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O. Buryanov, V. Chorney

Bogomolets National Medical University, Kyiv, Ukraine

METHODICAL DEVELOPMENT OF SESSIONS FOR TRAINING STUDENTS: " BONE TUMORS "

1. Background:

Tumors of the musculoskeletal system include tumors of bone, soft tissue and skin. Tumor is solitary or multiple abnormal uncontrolled multiplication of own cell from which it is derived. Modern theories of carcinogenesis (chemical, physical, biological, genetic) do not correspond fully to the origin and development of tumors. Tumors may originate not only from their own bone or cartilage elements, but also from other tissues that make up the bone, including the bone marrow, periosteum, blood vessels and nerves. In practice, there are considerable difficulties in distinguishing between benign and malignant tumors and tumor diseases.

In Ukraine in 2008, the incidence of malignant primary bone tumors and articular cartilage was 1,2 cases and deaths amounted 0,7 per 100 thousand of population (560 and 342 patients, respectively). The incidence was 1 in men and 0.6-0.7 cases in women per 100 thousand populations [1]. The incidence is higher in Kirovohrad, Rivne region. Mortality is higher in Crimea, Rivne region. The diagnosis is confirmed by histological examination in 67.7% of patients. Special treatment covered 63.3% of primary patients, only 30.7% received combined or complex treatment. Among patients who got a disease first in 2008, 37.8% lived less then 1 year afterwards [1].

Among all bone lesions [4] benign bone tumors account for 35.5%, primary malignant tumor – 29.5%, bone metastases – 15.7%, pseudotumor diseases – 13.7%, lesion system tumor diseases – 5.6%. Primary bone tumors occur most often between the ages of 15 and 40. Benign bone tumors are distributed as follows: osteochondroma – 28%, osteoid osteoma – 18.7%, giant cell tumor (GCT) – 15.4%, chondroma – 10.4%, fibrous dysplasia – 6.1%, fibrous histiocytoma – 5.8%, hondroblastoma – 4.5%. Among malignant bone tumors most often are found: osteosarcoma, in 41.4% cases, chondrosarcoma, in 21.3% cases, Ewing's sarcoma, in 17.9 % cases, the others take place significantly rarely. Most affected are long bones and pelvic bones. Joints are affected by tumor process in 50-60% cases.

Metastatic bone tumors occur in nature 6-20 times more often than primary bone tumors. Cancer metastases in the spine account for 59%, pelvis – 49%, edge –30%, tubular bones – 25% of the skull bones – 18-20%. Metastasis of breast cancer occur in 60 - 90% cases, lung cancer – in 40% cases, kidney cancer in 20-30% cases, prostate cancer – in 10 to 20% cases.

2. The specific objectives:

Educational tasks of the lesson:

1. To get acquainted with the general features and stages of medical care.
2. An overview of possible tumors and tumor-like bone diseases, known classification, complications of tumors.
3. To learn algorithm of clinical examination of patients with bone tumors.
4. To master algorithm of providing care to patients with bone tumors.
5. To read the radial image and other bone tumors instrumental methods of diagnosis.
6. To know the indications and principles of conservative and surgical treatment of tumors and tumor-like bone diseases.

Educational goals: formulating the future professional as individual taking into consideration deontological and professional responsibilities.

3. Basic knowledge and skills necessary for studying the themes of interdisciplinary integration.

Discipline	To know	To be able
1. Preceding disciplines (normal and topographical anatomy, operational surgery, radiology	1. Osteology. Anatomical structure of bone sections. 2. Syndesmology . Large joints, ligaments joints, tendon sheath. 3. The anatomic and topographic features of limbs, important neurovascular bundles. 4. Peculiarities of biomechanics of movement of large joints. Age characteristics of bones skeleton in the X-ray image.	X-ray examination and bone diseases semiotics Identifying bias fragments in fractures based on X-ray data
2. The following disciplines (normal physiology, pathophysiology, generalsurgery, oncology, internal propedeutics diseases)	Transport immobilization, desmurgy, timing immobilization fusion disability and loss. Care of patients in plaster bandages. Prevention ofpossible complications andways to prevent them.Clinic and chemoradiotherapy malignant bone tumors.	Conducting social, labor and householde xamination depending onthe nature of the damage and possible complications
3. Interdiscipline integration (themes of the given discipline with which it is integrated)	1. Indications and methods ofconservative treatment of bone tumors, external immobilization, skeletal elevator. 2. Indications, choice of method and implants in surgical treatment	1. Measuring amplitude movements of the joints and spine. 2. Measuring lengthlower extremity and analyzing the reasons leading to these changes. 3. Conducting transport and medical immobilization. 4. Identify places, means and methods of skeletal stretching depending on the nature of the damage.

