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Various Treatments Used in Bone Metastases

XU Chuan*

Department of Medicine, Chinese University of Hong kong, Hong kong, China

Medications

Medications used in people with bone metastasis include:

1. **Bone-forming drugs:** Drugs commonly used to treat people with thin bones (osteoporosis) may also help people with bone metastases [1]. These medicines can strengthen the bones, reduce the pain caused by bone metastases, and reduce the need for powerful painkillers. Bone-forming drugs can also reduce the risk of developing new bone metastases. These medicines can be given via a vein in the arm or by injection every few weeks. Oral forms of these drugs are available, but they are generally less effective than intravenous or injectable forms and can cause gastrointestinal side effects. Bone-forming drugs can cause temporary bone pain and kidney problems. Rarely, there is an increased risk of severe jawbone deterioration (bone necrosis).

2. **Intravenous radiation:** People with multiple bone metastases can be given a form of radiation called radiopharmaceuticals from the veins. Radiopharmaceuticals use a small amount of radioactive material that has a strong attraction to bones. Once inside the body, the particles move to the area of bone metastases and emit radiation. Radiopharmaceuticals help control the pain caused by bone metastases. Side effects can include bone marrow damage, which can lead to lower blood cell counts.

3. **Chemotherapy:** If the cancer has spread to multiple bones, your doctor may recommend chemotherapy. Chemotherapy goes through your body to fight cancer cells. Chemotherapy can be taken as tablets, given intravenously, or both [2]. Side effects depend on the particular chemotherapeutic drug you are receiving. For cancers that respond to chemotherapy, chemotherapy may be the best way to reduce the pain caused by bone metastases.

4. **Hormone therapy:** For cancers that are sensitive to hormones in the body, treatment that suppresses those hormones may be an option. Breast and prostate cancers are often sensitive to hormone blockade therapy. Hormone therapy may include taking medications that lower natural hormone levels or interfere with the interaction of hormones with cancer cells. Another possibility is the surgical removal of hormone-producing organs (ovaries and testicles).

5. **Painkillers:** Painkillers can reduce the pain caused by bone metastases. Analgesics can include over-the-counter analgesics or more potent prescription analgesics. It may take some time to determine which combination of painkillers is best for you [3]. Tell your doctor if you are still taking the medicine and still have pain. Pain specialists may be able to offer options to relieve additional pain.

6. **Steroids:** Drugs known as steroids often help reduce the pain associated with bone metastases by reducing swelling and inflammation around the cancer site. These steroids are different from the types of steroids that bodybuilders and athletes use to build muscle. Steroids can act fairly quickly to relieve pain and prevent some cancer complications, but they have side effects and should be used very carefully, especially when used for long periods of time.

7. **Targeted therapy:** Targeted drug therapy focuses on specific abnormalities in cancer cells. By blocking these abnormalities, targeted drug treatment can lead to the death of cancer cells.

Certain cancers may respond very well to these treatments. For example, breast cancer cells that are HER2 positive can respond to certain medications.

External radiation therapy

Radiation therapy uses high-energy rays such as x-rays and protons to kill cancer cells. Radiation therapy may be an option if bone metastases cause pain that is beyond the control of painkillers, or if the pain is confined to a small area.

Depending on the situation, the radiation to the bone can be given over many days with a single high dose or multiple small doses. The side effects of radiation depend on the area being treated and its size.

Surgery

Surgical procedures help stabilize bones at risk of fractures and repair broken bones.

1. **Bone Stabilizing Surgery:** If there is a risk of bone fracture due to bone metastases, the surgeon can stabilize the bone with metal plates, screws and nails (orthopedic fixation). Orthopedic fixation can reduce pain and improve function [4]. Radiation therapy is often given when healed after surgery.

2. **Surgery to inject cement into bone:** Bone that cannot be easily reinforced with metal plates or screws, such as pelvic bone or spinal bone, can benefit from bone cement. Doctors inject bone cement into bone that has been destroyed or damaged by bone metastases. This procedure can relieve pain.

3. **Surgery to repair a fractured bone:** If a bone metastasis causes a fracture, the surgeon can work to repair the bone. Metal plates, screws and nails are used to stabilize bones. Joint replacements, such as hip replacements, may be another option. In general, putting a cast on a fractured bone does not help the fracture caused by the bone metastasis.

