

Ewing's Sarcoma in an 18-Year-Old Girl. Clinical Case

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Abstract

Introduction: The Ewing sarcoma family of tumors comprises a group of small round blue cell neoplasms that primarily affect the skeleton in adolescent children. The incidence is approximately 2.8 per million in the United States and has remained relatively stable in recent decades.

Clinical Case: An 18-year-old female with an abscessed tumor mass on the left abdominal flank at the level of the axillary midline. The piece is removed and sent to the pathology service. The result of pathology was Ewing's Sarcoma of an extrahepatic type and the CD99 immunohistochemical analysis was positive.

Discussion: Ewing's sarcoma, the second most common primary bone tumor in pediatric age, is known for its scarcity of recurrent somatic anomalies. Apart from the chimeric oncoprotein that is derived from the fusion of EWS and FLI genes, recent genome-wide association studies have identified susceptibility variants near the EGR2 gene that regulate EWS-FLI DNA binding. However, to induce transformation, EWSFLI requires the presence of additional molecular events, including the expression of CD99, a cell surface molecule with critical relevance for the pathogenesis of Ewing sarcoma. The high expression of CD99 is a common and distinctive feature of Ewing sarcoma cells, and has been widely used for the differential diagnosis of disease; in the pathology service of immunohistochemically in our hospital reactions only CD 99 was positive.

Keywords: Primitive Neuroectodermal Tumor; Ewing Sarcoma; Pediatric Oncology; Immunohistochemistry; CD-99; Treatment; Survival

Introduction

To a large extent, progress in understanding, diagnosing, and treating cancer is the story of individuals: James Ewing was one of the giants. Despite personal tragedy and inherent weaknesses, he rose to become the leading pathologist of the tumors of his time and head the United States' first cancer center in New York [1,2]. The Ewing sarcoma (SE) family of tumors comprises a group of small round blue cell neoplasms that primarily affect the skeleton in adolescent children. The incidence is approximately 2.8 per million in the United States and has remained relatively stable in recent decades. Adult patients with these neoplasms have a worse prognosis than infantile groups probably related to earlier detection in children [3].

Ewing's sarcoma, primitive neuroectodermal tumor (PNET), Askin tumor, bone PNET and extra osseous SE together form the Ewing sarcoma (ESFT) family of tumors. These tumors originate from the neuroectoderm and are composed of undifferentiated neuroepithelial cells that have the ability to differentiate into neuronal, neuroglial, or other types of mesenchymal cells. The ESFTs are positive for periodic acid Schiff (PAS) and CD99 (MIC2).

The annual rates of incidence and mortality are 0.1/100,000 and 0.05/100,000, respectively. The ESFTs exhibit an irregular geographical pattern of incidence. Caucasians are affected much more often, while rates are much lower in populations in East Asia and Africa. ESFTs are considered a pediatric neoplasm, with ~ 80% of cases occurring before the age of 18 years. Diagnosis is often determined during the second decade of life. Approximately 20 - 30% of patients are younger than 10 years of age, and frequency decreases with increasing age [4].

SE is a highly aggressive and metastatic tumor in children and young adults caused by a chromosomal fusion between the Ewing sarcoma (EWSR1) point-1 region gene and the FLI1 transcription factor gene. ES is managed with standard treatments, including chemother-

apy, surgery, and radiation. Although the 5-year survival rate in primary ES has improved the survival rate of SE patients with metastasis or recurrence remains low. Several new molecular targets in SE have been recently identified and investigated in preclinical and clinical targeting and the function of receptor tyrosine kinases (RTKs), the fusion protein EWS-FLI1 and mTOR has been shown to be promising. Interest in the immunological responses of patients with ES has also increased. Immunotherapies have been considered using T cells, NK cells, cancer vaccines and monoclonal antibodies to SE, especially for patients with recurrences [5].