4. Content of educational material.

4.1. The list of key terms, parameters, characteristics which the students learn preparing for the lesson:

Term	Definition

Malignant tumor – a solitary or multiple abnormal uncontrolled multiplication of own cells from which it is derived.

Tumor a pathological process caused by uncontrolled multiplication of own cells, invasion of surrounding tissue and sometimes metastasis.

Combined treatment Combination of two or three methods of treatment.

Comprehensive treatment Using auxiliary methods of treatment together with the main ones, such as immunotherapy, hormone therapy, magnetic hyperthermia, etc

Pathological fractures Fractures of painfully altered bone malignant tumor

Benign bone tumors Osteoid osteoma, osteoblastoma, osteochondroma, chondroma, chondroblastoma, hondromixoid fibroma, desmoplastic fibroma, benign fibrous histiocytoma, giant cell tumor, haemangioma

Tumor-like lesions of bone (miscellaneous lesions) Aneurysmal bone cyst, simple bone cyst, fibrous dysplasia, osteofibrous dysplasia, Langerhans cell histiocytosis, synovial chondromatosis

Malignant bone tumors Osteosarcoma, parosteal osteosarcoma, periosteal osteosarcoma, chondrosarcoma, plasma cell myeloma, bone metastases, malignant fibrous histiocytoma, Ewing's sarcoma, chordoma, lymphoma, malignant giant cell tumor, angiosarcoma, fibrosarcoma, adamantinoma.

Bone sections Epiphysis, metaphysis, diaphysis, periosteum, cortical layer

Closed fracture A fracture, when there is no communication of fracture areas with the environment.

Immobilization Creating conditions of complete immobility or decreasing limb or joint mobility.

Bone calluses (callus) Plot bone that is formed in a violation of the integrity of the bone and connecting it to debris.

Signs of benign bone tumors Clear paths, sclerotic rim, correct structure, slow growth

Symptoms of malignant bone tumors Violation of bone formation defects, fuzzy, irregular shape diffuse, heterogeneous structure, no structure, periosteal reaction, needle-shaped periostitis (spicules), rapid growth, Codman triangle, the reaction of the periosteum, the lack of boundaries between tumor and healthy bones plot.

4.2. Information block:

Physical examination of patients with tumors of bone.

Complaints: 1) the appearance of neoplasm, 2) pain, 3) limb dysfunction, claudication, contracture, temperature, and so on (Fig. 1.)[2,3].

History of disease: patient's age, the time of the disease, the rate of tumor growth general condition of the patient.

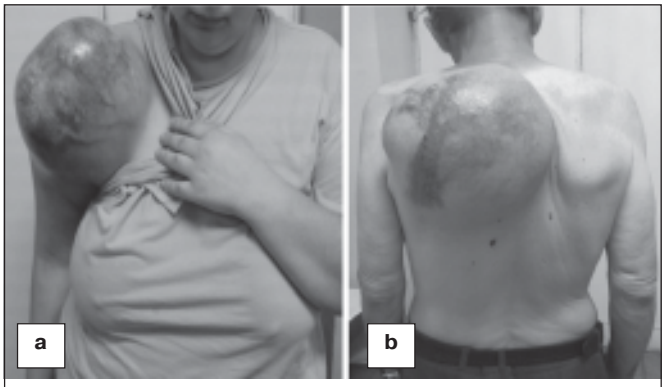

Fig. 1. Appearance of tumors, expansion saphenous veins, dysfunction of limbs, contracture (a,b).

