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Case Report

High Grade Osteoblastic Osteosarcoma of the Proximal Humerus in a 14 Years-Old Teenager: An Accidental finding after fall from a Bicycle

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Abstract

Conventional high-grade osteosarcoma is the most common primary malignant bone tumor and occurs most frequently in children, adolescents, and young adults. The majority of tumors are located in the lower part of the femur, upper part of the tibia, upper part of the humerus, and pelvis. The preferred local treatment consists of surgically removing the entire tumor and a layer of healthy tissue surrounding the tumor. This is essential for long-term survival. Limb-sparing surgery is often possible, preserving the function of the affected limb. After surgical removal of high-grade osteosarcomas in the limbs and pelvis, it is often necessary to reconstruct the resulting defect. This is most commonly done by implanting an endoprosthesis. Special mega-endoprostheses made of metal are used for this purpose. The choice of the optimal implant and reconstruction method depends on many factors, including the tumor's location and extent, as well as the patient's age, activity level, and prognosis. Therefore, the treating surgeon should be familiar with all possible reconstruction techniques. Approximately 20% of patients have distant metastases at the time of initial diagnosis of high-grade osteosarcoma, with about 90% located in the lungs and 10% in other bones. Even patients without detectable metastases on imaging may have undetectable micro metastases at the time of diagnosis. This explains why in the past, about 90% of patients developed distant metastases within a few months after undergoing surgery alone and died from their disease. Therefore, all patients with high-grade osteosarcoma require pre- and postoperative chemotherapy. This, combined with adequate surgical tumor removal, can increase the 5-year survival rate to over 60%. Comprehensive experience in the interdisciplinary treatment of high-grade osteosarcomas is necessary to determine which treatment offers optimal results for each individual patient. We present a case of a 14 years-old teenager with high grade osteosarcoma of the proximal humerus.

Keywords: Osteosarcoma, Humerus, Child, Chemotherapy

Introduction

Osteosarcoma, also known as osteogenic sarcoma, is the most common primary malignant bone tumor, commonly referred to as "bone cancer" in colloquial terms, but not entirely medically correct. Its proliferating cells are capable of forming bone and osteoid (uncalcified bone matrix). Osteosarcoma is characterized by aggressive growth with destruction of surrounding bone and, if present, joints. It metastasizes early through the bloodstream to the lungs. At the time of diagnosis, 20% of patients already have metastases, and an estimated additional 60% have non-visible micrometastases. The incidence in Central Europe is about 0.2-0.3 per 100,000. This type of cancer is therefore one of the rarer types of cancer. Extrapolated to all of Germany, there are about

200 new cases per year, and in Switzerland and Austria, about 10 to 15 cases each per year. The median age of onset is 18 years, and most cases are diagnosed in the age group between 10 and 25 years. Male patients are slightly more affected. Osteosarcomas mainly occur near joints in the long bones (femur, humerus, tibia) of the skeletal system. 50% of osteosarcomas are located in close proximity to the knee joint and about 10% near the shoulder joint. A localization on the skull bone or spine is rare. One of the possible causes of osteosarcoma is previous radiation therapy or radioactive exposure. In a cohort study over more than forty years of over 80,000 survivors of the atomic bombings in Hiroshima and Nagasaki, a linearly increasing risk for the development of malignant bone cancer was shown with a relative risk of 7.5 per gray radiation from a lower threshold of 0.85 Gray upwards. Histologically, the cells of osteosarcoma are highly polymorphic and irregular. Characteristic is that the tumors synthesize primitive bone substance (osteoid) without recognizable cartilage matrix. The classification divides into different types of osteosarcoma: Central (medullary) osteosarcoma, classical osteosarcoma (chondroblastic, fibroblastic, osteoblastic), telangiectatic osteosarcoma, well-differentiated central (low-grade) osteosarcoma. Furthermore small cell osteosarcoma, peripheral (surface) osteosarcoma, parosteal osteosarcoma, periosteal osteosarcoma are types that will be not so often found. As a secondary condition, osteosarcoma can occur after previous radiation exposure and in the disease osteodystrophia deformans Paget.

Case Report

We present a case of a to date of accident healthy 14 years-old teenager, who was fallen down by bicycle on the left shoulder. X ray evaluation confirmed the suspicicion of a bone tumor with a pathological fracture. A bone biopsy was performed and a high-grade osteoblastic osteosarcoma was confirmed. Preoperative chemotherapy was terminated and introduced to date of the publication.

Immunohistological Results

The spindle cell sections express SATB2 with recognizable nuclear size variations in the staining. p53 is predominantly weak, questionably negative in the lesional cells. The ki 67 proliferation index within the lesional cells is focal up to 40%. Questionable faint, single-cell positivity of the lesional cells for c-FOS. Negativity of the lesion for H3.3G34W.

Even considering the additional immunohistochemical stains, the striking, cell-dense, osteoid matrix-forming, giant cell-rich proliferation from the left proximal humerus is clearly proliferation-active. With immunohistochemical negativity of the lesion for H3.3G34W, there is no evidence for the presence of a (malignant) giant cell tumor, which is already unlikely for the age. Considering the result of the clinical-radiological correlation in the context of the interdisciplinary tumor conference, the finding is classified as a manifestation of an osteoblastic osteosarcoma (high grade).