Clinical Case

An 18-year-old female presented to the outpatient general surgery clinic for presenting an abscessed tumor mass on the left abdominal flank at the level of the axillary midline, assuming that it was an abdominal wall abscess, it is punctured and serohematic fluid is obtained weight without obtaining purulent material, soon it is proceeded to exéresis of the tumor type pseudo cystic of very thin walls which is broken when manipulating it observing trabecular tissue in its interior and abundant serohemático liquid and blood clots.

The piece is removed and sent to the pathology service. Previous ultrasound had reported: lobulated lipomas on the left flank of 8 cm. New ultrasound reported lobulated cystic lesion at L2-L3 level with irregular septa and reinforcing nodules of 7.2 x 7.8. X 7.6 cm (Figure 1, 2).

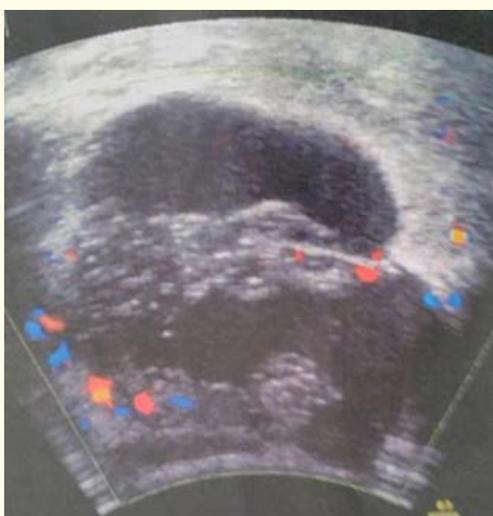


Figure 1: Lipomas lobulated on left flank.



Figure 2: Lobular cystic lesion at L2-L3 level with irregular septa and reinforcing nodules.

The result of pathology was Ewing sarcoma of an extra skeletal type with positive CD99 immunohistochemical analysis measuring 6.5 x 5.4 x 4.1 cm with positive tumor margins. The patient reports that 18 months earlier a "lipoma" had been removed at the same site and that she had grown again. The patient's file is obtained and the previous surgery is confirmed. CT scans of the abdomen; chest and skull were not found in any metastases. The patient is referred to a hospital of high specialty to the oncology service for its management and corresponding follow-up. Currently the patient has not presented new tumor growth with normal scarring at the surgical site.

Discussion

Ewing's sarcoma (EWS), the second most common primary bone tumor in pediatric age, is known for its scarcity of recurrent somatic anomalies. Apart from the chimeric oncoprotein that is derived from the fusion of the EWS and FLI genes, recent genome-wide association studies have identified susceptibility variants near the EGR2 gene that regulate EWS-FLI DNA binding. However, to induce transformation, EWSFLI requires the presence of additional molecular events, including the expression of CD99, a cell surface molecule with critical relevance for the pathogenesis of EWS. The high expression of CD99 is a common and distinctive feature of EWS cells, and has been used to a large extent for the differential diagnosis of disease, in the pathology service of our hospital immunohistochemical tests only the CD99 was positive [6].

The transcription factor Friend Leukemia Integration 1 (FLI-1) is also a useful marker in the diagnosis of Ewing's sarcoma / peripheral primitive neuroectodermal tumor, however, its positivity is more reliable when used in combination with other markers Set of differentiation CD99 [7].

Likewise, the likelihood that the molecular analysis of t (11; 22) reordering involving EWS / FLI-1 genes would have diagnostic value in Ewing's sarcoma (ES) and in primitive neuroectodermal tumors (PNET) was found That while EWS expression does not appear to be specific for ES/PNET, analysis of FLI-1 expression along with CD-99 is a powerful marker for ES/PNET and important factors in the differential diagnosis of SRCT [8].

One aspect we were worried about was metastasis because our patient reported intermittent dizziness and headaches, but the body scan did not show any. CNS metastases are rare and late in children with sarcomas of bone/soft tissue, although in the work of Bekiesinska-Figatowska M., *et al.* [9] is more frequent (3.45%) than in other reports (0.7%). Ewing's sarcoma tends to metastasize to the bones of the skull and soft tissue sarcomas have several morphological forms.