Status localis:

- run (for the lower limbs), using additional support, the presence of splints, Extent of movement of the affected parts of the skeleton;
- condition and changes in the skin (subcutaneous veins expand, the availability of post-surgical scars, wounds, ulcers, their origin and state of decay tumor bleeding, infection);
- tumor in the bone segment (top, middle or bottom) and on its surface (front, inside, outside, back);
- tumor size, circumference sick and healthy limbs over the tumor;
- pain tumors consistency tumor mobility;
- status of regional lymph nodes (mobility, tenderness, texture, shape, size)[2,7].

X-ray studies. Radiography can give the following information: location of the tumor in segments (epiphysis, metaphysis, diaphysis, periosteum, cortical layer or endosteal) solitary or plurality of defeat. Benign tumor is indicated by sharp contours, normal structure, and slow growth (Fig. 2). Malignant tumor characteristics are: violations of bone formation de-

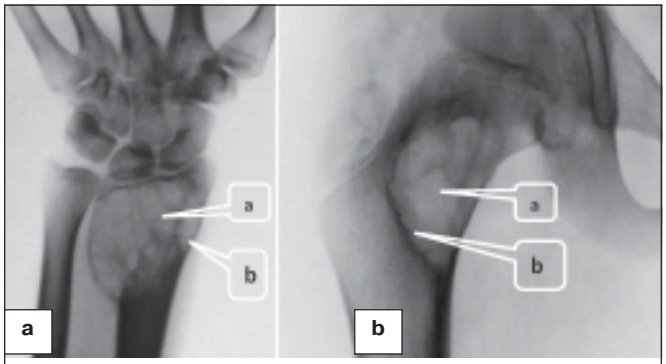

Fig. 2. A.Cellular-trabecular form of Giant cell tumor of radius. Foci of destruction (a) are separated by a sharp bony septa (b), but the rim of osteosclerosis is not typical; B. Radiographs solitary cysts of the femur.
Multilocular focus destruction (a), which is often located centrally in the proximal long bones metadiaphysis, (b) rim osteosclerosis.

fects, fuzzy, irregular shape diffuse, heterogeneous structure, no structure, periosteal reaction, needle-shaped abscess (spicules), rapid growth, Codman triangle, the reaction of the periosteum, the lack of boundaries between tumor and healthy section of bone (Fig. 3,4). To clarify the location of the tumor X-ray

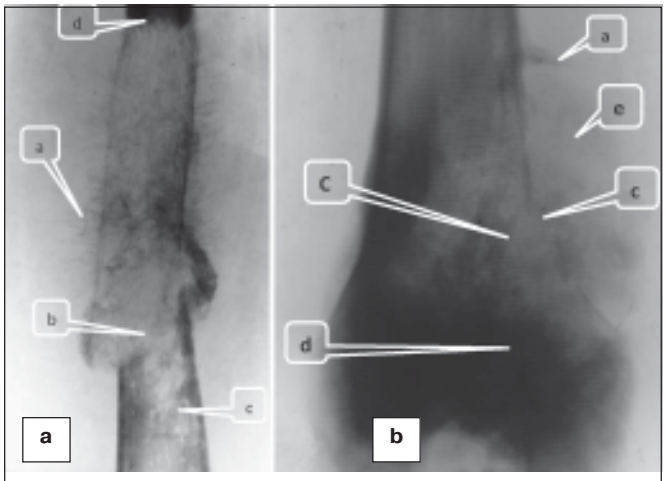

Fig. 3. A. Lymphoma of the femoral shaft: (a) soft tissue component with spicules, (b) pathological fracture, (c) small focal bone destruction ("moth-eaten"), (d) destruction of all segments of bone; B. Radiographs of the mixed form osteosarcoma of the femur metaepiphysis, the threat of pathological fracture: (a) Codman triangle,(b) osteolityc destruction, (c) the destruction of the cortical layer, (d) destruction all segments of bone, (e) soft tissue component.

examinations in two or more projections should be performed. In case of small fire, such as osteoid osteoma, your computer tomography should be used.

To identify the multiplicity of lesions, total X-ray is used (such as myeloma (Fig. 5.), lymphoma, multiple exostosis), which can detect asymptomatic lesions of bone.

