EWING SARCOMA

Ewing sarcoma are malignant tumors that usually occur in bone. Any bone can be the site of origin of an Ewing sarcoma. Rarely, they arise in soft tissues. The disease is named after James Ewing (1866-1943), a New York Pathologist and Cancer Researcher who first described this tumor back in 1921. Most Ewing sarcomas grow and spread very rapidly, making the disease fatal without effective treatment. In about a quarter of patients, visible metastases are already present at the time of diagnosis, mostly in the lungs, but also in bones or bone marrow. In addition, almost all patients have the smallest not yet visible metastases - so-called micro-metastases - which cannot yet be detected with conventional examination methods. Ewing sarcoma are therefore always considered diseases that affect the entire body (systemic disease). Current treatment protocols consist of multiagent systemic therapy and local control with either surgery, radiotherapy or both.

If a malignant bone tumor is suspected, an experienced center should be consulted: A sarcoma center with Pediatric Oncology/Hematology, for the treatment of children and experienced sarcoma surgeons. This is the case in our clinic. The Sarcoma Center of the West German Tumor Center is one of the largest sarcoma centers in Europe and treats the most people with a sarcoma disease in Germany. A highly specialized team of pediatric and adult oncologists, surgeons, radiation therapists, WPE, radiologists and pathologists work together at the Sarcoma Center. All patients are discussed in tumor conferences several times during the treatment to enable an optimal treatment.

If such a rare tumor is suspected, extensive examinations and the cooperation of specialists from different fields are necessary to determine whether a malignant bone tumor is present and, if so, what form of tumor it is and how far the disease has spread in the body. Clarification of these questions is a prerequisite for optimal treatment and prognosis of the patient. Subsequent treatment is carried out within the framework of a protocol established by experts in the field of Ewing Sarcoma. The Cooperative Ewing Sarcoma Study Group at Essen University Hospital is one of the world's leading research groups in the field.

ARE THERE RISK FACTORS FOR EWING SARCOMA?

Ewing sarcoma is rare and approximately three out of 1 million children, adolescents and (young) adults are affected by this disease each year. Ewing sarcoma is most frequently diagnosed in the second decade of life. The average age of onset is about 15 years, with boys and men more commonly affected than women and girls (gender ratio 1.3:1). However, Ewing's sarcoma can also occur in infants and in older adults. Ewing sarcoma mainly affects white people, is less common in people of Asian descent, and almost never occurs in black people.

It is still not known why the disease develops. The cancer cells develop from immature (undifferentiated) tissue cells, so-called mesenchymal stem cells, or from primitive neuroectodermal stem cells.

HOW DO EWING SARCOMA CELL LOOK LIKE?

Ewing sarcoma cells are classified histologically as mesenchymal small-, blue-, and round-cell tumors. Because of the rarity of the tumors, such differentiation is done in pathology laboratories that specialize in it. The Ewing sarcoma cells carry chromosomal changes in which a part of one gene is transferred to another gene. This is called translocation. This causes activation and signaling pathways in the cells to be altered so that the cells

degenerate, i.e., become malignant. In the most common translocation (85%), a piece of chromosome 22 (EWS) is joined to a piece of chromosome 11 (Fli1) [called a t(11;22) (q24;q12) translocation]. The translocations are so typical for Ewing sarcomas that their detection allows the diagnosis of the disease. Generally, such gene alterations detectable in tumor tissue are not inherited. Very rarely, Ewing sarcoma occurs as part of a so-called cancer predisposition syndrome, a hereditary predisposition to the development of tumors, or as a secondary malignancy, even many years after treatment of a primary cancer.

WHAT KIND OF SYMPTOMS DOES EWING SARCOMA CAUSE?

By far, the most common symptoms caused by Ewing sarcoma are pain and swelling in the area affected by the tumor.

