ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of Ewing’s sarcoma of bone

Incidence

- The incidence rate is ∼0.1 cases/100000/year. It occurs mainly in childhood and adolescence with a median age of 14 years and 90% of patients are <20 years. Fifty per cent of patients have extremity and 20% have pelvic tumours. The mortality is ∼0.05/cases/100000/year.

Diagnosis

- Patients with radiological findings suggesting a bone sarcoma should be referred without prior biopsy to a centre with particular bone sarcoma experience. Ewing’s sarcoma is usually dominated by a large soft tissue component. Histological diagnosis is made by needle biopsy or open surgical biopsy. The Ewing family of tumours (ES) includes classical Ewing’s sarcoma and primitive neuroectodermal tumour (PNET), and these are treated identically. ES are rare tumours arising in the bone marrow from primitive neural elements and constitute ∼10% of bone sarcomas. ES can be distinguished immunohistochemically from other pediatric ‘blue tumours’ by expression of the MIC2 gene. Detection of the translocation t(11;22)(q24;q12) by cytogenetics or PCR is diagnostic (present in >90%).

Staging and risk assessment

- Prior to biopsy, the entire affected bone should be evaluated radiologically. Pulmonary metastases should be evaluated by CT scan and bone metastases should be ruled out by bone scintigraphy. Bone marrow aspirates are mandatory for light microscopy examination. Sperm banking should be considered.
- Approximately 20% of patients have detectable metastases at diagnosis, most commonly in the lungs and/or bone/bone marrow. Adverse prognostic factors include metastatic disease, pelvic localisation, tumour diameter >8–10 cm, age >15 years, elevated serum LDH, poor histological response to preoperative chemotherapy and radiotherapy as the only local treatment [III, B]. Lung metastases alone have a better prognosis than skeletal metastases (30% versus 10% 5-year survival [IV, C]).

Treatment plan

Localised disease

- Combination chemotherapy as part of a multidisciplinary approach has significantly increased 5-year survival rates from <10% to ∼60% [III, B]. The most commonly used drugs are doxorubicin, vincristine, cyclophosphamide, ifosfamide, dactinomycin and etoposide. The number of courses is 12–15 and total treatment time is 8–12 months. Some protocols differentiate treatment intensity and duration according to risk groups. Treatment is divided into induction chemotherapy (3–6 courses) followed by local therapy and consolidation chemotherapy (8–10 courses). Local therapy is surgery, radiotherapy (RT) or a combination of both. Despite Ewing’s sarcoma being a radiosensitive tumour, surgery is the preferred treatment for local control. A wide surgical margin should be attempted, and RT should be limited to patients with marginal or intralesional surgery, or with inoperable tumours. Radiation dose will depend on tumour site but should be 40–45 Gy for microscopic residual disease and 50–60 Gy for macroscopic disease.

Metastatic and recurrent disease

- Patients with metastatic disease at diagnosis should have the same standardised chemotherapy as patients with localised disease [III, C]. For patients with lung metastases who are in complete remission, total lung irradiation should be considered, and thoracotomy should be considered for patients with limited residual macroscopic disease. Supplemental irradiation of bone metastases is usually indicated. With the possible exception of patients with a limited relapse after a long disease-free interval, patients relapsing systemically or locally from ES should be considered to be in a palliative situation [III, C].

Follow-up

- Patients should be followed at 3-month intervals until 3 years after the end of treatment, then at 6-month intervals until 5 years and at 8–12 month intervals until at least 10 years after the end of treatment. Ideally patients should be followed longer due to long-term toxicity and a 5% risk of second cancers (particularly acute myelogenous leukaemia irrespective of RT and secondary sarcoma in the RT field) [III, B].

Note

Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the expert authors and the ESMO faculty.

Literature


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