Angiography. This method is the introduction of a specific substance (Cardiotrastum, Triombrastum) in the vascular patient limb. A dense grid of atypical newly drive (afferent) vessels, the presence of numerous gaps, curls are the evidence of malignancy.

Angiography is performed invasively during vessel puncture. Today CT angiography with three-dimensional reconstruction image has become widespread (Fig. 6).

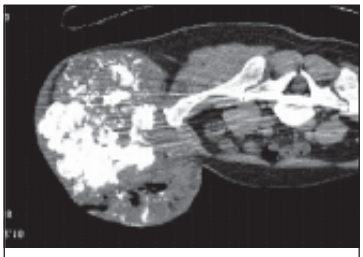

Fig. 4. CT scan of the giant secondary peripheral chondrosarcoma (G3-4) wing of the ilium, which developed against the backdrop of multiple exostosis.

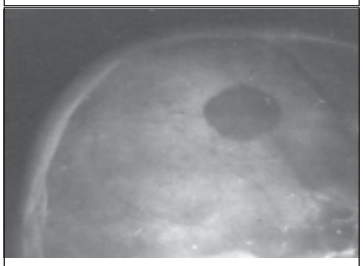

Fig. 5. Typical lesion of the skull bones in multiple myeloma (multiple "punched-out" holes).

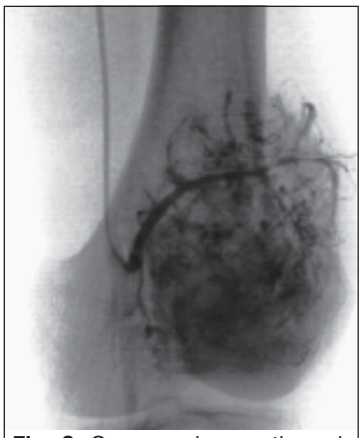

Fig. 6. On an angiogram through the intra-arterial catheter contrasting branches of the femoral artery, which supplies the osteosarcoma of the distal femur.

Radionuclide studies (bone scintigraphy) determine the prevalence of the whole process in pigtails skeleton. Bone tissue has the ability to accumulate radiopharmaceuticals (technetium, strontium). Characteristic of malignant tumors is the accumulation of radiopharmaceuticals 200% or more.

Laboratory diagnosis. In laboratory diagnostics at tumors of bone today is the concept of molecular tumor markers. These are mainly proteins that emit or contain some kind of tumor cells. Their value lies in the diagnosis, prognosis and disease "target" (targeted) therapy. The level of alkaline phosphatase, calcium, Ki67, p53, Her-2, S100, vascular endothelial growth factor (VEGF) becomes higher. They are determined by immunohistochemical methods (in tumor tissue) and enzyme-linked immunosorbent assay (serum).

Pathological research is basic and the most accurate means of diagnosing mandatory origin tumors. The most informative is biopsy during surgery or bone marrow aspiration and biopsy. Less informative in case of bone tumors is needle biopsy. Disregard to this diagnostic method is unacceptable and has serious consequences for the patient.

Classification of bone tumors (WHO ICD -10, 2002)

CARTILAGE TUMOURS
Osteochondroma 9210/0*
Chondroma 9220/0
Enchondroma 9220/0
Periosteal chondroma 9221/0
Multiple chondromatosis 9220/1
Chondroblastoma 9230/0
Chondromyxoid fibroma 9241/0
Chondrosarcoma 9220/3
Central, primary, and secondary 9220/3
Peripheral 9221/3
Dedifferentiated 9243/3
Mesenchymal 9240/3
Clear cell 9242/3
OSTEOGENIC TUMOURS
Osteoid osteoma 9191/0
Osteoblastoma 9200/0
Osteosarcoma 9180/3
Conventional 9180/3
chondroblastic 9181/3
fibroblastic 9182/3
osteoblastic 9180/3
Telangiectatic 9183/3
Small cell 9185/3
Low grade central 9187/3
Secondary 9180/3
Parosteal 9192/3
Periosteal 9193/3
High grade surface 9194/3
FIBROGENIC TUMOURS
Desmoplastic fibroma 8823/0
Fibrosarcoma 8810/3
FIBROHISTIOCYTIC TUMOURS
Benign fibrous histiocytoma 8830/0
Malignant fibrous histiocytoma 8830/3
EWING SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOUR
Ewing sarcoma 9260/3
HAEMATOPOIETIC TUMOURS
Plasma cell myeloma 9732/3
Malignant lymphoma, NOS 9590/3
GIANT CELL TUMOUR
Giant cell tumour 9250/1
Malignancy in giant cell tumour 9250/3
NOTOCHORDAL TUMOURS
Chordoma 9370/3
VASCULAR TUMOURS
Haemangioma 9120/0
Angiosarcoma 9120/3
SMOOTH MUSCLE TUMOURS
Leiomyoma 8890/0
Leiomyosarcoma 8890/3

