Introduction

Ewing’s sarcoma (ES) is a malignant tumour composed of small round cells. It is related to peripheral primitive neuroectodermal tumours (PNET) having the same genetic alteration and response to chemotherapy. These tumours present a specific 11;22 translocation that can be used to establish the correct diagnosis. PNETs have multimodal treatment: surgery for the resection of the tumour, chemotherapy and radiotherapy for the control of systemic disease. This type of approach has improved the survival rate for the patients with PNET.

Keywords: Ewing’s sarcoma; peripheral primitive neuroectodermal tumours (PNET); treatment.

Material and Methods

The paper presents theoretical and practical aspects of Ewing’s sarcoma/PNET and appropriate treatment. Because of the rarity of this disease, there are few scientific papers on this topic.
Ewing’s sarcoma is part of a group of tumours called “small round cell tumour of childhood” along with neuroblastoma, lymphoblastic lymphoma, rhabdomyosarcoma. The tumours belonging to this group have multiple histological and immunohistochemical similarities and it is quite difficult to differentiate one from another. Every tumour has its own immunohistochemical pattern that must be searched and identified in order to establish the correct, definitive diagnosis. For example, lymphoblastic lymphoma has high immunoreactivity to CD99 and to leukocyte common antigen (LCA) (CD45), while ES/PNET has no/low immunoreactivity to LCA; both lymphoblastic lymphoma and ES/PNET have the same membrane pattern. Neuroblastoma is immunoreactive to NSE, S-100 and neurofilament protein, while ES/PNET is not. Rhabdomyosarcoma is immunoreactive to CD99 like the ES/PNET, but the staining is usually focal, weak, and cytoplasmic; Rhabdomyosarcoma is also immunoreactive to desmin and actin and weakly positive to NSE like neuroblastoma, but negative to LCA (CD45) like ES/PNET.

Ewing’s sarcoma typically occurs in children and adolescents. It can very rarely be found in adult individuals. There have been described two types of Ewing’s sarcoma: skeletal and extraskeletal, having similar histological, immunohistochemical, molecular and genetic features. The most frequent site of appearance is the long bones of the limbs and the pelvis. The development of Ewing’s sarcoma in the head and neck area is rare, about 2-3%, the mandible and maxilla being

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the most common location. ES/PNET rarely occurs in the nasal cavity and paranasal sinuses; in the English literature were reported only 12 cases until 2007, most of them described in the nasal cavity and maxillary sinus.

Epistaxis, nasal obstruction and discharge, facial pain, swelling of the face with asymmetry are the most encountered symptoms of the ES/PNET in the rhinological area. The unilaterality of the symptoms is characteristic for these tumours.

Figure 2: Ewing’s sarcoma of the nose with extension in the pterygopalatine region

The imagistic investigation (CT/MRI) establishes the tumour true dimension, its relationships with the surrounding structures (soft tissue invasion, bone erosion) and offers the surgeon a key for the complete resection of the tumour.

The correct, complete and definitive diagnosis is based on tissue biopsy after histological, immunohistochemical and molecular genetic investigations. The histological findings consist of small, round cells with round or oval nuclei and scant cytoplasm. The presence of CD99 (MIC-2) in immunohistochemical investigations is characteristic of Ewing’s sarcoma, as well as the identification of 11;22 translocation in the genetic analysis. This translocation – t(11;22)(q24;q12) – can be identified in 85% of ES/PNET cases by PCR molecular analysis. In 30% of the cases can be observed trisomies 8 and/or 12 along with the specific translocation.

The treatment of ES/PNET is multimodal: surgical approach for complete resection of the tumour, when possible in association with systemic radiotherapy and chemotherapy. The five-year survival rate has increased with the multimodal strategy of treatment by 70% compared to single or dual therapy, according

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3 Masaki Kawabata, Kosuke Yoshifuku, Yukari Sagara, and Yuichi Kurono, op. cit. pp. 75-78.
Figure 3: Coronal CT image-naso-sinusal tumour

Figure 4: Axial CT image-naso-sinusal tumour
to some authors\textsuperscript{5}. The longest disease free interval reported after multimodal treatment for ES is 59 months\textsuperscript{6}. An important role in choosing the treatment strategy for head and neck ES/PNET is played by the localisation of the tumour, dimension of the tumour, age of the patient, and general clinical status of the patient\textsuperscript{7}. Multi-agent systemic induction chemotherapy can be administered preoperatively in order to improve the result of the surgery to obtain complete resection of the tumour and maintenance chemotherapy can be applied after surgery. Chemotherapy uses a combination of the following drugs: vincristine, doxorubicin, cyclophosphamide, adriamycin, etoposide, actinomycin D and ifosamid\textsuperscript{8}. Radiotherapy is used to control subclinical micrometastases and can be associated with polichemotherapy. The dose of radiotherapy used for the treatment of ES/PNET is 40-45 Gy for postoperative radiotherapy and 45-60 Gy for definitive radiotherapy in order to achieve the best outcome\textsuperscript{9}. For children, radiotherapy can be avoided if the local control of the tumour is achieved with surgery, due to the long term effects of this treatment. Radiotherapy is related to growth defects, late toxicity, risk of malignancies (leukemia or solid malignant tumour), and it is eluded every time the complete removal of the tumour with free resection margins can be accomplished\textsuperscript{10}. Aggressive surgery with complete removal of the tumour and tumour free resection margins is essential for a good long-term outcome of the patient, especially when treating children with ES/PNET\textsuperscript{11}, but the multimodal approach to these “small round cell tumours” is the golden standard of treatment.

The follow up of the patients with ES/PNET must be thoroughly planned and it consists of CT or MRI for entire body (chest, abdomen, brain, bones)


\textsuperscript{7} J. Thariat, A. Italiano, F. Peyrade, I. Birtwisle-Peyrottes, L. Gastaud, O. Dassonville, and A. Thyss, \textit{op. cit.}


\textsuperscript{10} Ibidem.

to search for second tumours, complete blood tests and periodic endoscopic examination (for the ES/PNET in the head and neck region).

In the literature are described two types of metastatic relapses: early (within the first three years from the first diagnostic tumour) and late (after five years from the diagnosis of primary tumour). The early metastases are proven to have a poorer prognosis and there are authors who claim that 85% of the metastases occur in the first three years\textsuperscript{12}. In case of late relapse, curative treatment can be performed – surgery for the complete removal of the metastatic tumour, multi-agent chemotherapy and radiotherapy (if the patient was not irradiated for the primary tumour)\textsuperscript{13}.

**Conclusions**

The treatment of choice for the ES/PNET is multimodal: surgery for local control of the tumour associated with multi-agent chemotherapy and radiotherapy. This type of management has proved its efficacy by increasing long-term survival rates in military personnel. An important element in the therapy of ES/PNET is the “aggressive” follow up (periodic CT/MRI of chest, abdomen, brain, bones; periodic endoscopic examination, complete blood counts) for early detection of the metastatic relapses.