General Therapy Options

A simplified overview in chronological order recommends a biopsy with a tissue sample from suspicious areas. Preoperative chemotherapy, according to neoadjuvant therapy, is administered before surgery. Surgery with complete tumor removal and free histological margins are of upmost importance. A postoperative adjuvant chemotherapy, possibly with immunomodulator (Mifamurtide), are necessary after surgical excision of the tumor. Neoadjuvant chemotherapy according to study protocol (COSS, EURAMOS, EUROBOSS) in an oncology center is necessary. After neoadjuvant chemotherapy, biopsies are re-examined for tumor size, tumor type, resection status, and regression grade. To determine the regression grade, processing of a tumor slice in the largest diameter is necessary. It is crucial how much residual tumor is found in this slice (responder: less than 10% residual tumor). This allows a prediction of the need for a change in treatment in case of metastasis. The amount of healthy tissue varies, 2 cm for bones up to a fat lamella (1 mm) for vessels/nerves are recommended. Depending on the location of the tumor and its contact with vessels/nerves, this can lead to large remaining defects that can be reconstructed in various ways:

Methods of Biological Reconostruction

i) Bone shortening, rotationplasty, amputation

ii) Bone transplantation with own bone with or without vascular connection, rotations (clavicle pro humerus)

iii) Allogeneic bone transplantation (allograft)

iv) Replantation of "e.g., radiation-sterilized" own bones

Endoprosthetic Management

i) Tumor megaendoprostheses

Chemotherapy

i) Adjuvant chemotherapy to reduce the risk of metastasis (possibly also surgical removal of metastases)

ii) Possibly additional Mifamurtide (immunomodulator, approved in the EU since 2009)

iii) Tumor follow-up every 3 months using thoracic CT to detect possible lung metastases and the surgical area for 2 years

iv) Tumor follow-up every 6 months using thoracic CT to detect possible lung metastases and the surgical area for another 3 years

v) Tumor follow-up every 12 months using thoracic CT to detect possible lung metastases and the surgical area for another 5 years

vi) Tumors can only be treated with neoadjuvant chemotherapy. An exception are the very rare parosteal

osteosarcomas (G1), which are classified as having very slow division and metastasis rates.

Surgery

All tumors (primary and metastases) are surgically removed in healthy tissue (= with a safety margin). Osteosarcoma is not very sensitive to radiation, so radiation is generally not used.

Course and Prognosis of Osteosarcoma

With treatment, the 5-year survival rate averages 70%. Lung metastases are a poor prognostic sign, but they can be treated through surgery, allowing patients with lung metastases to achieve a cure. The most important prognostic factor is the response to chemotherapy (COSS scheme): If the chemotherapy is not effective, meaning less than 90% of tumor cells were killed, the survival chance is less than 50%. The number of killed cells is determined on the surgical specimen (tumor-bearing bone) after completion of preoperative chemotherapy. Almost always, an endoprosthesis must be implanted or reverse plastic surgery must be applied.

Discussion

Osteosarcoma is a rare, mostly highly malignant mesenchymal tumor with an incidence of 2-3/1,000,000 per year, whose cells directly form bone or osteoid [1-33]. It is the most common primary malignant bone tumor [1-33]. The peak incidence is in the second decade of life [2,7,9,23]. The primary tumor usually affects the metaphysis of a long bone, especially in the knee region [1,5,7]. Both primary (10-20%) and occult (approximately 80%) metastases primarily affect the lungs, and secondarily the skeleton. Osteosarcomas are mostly high-grade malignancies, but there are also higher differentiated tumors with lower metastatic potential (low-grade) [5,20,21]. About 80-90% of all osteosarcomas are "conventional," arising centrally in the bone marrow space as highly malignant osteosarcomas. Biologically similar tumors include telangiectatic osteosarcomas, high-grade surface osteosarcomas, small cell osteosarcomas, and extra skeletal osteosarcomas, which are classified as soft tissue sarcomas by the WHO. Paro steal and periosteal osteosarcomas originate from the bone surface [3,7,10,12]. Paro steal osteosarcomas are low-grade but can dedifferentiate into high-grade tumors (primary or in recurrence). Periosteal osteosarcomas have an intermediate malignancy grade (G2). In the current 8th version of the TNM classification by UICC and AJCC, the T-stage is based on the largest tumor diameter (≤ / >8 cm). If skip metastases - synchronous metastases in the tumor-bearing bone that are separate from the primary tumor - are present, the situation is classified as T3 regardless of tumor size. Lymph node metastases are very rare, so NX is considered as N0. Osteosarcomas with distant metastases limited to the lungs are classified as M1a, and those with extrapulmonary metastases as M1b [10,14,23]. The disease stages resulting from the TNM classification are listed in the table. Over 80% of osteosarcomas manifest in stage II. In addition to a subdivision into four grades of malignancy, scales with only three or even two grades (low or high malignancy) are used.

The median duration from the onset of the first symptoms and signs to diagnosis is 10 to 15 weeks. Clinically, the leading symptoms are usually increasing, initially perceived as load-dependent pain in the affected region [3,4]. Occasionally, the pain may not be directly in the tumor region but in another part of the affected skeletal segment. A local swelling may be noticed later, along with possible restriction of movement in the adjacent joint [14,16]. In jaw osteosarcomas, tooth loosening and early swelling may be apparent. For some patients, a pathological fracture is the first symptom. General symptoms are usually absent and, if present, indicate advanced metastasis.

Disclaimer (Artificial Intelligence)

Author hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Ethical Approval

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Conflict of Interest

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Contributor Statement

S.B. performed the analysis, wrote the manuscript and finished it according to the instructions for authors. E.L. and E.M. read the manuscript carefully and proved references and made recommendations to optimize the text.

Data Availability Declaration

The data that support the findings of this study are available on request from the corresponding author.

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