MORPHOLOGICAL ASPECTS OF EWING'S SARCOMA IN CHILDREN AND ADOLESCENTS

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Abstract

Ewing's sarcoma, first describes by James Ewing, is an aggressive type of bone and soft tissue cancer that occurs mainly in children and young people. Ewing's sarcoma is the second most common type of bone cancer in children and young adults.

It occurs mainly in adolescents between the ages of 10 and 20. Only about **1% of cases occur in adults over the age of 40**. Despite its rarity in older populations, Ewing's sarcoma is a critical diagnosis to consider in adults with persistent bone pain or unusual soft-tissue masses. Ewing's sarcoma accounts for about 2% of childhood cancers and can occur in any part of the body, but most often affects the pelvis and the proximal sections of long tubular bones.

Ewing's sarcoma is part of a family of tumors known as Ewing sarcoma family of tumors (ESFT), which includes Ewing's sarcoma of bone, extraskeletal Ewing's sarcoma, and peripheral primitive neuroectodermal tumors (pPNET)

Location	Percentage (%)
Bone (~80%)	
- Axial Skeleton (45%)	
• Pelvis	20%
• Ribs	10%
• Other Axial Bones	15%
- Distal Skeleton (35%)	
• Femur	12%
• Humerus	4%
• Other Distal Bones	19%

Extraosseous (~20%)
Nonskeletal Primary Cancers
• Retroperitoneum
• Esophagus
• Pancreas
• Ileum
• Kidney
• Bladder
• Vagina
• Uterus
• Penis
• Adrenal Gland
• Lung
• Breast
• Spinal Cord
• Orbit
• Intracranial Tissue

Ewing's sarcoma is more prevalent in males than females, with a male-to-female ratio of approximately 1.5:1. It is also more common in individuals of European

descent and rare in individuals of African or Asian ancestry. The precise ethiology of Ewing's sarcoma remains unclear. Unlike other cancers, there is no strong association with environmental or hereditary factors. The only known risk factor is the presence of a specific genetic mutation involving the EWSR1 gene, which is discussed further in the pathology section.

The clinical and pathological symptoms of Ewing's sarcoma are highly different, therefore in many cases patients complain about localized pain, swelling at the site of the tumor and very frequently the bone fractures. Furthermore, there could be noticed nonspecific symptoms as night sweets, fatigue, weight loss and fever.

Key words: Ewings' sarcoma, bone cancer, pediatric oncology, EWS-FLI1 fusion, chemotherapy

Material and method of research

We had a retrospective study of works related to Ewings' sarcoma and its' morphofunctional changes in children and adults in the period of cancer's progression. All the articles and books that we, with our team, studied and observed were published under well-known doctors and scientists such as: **Dr. Paul Meyers, he** has published extensively on the treatment of Ewing's sarcoma, focusing on chemotherapy and clinical outcomes in pediatric and adolescent populations; Dr. Cristina R. Antonescu, she is a leading figure in the genetic and molecular pathology of sarcomas, including the identification of the EWS-FLI1 fusion in Ewing's sarcoma; Dr. Uta Dirksen, he has led several large-scale European clinical trials on Ewing's sarcoma, including the EURO-EWING consortium, which explores treatment protocols and long-term outcomes in children and adolescents with Ewing's sarcoma; Dr. Denise Reike Brohl, he has researched and published on the potential for immunotherapy in Ewing's sarcoma, as well as new therapeutic strategies targeting molecular pathways in sarcoma patients, and many others.

According to these studies we had brief information about all the types of Ewings' sarcoma, and what are the most efficient therapies for the patients with this aggressive cancer.

Results of the research and discussion

Ewing's sarcomas are most commonly found in adolescents because this sarcoma arises during developmental stage of the bones. Adolescents are in developmental phase hence prone to the disease. Adolescents are having immature immune system which is also one of the reasons.

Ewing sarcoma arises from primitive neuroectodermal cells. The hallmark of this cancer is a genetic mutation, specifically a translocation between chromosomes 11 and 22, which results in the formation of the **EWSR1-FLI1 fusion gene.** This genetic change drives the uncontrolled growth of the tumor cells. The

tumor typically originates in the long bones, such as the femur, tibia, or humerus, but it can also occur in flat bones like the pelvis, ribs, or even the spine.

While Ewing sarcoma primarily affects bones, it can also arise in soft tissues, including muscles and connective tissues. When this happens, it is referred to as extraosseous Ewing sarcoma. Both forms of the disease have similar genetic profiles and behaviors, although bone-based tumors are more common. The overall survival rate for localized Ewing sarcoma is around 70-80%, but this drops to 15-30% for patients with metastatic disease. The clinical and pathological symptoms of Ewing's sarcoma are highly different, therefore in many cases patients complain about localized pain, swelling at the site of tumor and very frequently the bone fractures. Furthermore, there could be noticed nonspecific symptoms as night sweets, fatigue, weight loss and fever. Parallel, lamellate periosteal new bone formation (onion skin) or less frequently, radiating spicules may be present

Ewing sarcoma is typically diagnosed using a combination of medical history, physical examination, imaging studies, biopsy, and laboratory tests. Studies implicate EWS-FLI1 in reducing TGF-β receptor levels, potentially targeted by antisense oligonucleotides to restore sensitivity and inhibit tumorigenicity.

Conclusion

Early recognition of symptoms, rapid imaging, and confirmatory genetic testing are essential to diagnosing Ewing sarcoma in its early stages. This approach increases the chances of successful treatment, reduces the risk of metastasis, and improves overall survival rates. Knowing that this cancer is more common in teenagers, especially during periods of rapid growth, can encourage healthcare providers and families to be more alert to symptoms like unexplained bone pain or swelling in this age group. Furthermore, physicians can prioritize age-appropriate differential diagnoses when teenagers present with persistent bone pain or swelling. Recognizing that Ewing sarcoma is a possibility in this age group helps avoid misdiagnosis or delays in treatment.

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