Heating and freezing cancer cells

Procedures that use heat or cold to kill cancer cells can help control pain. These steps may be an option if there are one or two areas of bone metastases and other treatments do not help. In a procedure called radiofrequency ablation, a needle with an electric probe is inserted into a bone tumor. An electric current flows through the probe and heats

***Corresponding author:** XU Chuan, Department of Medicine, Chinese University of Hong kong, Hong kong, E-mail: chuan.xu@123.com

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the surrounding tissue. Allow the tissue to cool and repeat this process. Tumors are frozen and then thawed using a similar procedure called cryoablation [5]. This process is repeated several times. Side effects may include damage to nearby structures such as nerves and bone damage that may increase the risk of fractures.

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Board 1: Bone tumors with aneurysmal content.

Giant Cell Tumor	Non Ossifying Fibroma	Telangiectatic Osteosarcoma
Osteoblastoma	Chondromyxoid Fibroma	Fibrosarcoma
Chondroblastoma	Bone Cysts with Fracture	Metastasis of Carcinoma
Fibrous Dysplasia	Eosinophilic Granuloma	

Table 1: Decision algorithm.

Score	**2**	**1**	**0**
Age		≤ 18 years old	> 18 years old
Long bones		Yes	No
Tumors in the spine	≥ 50 years		
Bone destruction (radiographic or MRI)		IC, moth-eaten, permeative	IA- IB
Fluid-fluid level	≤ 1/3	1/3 - 2/3	≥ 2/3
Solid content		Yes	No
Aggressiveness characteristics (cortical rupture, periosteal reaction, soft tissue mass, mineralized matrix, perilesional bone edema)		Yes	No
Pathological fracture		Yes	No

Table 2: Comparison between classification for bone destruction types in radiography and MRI.

Diagnosis n=15	**Age**	**Location**	**Classification Radiography**	**Classification RM**	**Concordance**
ABC	13	Tibia	IB	IB	Yes
ABC	33	Tibia	IA	IA	Yes
ABC	18	Clavicle	IB	IB	Yes
ABC	48	Humerus	IB	IB	Yes
ABC	12	Ulna	IB	IB	Yes
ABC	11	Tibia	IB	IB	Yes
ABC	15	Column	IC	IB	No
ABC	12	Fibula	IB	IB	Yes
GTC	19	Fibula	IC	IC	Yes
CMF	22	Femur	IB	IB	Yes
GCT	21	Tibia	II	IC	No
GCT	47	Femur	IB	IC	No
CMF	22	Basin	IB	IB	Yes
FD	12	Femur	IA	IA	Yes
TO	22	Tibia	III	III	Yes

ABC: aneurysmal bone cyst; GCT: giant cell tumor; CMF: chondromyxoid fibroma; FD: fibrous dysplasia; TO: telangiectatic osteosarcoma

Table 3: Decision algorithm of primary ABC, secondary ABC, and telangiectatic osteosarcoma cases.

Diagnosis	Age	Location	MRI Classification	Fluid-fluid level	Aggressiveness characteristics	Solid content	Fracture	Score
ABC	13	Tibia	IB	Complete	Present (perilesional bone edema)	Absent	Absent	3
ABC	33	Tibia	IA	≥2/3	Absent	Present	Present	3
ABC	18	Clavicle	IB	Complete	Present (perilesional bone edema)	Absent	Absent	3
ABC	29	Tibia	IC	≥2/3	Present (soft tissue mass)	Present	Absent	4
ABC	8	Spine	IC	Complete	Present (perilesional bone edema)	Absent	Absent	3
ABC	48	Humerus	IB	≥2/3	Present (perilesional bone edema)	Present	Absent	3
ABC	12	Ulna	IB	Complete	Absent	Absent	Absent	2
ABC	11	Tibia	IB	Complete	Absent	Absent	Absent	2
ABC	15	Spine	IB	Complete	Present (perilesional bone edema)	Absent	Absent	2
ABC	12	Fibula	IB	≥2/3	Absent	Present	Absent	3
GCT	19	Fibula	IC	≥2/3	Present (periosteal reaction)	Present	Absent	4
CMF	22	Femur	IB	≤1/3	Present (perilesional bone edema)	Present	Absent	6
GCT	24	Radio	IB	≥2/3	Present (perilesional bone edema)	Present	Absent	3
GCT	21	Tibia	IC	≤1/3	Present (soft tissue mass)	Present	Absent	6
GCT	47	Femur	IC	≤1/3	Present (perilesional bone edema)	Present	Present	7
CMF	22	Pelvis	IB	≤1/3	Present (perilesional bone edema)	Present	Absent	4
FD	12	Femur	IA	1/3-2/3	Absent	Present	Absent	4
OT	69	Humerus	III	≤1/3	Present (soft tissue mass)	Present	Absent	6