Standard first-line treatment for patients with these tumors includes chemotherapy with a five-drug regimen of vincristine, doxorubicin (Adriamycin®) and cyclophosphamide, alternating with ifosfamide and etoposide (VAC/IE). In cases of inadequate response, a number of second-line regimens are available. However, more treatment options are required for those patients with disease that do not respond to standard treatment. Trabectedin is a new treatment option for patients with ESFT [10].

Eribulin at cytotoxic concentrations and co-treatment with Eribulin at subtoxic concentrations together with BI 6727 arrest cells act at the M-phase of the cell cycle before the onset of cell death. This mitotic arrest is followed by increased phosphorylation of BCL-2 and BCL-xL, as well as deregulation of MCL-1, suggesting the inactivation of these anti-apoptotic proteins of the BCL-2 family [11].

Children, adolescents, and young adults treated with Ewing's sarcoma (ES) are at risk for complications related to disease and treatment-related. Therefore, they are at high risk of relapse/progression and secondary cancers [12].

Conclusion

The Ewing tumor is rare in our country and given that our hospital does not have the oncology service, our patient was referred to a Regional High Specialty Hospital in the Peninsula for follow-up and control. This tumor is the first to be reported in our hospital and was initially managed by the general surgery service of our hospital.

Conflict of Interest

None.

Ethical Approval

None for being a retrospective study.

Financial Support

None.

Bibliography

1. Huvos AG. "James Ewing: cancer man". *Annals of Diagnostic Pathology* 2.2 (1998): 146-148.
2. Brand RA. "The Classic. The Bulkley Lecture: The Modern Attitude Toward Traumatic Cancer". *Clinical Orthopaedics and Related Research* 470.3 (2012): 642-662.
3. Verma V., *et al.* "A Comparison of Pediatric vs. Adult Patients with the Ewing Sarcoma Family of Tumors". *Frontiers in Oncology* 7 (2017): 82.
4. Uyeturk U., *et al.* "Clinical outcomes and prognostic factors of adult's Ewing sarcoma family of tumors: single center experience". *Contemporary Oncology (Pozn)* 20.2 (2016): 141-146.
5. Yu H., *et al.* "Potential approaches to the treatment of Ewing's sarcoma". *Oncotarget* 8.3 (2017): 5523-5539.
6. Martinelli M., *et al.* "CD99 polymorphisms significantly influence the probability to develop Ewing sarcoma in earlier age and patient disease progression". *Oncotarget* 7.47 (2016): 77958-77967.
7. Ahmed S., *et al.* "Immunohistochemical detection of FLI-1 protein expression in Ewing Sarcoma/ peripheral primitive neuroectodermal tumour: A study of 50 cases". *Journal of Pakistan Medical Association* 66.10 (2016): 1296-1298.

8. Llombart-Bosch A and Navarro S. "Immunohistochemical detection of EWS and FLI-1 proteins in Ewing sarcoma and primitive neuroectodermal tumors: comparative analysis with CD99 (MIC-2) expression". *Applied Immunohistochemistry and Molecular Morphology* 9.3 (2001): 255-260.
9. Bekiesinska-Figatowska M., et al. "CNS Metastases from Bone and Soft Tissue Sarcomas in Children, Adolescents, and Young Adults: Are They Really So Rare?" *BioMed Research International* (2017): 1456473.
10. Hernando-Cubero J., et al. "Metastatic extraskeletal Ewing's sarcoma treated with trabectedin: A case report". *Oncology Letters* 12.4 (2016): 2936-2941.
11. Weiß LM., et al. "Eribulin alone or in combination with the PLK1 inhibitor BI 6727 triggers intrinsic apoptosis in Ewing sarcoma cell lines". *Oncotarget* (2017).
12. Friedman DN., et al. "Morbidity and mortality after treatment of Ewing sarcoma: A single-institution experience". *Pediatric Blood and Cancer* (2017).

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