LIPOGENIC TUMOURS
Lipoma 8850/0
Liposarcoma 8850/3
NEURAL TUMOURS
Neurilemmoma 9560/0
MISCELLANEOUS TUMOURS
Adamantinoma 9261/3
Metastatic malignancy
MISCELLANEOUS LESIONS
Aneurysmal bone cyst
Periosteal 9193/3
High grade surface 9194/3
FIBROGENIC TUMOURS
Desmoplastic fibroma 8823/0
Fibrosarcoma 8810/3
FIBROHISTIOCYTIC TUMOURS
Benign fibrous histiocytoma 8830/0
Malignant fibrous histiocytoma 8830/3
EWING SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOUR
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HAEMATOPOIETIC TUMOURS
Plasma cell myeloma 9732/3
Malignant lymphoma, NOS 9590/3
GIANT CELL TUMOUR
Giant cell tumour 9250/1
Malignancy in giant cell tumour 9250/3
NOTOCHORDAL TUMOURS
Chordoma 9370/3
VASCULAR TUMOURS
Haemangioma 9120/0
Angiosarcoma 9120/3
SMOOTH MUSCLE TUMOURS
Leiomyoma 8890/0
Leiomyosarcoma 8890/3
LIPOGENIC TUMOURS
Lipoma 8850/0
Liposarcoma 8850/3
Simple cyst
Fibrous dysplasia
Osteofibrous dysplasia
Langerhans cell histiocytosis 9751/1
Erdheim-Chester disease
Chest wall hamartoma
JOINT LESIONS
Synovial chondromatosis 9220/0

* Morphology code of the International Classification of Diseases for Oncology (ICD-O) [5] and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for in situ carcinomas and grade III intraepithelial neoplasia, and /3 for malignant tumours.

TNM Classification of bone tumours [6]

Primary tumour (T)	TX: primary tumour cannot be assessed T0: no evidence of primary tumour T1: tumour ≤8 cm in greatest dimension T2: tumour > 8 cm in greatest dimension T3: discontinuous tumours in the primary bone site
Regional lymph nodes (N)	NX: regional lymph nodes cannot be assessed N0: no regional lymph node metastasis N1: regional lymph node metastasis

Note: Regional node involvement is rare and cases in which nodal status is not assessed either clinically or pathologically could be considered N0 instead of NX or pNX.

Distant metastasis (M)	MX: distant metastasis cannot be assessed M0: no distant metastasis M1: distant metastasis M1a: lung M1b: other distant sites

G Histopathological Grading

Translation table for 'three' and 'four grade' to 'two grade' (low vs. high grade) system.

TNM two grade system	Three grade systems	Four grade systems
Low grade	Grade 1	Grade 1
		Grade 2
High grade	Grade 2	Grade 3
	Grade 3	Grade 4

Note: Ewing sarcoma is classified as high grade.