Figure 1: ABC, female, 13 years old, proximal tibia, type IB (radiography and MRI) filled with fluid-fluid level, perilesional bone edema, no fracture. Score 3.

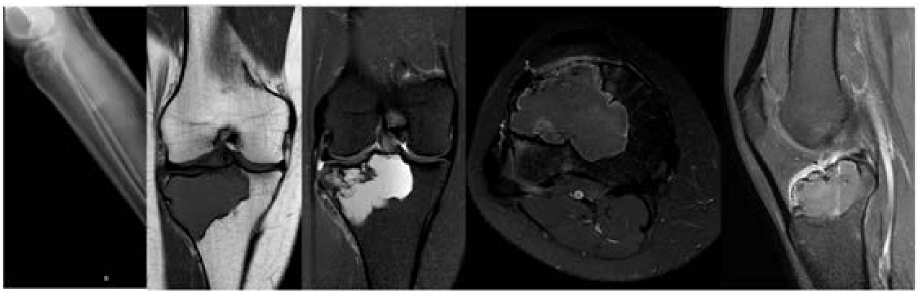

Figure 2: ABC, female, 33 years old, proximal tibia, type IA (radiography and MRI), fluid-fluid level ≥2/3, and small incomplete fracture. Score 3

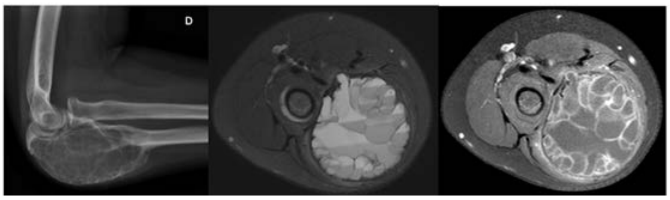

Figure 3: ABC, female, 12 years old, proximal ulna, type IB (radiography and MRI), filled with fluid-fluid level, no solid component, no aggressive imaging characteristic, no fracture. Score 2.

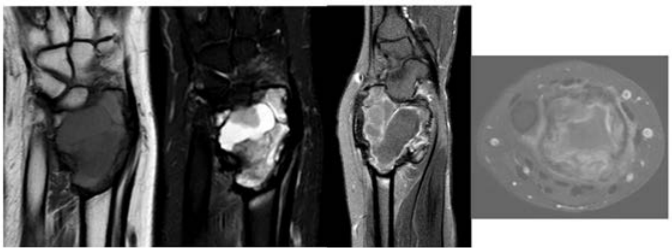

Figure 4: Giant cell tumor, male, 24 years old, distal radius, type IB (MRI), fluid-fluid level ≥ 2/3, solid component, perilesional bone edema, no fracture. Score 3.

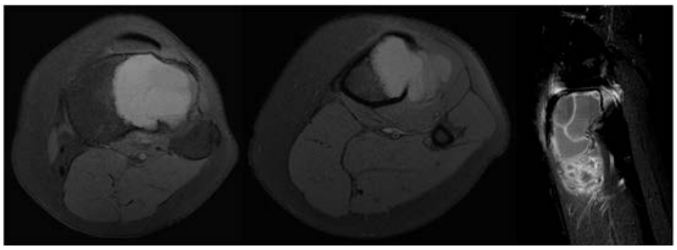

Figure 5: ABC, female, 29 years old, proximal tibia, type IC (MRI), fluid-fluid level ≥ 2/3, solid content, soft tissue mass, no fracture. Score 4.

