

Osteosarcoma

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Osteosarcoma is the most common malignant bone tumour found in children and young adults. The annual incidence is 65 cases per year which represents 5% of all childhood cancers (0.5 cases per 100 000 per year). Non-metastatic osteosarcoma is currently curable in about 70% of cases.

These guidelines do not relate to radiation-induced osteosarcoma or that occurring in Paget's disease. They were validated in December 1998 and will be updated according to the publication of new data.

DIAGNOSIS

Plain X-rays of bone remain indispensable for confirming the presence of bone pathology. Lesions are typically localized in the metaphyseal region of long bones, as mixed osteolytic osteoblastic lesions or cortical lytic lesions, with periosteal reaction and adjacent soft-tissue mass.

Technetium bone scanning is used to detect the growth plates, and also skip metastases and distant spread. The examination should be done in three phases to study the functional characteristics of the radio-isotope uptake over time. A thoracic CT scan detects lung metastases not visible on chest X-ray. Thin (about 1 cm) cuts should be taken, if possible by spiral scanning (level of evidence B). MRI and bone scan must be done before surgical biopsy to avoid artefacts from haemorrhage, oedema and bone healing. CT scanning and arteriography are no longer used routinely to study the primary tumour. An arteriogram done immediately preoperatively can in some cases identify venous tumour emboli, provided this is a dynamic scan.

DIAGNOSIS

The biopsy must be taken by the surgeon who is to eventually do the definitive surgery. He/she must be experienced in this type of surgery. The biopsy should be of adequate size and representative of the tumour. Surgical drainage should be avoided. The incision must be placed in an area that will be excised at the time of eventual resection. In some very specialized units, a core-needle biopsy may be sufficient to make a firm diagnosis, but this requires particular expertise with regard to interpretation and is not yet standard practice. The role of the pathologist is very important for both the diagnosis and in evaluating the subsequent response to chemotherapy (level of evidence A).

STAGING

Patients are generally classified as having metastatic or non-metastatic disease. Age, tumour volume and site of tumour have been reported as prognostic variables, but these are not consistent.

Alkaline phosphatase, LDH, renal function and cardiac echogram should be documented prior to therapy.

TREATMENT MODALITIES

Children should be treated according to an appropriate multicentre trial, such as SFOP and adults within FNCLCC or EORTC protocols.

Chemotherapy

Protocols combining neo-adjuvant chemotherapy and adjuvant chemotherapy have superior efficacy to protocols of adjuvant chemotherapy alone (level of evidence B). However, there are no randomized trials comparing these therapeutic options. Chemotherapy must be given by teams experienced in the use of aggressive and toxic protocols with provision of full medical and haematological supportive care. Preoperative chemotherapy generally combines a number of agents (standard). A variety of protocols can be proposed: high-dose methotrexate + doxorubicin, doxorubicin + cisplatin, high-dose methotrexate + cisplatin + doxorubicin, ifosfamide + cisplatin (Figure 1).

High-dose methotrexate is effective and widely used in children (level of evidence B). It is generally given at a dose of at least 12 g m⁻² to children. In adults, a test dose may be used to define the dose that will give an identical area under the concentration curve for all patients, and is usually at least 8 g m⁻². In general, the scheduling of methotrexate is identical in adults to children. It must be possible to measure methotrexate levels and to support with dialysis if necessary. The methods of high-dose methotrexate administration will vary according to different protocols, but facilities to provide rigorous hydration, clinical surveillance, regular blood tests and folic acid rescue must be in place at all times.

Randomized trials have suggested a combination of cisplatin and doxorubicin may be comparable to more complex multiagent regimens (level of evidence B).

Surgery

Surgery must be undertaken by an experienced surgeon who is familiar with the indications for amputation if conservative surgery is contraindicated. For localized disease, the biopsy scar should be resected and the tumour removed 'en bloc' without being opened (level of evidence B) (Figure 2). The limits of excision must be wide and clear histologically. A sample of the proximal marrow must be taken for analysis. Several surgical options are possible: reconstructive surgery using prostheses, reconstruction using bone graft, either autologous or allogeneic, and rotationplasty.