Stage IA	T1	N0,NX	M0	Low grade
Stage IB	T2	N0,NX	M0	Low grade
Stage IIA	T1	N0,NX	M0	High grade
Stage IIB	T2	N0,NX	M0	High grade
Stage III	T3	N0,NX	M0	Any grade
Stage IVA	Any T	N0,NX	M1a	Any grade
Stage IVB	Any T	N1	Any M	Any grade
	Any T	Any N	M1b	Any grade

Treatment: The main treatment of tumors of the musculoskeletal apparatus is surgery (S), chemotherapy (ChT) and radiotherapy (RT). By chemotherapy the following cytotoxic drugs are used: methotrexate at a high dose, doxorubicin, cisplatin, ifosfamide, bisphosphonates and others. Radiotherapy is conducted in total focal dose of 30-60 Gray. Combined treatment is combination of two or three main methods of treatment, such as:

1. preoperative chemotherapy (2-3 courses at 3 weeks).
2. surgery (resection of the lower third of the thigh bone tumor and knee replacement).
3. postoperative chemotherapy (4-6 courses at intervals of 3 weeks). Complex treatment is combination

of main basic methods with additional basic methods, such as hormone therapy, immunotherapy, and hyperthermia. The volume of surgery depends on the location, nature and size of the tumor [2,7].

Scheme of the main treatments for bone tumors

Surgery:	**Combined treatment** (chemotherapy + operation):	**Complex treatment:**
▪ Benign bone tumors, ▪ Chondrosarcoma ▪ parosteal osteosarcoma ▪ Hordoma, ▪ Adamantinoma	▪ Osteosarcoma, ▪ Angiosarcoma of bone, ▪ Fibrosarcoma bone ▪ Mesenchymal chondrosarcom, ▪ Malignant fibrous histiocytoma ▪ Malignant giant cell tumor.	▪ Myeloma, ▪ Ewing's sarcoma, ▪ Reticulosarcoma, ▪ Lymphoma, ▪ Bone metastases

Surgical intervention in oncosurgery is divided into organ surgery and those who mutilate, radical, non-radical and symptomatic. Among them are distinguished:

- bone biopsy (biopsy trepan, or open biopsy);
- curettage or inside bone resection with plastic ceramic implants (tricalcium phosphate, hydroxyapatite), used in benign tumors, or bone cement – with aggressive metastases and benign tumors;
- wide resection of bone section (regional, wedge, segmental) + auto- or alograft + osteosynthes with plates or external fixation devices;
- articular resection of bone section with tumor + section arthroplasty articular bone - malignant tumors;
- extirpation (complete removal of bone - scapula, clavicle, calcaneus);
- amputation limb or finger, disarticulation;
- cryodestruction tumors; X-surgery.

5.1. Theoretical questions for the class.

1. General peculiarities of bone tumors and phases of medical assistance.
2. Algorithm of clinical examination of patients with bone tumors. To be able to identify the leading clinical manifestations.
3. Etiology and pathogenesis of tumors.
4. Clinic, differential diagnosis of benign and malignant tumor of bone tumors.
5. Known classification of bone tumors.
6. Algorithms for the treatment of bone tumors.
7. X-ray picture, CT, MRI diagnosis of bone tumors.
8. Indications and principles of conservative and surgical treatment of benign tumor and malignant bone tumors.

5.2 Practical tasks for lesson preparation.

1. To master algorithm of clinical examination of patient with a bone tumor.
2. To capture algorithm of medical care to the tumor of bone.
3. To be able to carry out clinical and radiological differential diagnosis of benign and malignant bone tumors.
4. To know the basic principles of surgery for tumor diseases, benign and malignant tumors of bone.
5. To know the principles of conservative and surgical treatment of this disease.

5.3. Tasks and tests for self-control.

1. Often metastasizes to bone:
   a) breast cancer b) kidney cancer
   c) lung cancer d) the correct answer a) and b)
   e) all correct answers.
2. Benign osteogenic tumors of bone are:
   a) osteoblastoma, osteoid osteoma,
   b) osteochondroma, chondroma, Chondroblastoma, hondromiksoid fibroma,
   c) all answers are correct.
3. The main method in the diagnosis of bone tumors is:
   a) X-ray c) computed tomography
   b) bone scan **g)** pathomorphological investigation.
4. Bone marrow tumors:
   a) Ewing's sarcoma b) lymphoma of bone
   c) multiple myeloma **d)** all answers are correct.
5. Benign tumors of cartilage:
   a) chondroma, chondroblastoma, hondromiksoidnaya fibroma, osteochondroma
   b) osteoblastoma, osteoid osteoma,
   c) chondrosarcoma

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