masses in order to increase the response to chemotherapy and radiotherapy, to relieve pain symptoms, and to control bleeding from ulcerated lesions. However, further studies are needed to better clarify the benefit of embolization in STS cases.

In our study, there were 3 patients with the diagnosis of STS. One had preoperative, one had palliative, and one had adjuvant embolization. Blood loss of the hypervascularized mass case was reduced during surgery, in the other case, bleeding from the giant mass was stopped, and in the last case, growth of the lesion size was evident during the chemotherapy regime. Adjuvant embolotherapy was carried out. Mass size was stable at the first month follow-up.

In conclusion, preoperative and palliative embolization of primary or metastatic bone tumors, which have suitable hemodynamics, is an effective method because it reduces blood loss intraoperatively, thus facilitating surgical manipulation and tumor excision. Moreover, aided by embolization, inoperable lesions can also be included in the surgical treatment criteria, so more that patients can have a surgical option. To determine which cases are suitable for embolization, vascular mapping and the hemodynamic status of the tumor must be determined, along with the anatomic region, using selective angiography before the procedure. Arteries feeding the tumor, risky vessels, and collaterals must be evaluated carefully. For a sufficient result, feeding arteries must be catheterized superselectively and the procedure must be undertaken with the most appropriate embolizing agent, protecting the hemodynamics of normal bone tissues as much as possible. Curative embolization improves the hemodynamics of primary bone tumors.

References