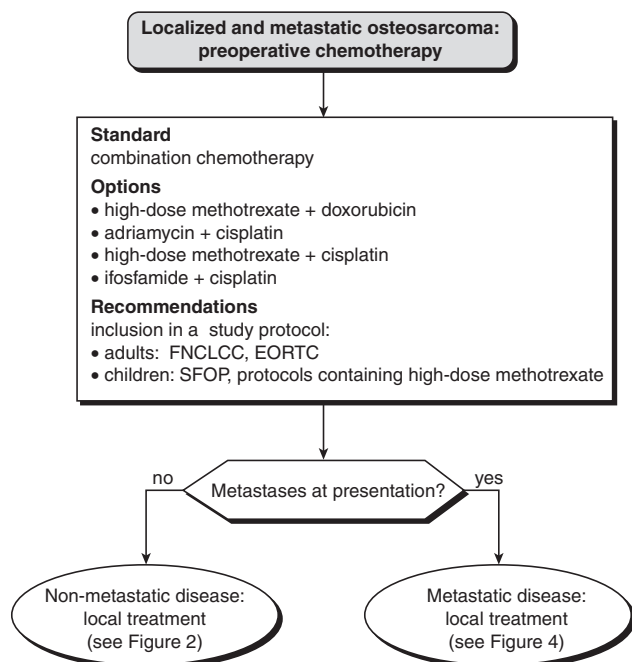


Figure 1 Preoperative chemotherapy for osteosarcoma

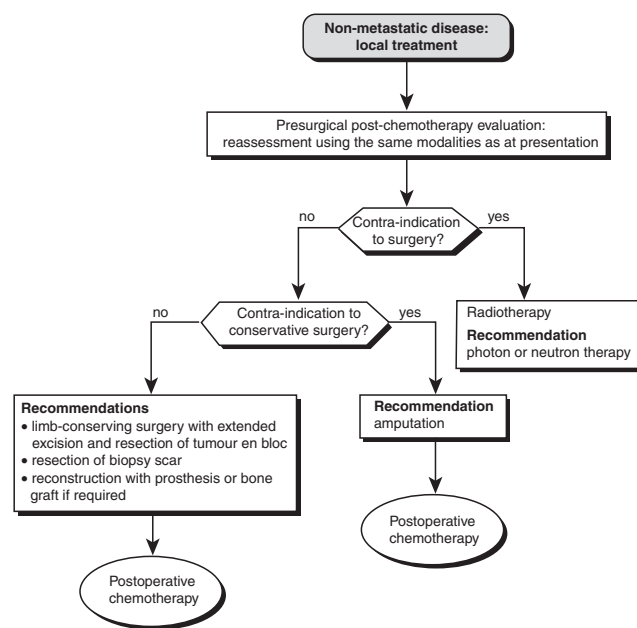


Figure 2 Treatment of local disease

The result of primary chemotherapy is documented by Huvos' histological grading on excised tumour (Figure 3). Good and bad responders to chemotherapy are defined. At present in France, the definition of a good response is if there is less than 10% of viable tumour cells in the sample. The response to preoperative chemotherapy is the single most important prognostic factor (level of evidence B). Various medical imaging techniques are under evaluation to determine the efficacy of chemotherapy. These include MRI, PET and Thallium scans. The results are at present unreliable in predicting response (level of evidence A). These tests should only be done in the context of an evaluable protocol.

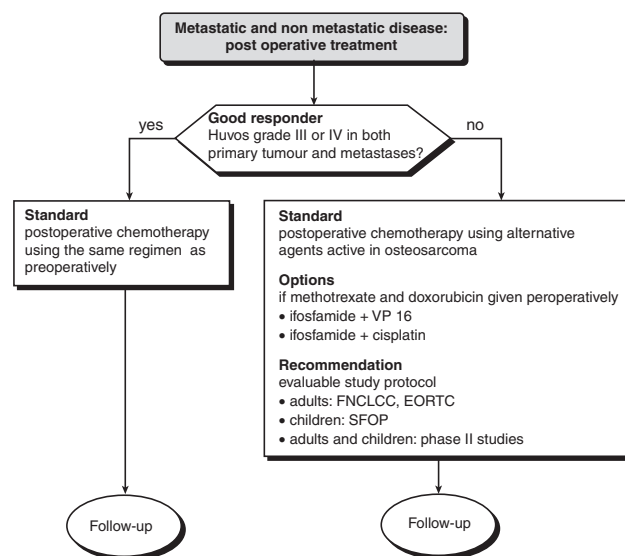


Figure 3 Postoperative treatment

The existence of metastases at presentation, in particular if they are single, should not lead to abandoning the possibility of curative treatment (level of evidence B). Amputation of limbs is only done under exceptional circumstances. Aggressive surgery to lung metastases following primary chemotherapy may be appropriate (Figure 4).

Radiotherapy

Radiotherapy may be indicated in the case of inoperable tumour. Options for irradiation include high dose, between 55–70 Gy according to site, and also photon or neutron therapy. Radiotherapy may also be useful for palliation of locally recurrent disease.

FOLLOW-UP

Few studies have compared the method and timing of follow up for osteosarcoma. Recommendations are as follows (level of evidence B):

- Chest X-ray every 2 months, for years 1 and 2, every 3 months for years 3 and 4, every 6 months for years 5 and 6, then annually.
- CT scan (if there were lung metastases at presentation) every 6 months for the first year and then every year until the fourth year.
- Plain X-ray of bone and MRI are only done in the case of local symptoms. Technetium bone scan may be done every 4 months for years 1 and 2, every 6 months for years 3 and 4 and then only in the case of symptoms. The role of bone scan remains debatable, however, as there is no useful therapeutic intervention in the event of distant bone metastases.

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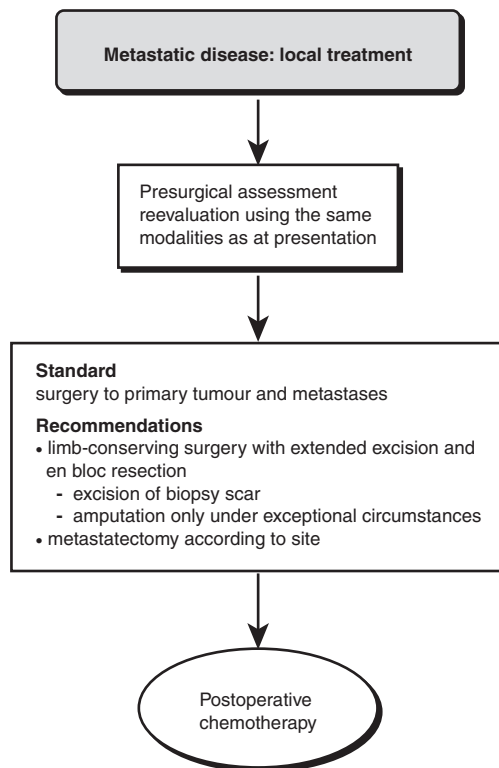


Figure 4 Treatment of metastatic disease

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