The pain may be intermittent and often occurs initially after physical activity. In the course, the pain is also noticed during the night. The pain may be accompanied - with increasing tumor growth - by visible and/or palpable swelling, which may be accompanied by loss of function. It is not uncommon for these signs of disease to be initially misinterpreted as growing pains, an inflammation of the bone, or as the result of a sports injury.

Because Ewing sarcomas can arise in virtually any bone and soft tissue, further symptoms vary from person to person. A few affected individuals experience general symptoms such as fever, feeling ill, weight loss and/or general fatigue, which may indicate that the disease is already advanced. Several weeks or months may pass between the first symptoms and the diagnosis.

Good to know: Children and adolescents with symptoms such as those described here do not, of course, always have Ewing's sarcoma or another malignant bone tumor. Nevertheless, it is advisable to have any form of bone pain in childhood and adolescence that lasts longer than 4 weeks and cannot otherwise be explained carefully clarified to rule out a malignant disease.

HOW TO DIAGNOSE EWING SARCOMA?

A malignant bone tumor shows typical findings in the X-ray. With the help of additional imaging procedures such as magnetic resonance imaging (MRI) and/or cat scan (CT), the exact local extend and size of the tumor as well as its demarcation from neighboring structures (such as muscle and tendon tissue or joint capsules) can be visualized. The exact procedure is selected by the treating physician, depending on the tumor site. Carefully planned images are required for the planning of surgery and for monitoring the course of the disease during chemotherapy.

To confirm the diagnosis of Ewing sarcoma, a tissue sample (biopsy) must be taken in every case. The biopsy should be taken at a center experienced in the treatment of such tumors. This ensures that the access chosen for the biopsy does not lead to problems later in further treatment, i. e. impairs the definitive surgery.

The biopsy will be examined under the microscope (histologically). An additional molecular genetic examination detects the genetic alteration typical of Ewing sarcoma. Such examinations must be performed by experienced pathologists.

Further examinations follow to assess whether the disease has spread into other tissues (metastasis). Here, too, imaging techniques are used, and possibly further samples are taken. We need to know whether the tumor has spread into other tissues before starting treatment. A computed tomography scan of the chest is

performed to rule out lung metastases. An examination that images the entire body is also performed to rule out other foci. To determine if the bone marrow is affected, a bone marrow puncture is also performed.

WHAT HAPPENS DURING THE TREATMENT OF EWING SARCOMA?

The treatment of a patient with Ewing sarcoma consists of chemotherapy and local treatment with surgery and/or radiotherapy.

Treatment begins in all patients with several weeks of intensive chemotherapy (also called induction chemotherapy). The goal of this chemotherapy is to shrink and kill the tumor and any metastases that may be present, thus making the subsequent surgery safer. In addition, chemotherapy is used to combat the smallest, not yet visible metastases (micro-metastases) and is intended to prevent the tumor from spreading further.

To destroy as many malignant tumor cells as possible, a combination of different cell growth-inhibiting substances (chemotherapy) is used, which have proven to be particularly effective in combating Ewing sarcoma cells. The patients in Germany and many countries in Europe are being treated according to the study protocols and treatment recommendations of the Essen-based Cooperative Ewing Sarcoma Study Group.

Local treatment is usually given between the induction and adjuvant chemotherapy phases. Local treatment may consist of surgery and/or radiotherapy. The University Hospital Essen has a specific focus on the treatment of sarcomas with a highly specialized sarcoma surgery and radiation therapy, WPE, for the treatment of Ewing sarcoma. After local therapy, chemotherapy is continued. The intensity of the adjuvant treatment depends on the response to the induction chemotherapy or on the size and extent of the tumor at the time of diagnosis. For some patients, high-dose chemotherapy followed by autologous stem cell transplantation may be considered. In this case, the team specialized in cellular therapies will take care of you. The duration of treatment is about ten months.

WHAT HAPPENS WHEN THE TREATMENT IS FINISHED?

The follow-up investigations are performed according to a specific protocol. This provides for very close controls in the first two years and later controls at greater intervals.

You can find further and detailed information on the following webpage
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