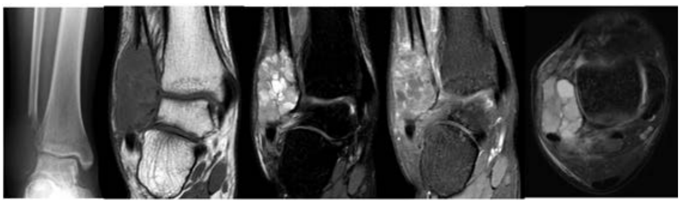

Figure 6: Giant cell tumor, male, 19 years old, distal fibula, type IC (radiography and MRI), fluid-fluid level >2/3, solid component, periosteal reaction, no fracture. Score 4.

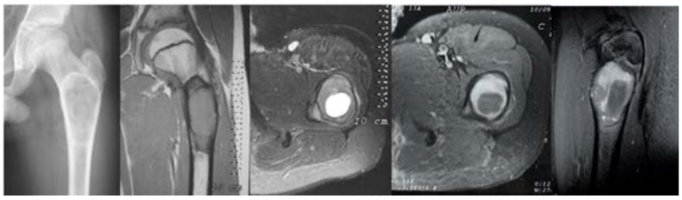

Figure 7: Fibrous dysplasia, male, 12 years old, proximal femur, type IA, fluid-fluid level between 1/3 and 2/3, no aggressive imaging characteristics, solid component, no fracture. Score 4.

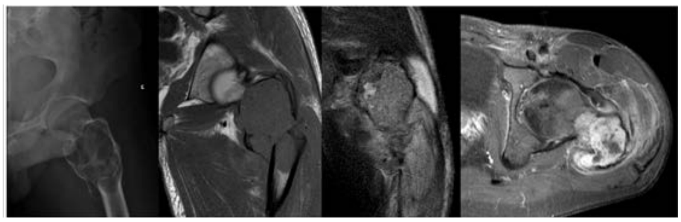

Figure 8: Chondromyxoid fibroma, male 22 years old, proximal femur, type IB, fluid-fluid level <1/3, perilesional bone edema, solid component, with pathological fracture. Score 6.

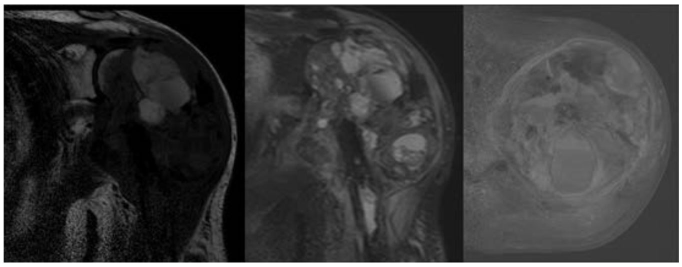

Figure 9: Telangiectatic osteosarcoma, 55 years old, proximal humerus, type III, fluid-fluid level <1/3, soft tissue mass, solid component, no fracture. Score 6.

Table 4: Obtained score versus the need for biopsy.

Variable	Need for Biopsy		Total (N = 19)	p
	No (N = 10)	Yes (N = 9)		
Score				**<0.001**
median (min.; max.)	3 (2; 4)	6 (3; 7)	3 (2; 7)	

Table 5: Diagnostic measures of the threshold.

AUC	CI (95%)		Threshold	Sens. (%)	Spec. (%)	PPV	NPV
	Lower	Upper		CI (95%)	CI (95%)	CI (95%)	CI (95%)
0.939	0.829	1	3.5	88.9	90	88.9	90
				(51.8; 99.7)	(55.5; 99.7)	(51.8; 99.7)	(55.5; 99.7)
AUC: Area under the Curve; CI: Confidence Interval; Sens.: Sensitivity; Spec: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value							

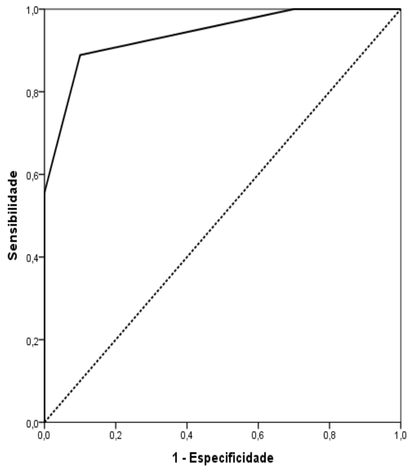

Figure 10: Area under the ROC curve.