CLINICAL REPORT

Fatal lung metastasis secondary to index finger giant cell tumor in an 8-year-old child


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**KEYWORDS**

Pediatric bone tumor; Giant cell tumor bone; Lung metastasis; Lethal complication

**Summary**

We report the case of a 7-year-old girl presenting with giant cell tumor (GCT) of the index finger, complicated by lung metastases. Index disarticulation, pulmonary metastasectomy and chemotherapy failed to produce a cure, and the child died at the age of 8 years after 1 year’s evolution. The pulmonary metastases were discovered following hypoxia during initial biopsy. A review of the literature shows this observation to be original, in terms of the patient’s age and of the location, onset and fatal outcome of metastasis. The hypoxic episode complicating biopsy raises the issue of early screening for lung metastases in GCT. Pulmonary dissemination of GCT is of severe prognosis.

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**Introduction**

Giant cell tumor (GCT) usually concerns young adults and presents as epiphyseal osteolytic long-bone tumor [1—3]. Lung metastasis is a rare complication, with low associated mortality [4,5]. We report a case of GCT in an 8-year-old girl who died following respiratory distress caused by lung metastasis. The case is original due not only to the patient’s young age but also to the GCT site on the distal phalanx of the index finger with lung metastases discovered on biopsy of the primitive lesion. Varied chemotherapy was unable to control pulmonary dissemination.

**Observation**

A 7-year-old girl presented with inflammatory pain in the index finger. X-ray found heterogeneous osteolysis of the third phalanx (P3) (Fig. 1). The bone was swollen, with cortical lysis involving the growth cartilage. MRI (Fig. 2) showed medullary replacement in iso-signal with respect to joint and conjunctive cartilage on the various sequences. Gadolinium injection sharply enhanced the lesion; there was also soft-tissue contrast uptake.

Surgical biopsy was prescribed, and was complicated by a perioperative episode of hypoxia requiring prolonged oxygen
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therapy. Chest X-ray (Fig. 3) was performed immediately, and found numerous bilateral parenchymatous pulmonary nodules suggestive of multiple bilateral pulmonary metastases. The hypoxia was controlled by nasal cannula oxygen therapy at 2 l/min.

Anatomopathologic examination of the bone biopsy sample diagnosed cytologically benign giant-cell tumor (Fig. 4). Extension was assessed: technetium 99 bone scan found a single hyperfixation zone on P3 of the index. Chest MRI confirmed the presence of bilateral pulmonary nodules. PET scan confirmed metabolic hyperactivity in P3 and the two pulmonary fields (Fig. 5).

Pulmonary nodule biopsy by thoracotomy demonstrated GCT metastasis without malignancy criteria (Fig. 6). Chemotherapy was initiated, but the progression observed in the inflammatory aspect of the primitive tumor led to distal trans-interphalangeal disarticulation.

Analysis of the surgical sample confirmed the initial diagnosis, and the absence of any necrosis demonstrated the inefficacy of the chemotherapy. Although the cytological and architectural aspect was normal, there were numerous tumoral lymphatic emboli; the resection edges were healthy.

Histology of the primitive tumor and pulmonary metastasis biopsies was checked and confirmed by the French Bone Pathology Group (Groupe français de pathologie osseuse [GFPO]).

Varied chemotherapy failed to prevent impairment of respiratory function. The first course associated etoposide, carboplatin and bisphosphonates, and the second

Figure 1  Index finger X-ray: heterogeneous osteolysis of the third phalanx.

Figure 2  MRI of lesion with Gadolinium injection: sharp enhancement of lesion and neighboring soft tissue.

Figure 3  Chest X-ray following biopsy: numerous bilateral pulmonary parenchymatous nodules.

Figure 4  Bone biopsy histology, with hematoxylin-phloxine-saffron (HPS) staining: numerous multinuclear giant cells.
doxorubicin and gemcitabine. Both having failed, an anti-angiogenic association was tried: very small “metronomic” daily doses associating cyclophosphamide—celecoxib, then etoposide—celecoxib, provided only transitory respiratory improvement and were stopped; a palliative anti-EGFR monoclonal antibody/cetuximab treatment was finally given.

The patient died of acute respiratory distress 15 months after the primitive tumor biopsy.

Discussion

The present observation combines several points that are unusual in bone GCT, with a hand locus in a child less than 10 years old, complicated by fatal lung metastasis: the case is quite exceptional.

GCT usually occurs in young adults, generally in their 20s [1]; it is rarely found in the second decade and even more rarely before growth cartilage closure [2,3,6]. Picci et al. [3], in a meta-analysis, found only 1.7% of cases under the age of 15 years. When earlier than bone cartilage closure occurs, the tumor is located metaphysically, generally respecting the physis [7,8]. GCT generally occurs in the long bones, especially distal femur and proximal tibia; the hand is rarely involved, with only five out of 248 cases in one single-center series [1].

GCT is to be managed surgically. Resection may consist in curettage or monoblock excision [6]. The almost complete bone lysis found in the present case made curettage impossible and index disarticulation unacceptable without histologic diagnosis. Simple biopsy was therefore initially performed.

Bone defect secondary to curettage can be treated by autologous or synthetic bone graft [6].

Overall recurrence is about 30% [9], but higher in case of location in the hand [10]. Various adjuvant treatments (acrylic cement [6], or phenolization and cryotherapy [11,12]) have been reported in an attempt to reduce recurrence, but their contribution is debatable: the quality of the curettage or resection would seem rather to be the determining factor for recurrence [13].

Lung metastasis following GCT treatment has been known for many years [14,15]. Such unfavorable evolution is rare but not unprecedented: Dominkus et al. [16] found a 2.1% rate in a series of 649 GCTs, and Bertoni et al. [4] 7.2% in a series of 97. Extrapulmonary metastasis is extremely rare [8,17]. Lung metastasis secondary to GCT in a hand or foot bone is rare, with only two cases reported [18,19].

Unlike in the present case, lung metastasis is very rarely discovered during diagnosis of the initial GCT, but rather in case of recurrence, at a mean 2 to 3 years. Local recurrence is indeed a known risk factor for lung metastasis, with a six-fold higher risk according to Rock [13].

We were surprised to discover lung metastases on biopsy. The immediate postoperative respiratory distress might have been prevented if preoperative chest X-ray had been performed. Systematic preoperative chest X-ray should perhaps be considered in case of bone lesion biopsy suggestive of lung metastasis. Other than local recurrence, an analysis of the literature found several other lung metastasis risk factors in GCT: an aggressive X-ray aspect (Enneking grade 3) [4,16,20], Ki 67 antigen expression [21], and a distal radius location [22]. Tumoral lymphatic emboli, found in the present case, on the other hand, are non-predictive of generalized dissemination [4].

Although lung metastases tend to occur only some years after diagnosis [4,5], chest X-ray and CT scan should nev-
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Lung metastases are usually excised [4,13,19]; where surgery is unfeasible, chemotherapy is sometimes able to control evolution [16], and comprises adriamycin, dacarbazine, vincristine, cytoxan, actinomycin, or bleomycin [4,5,16]. Lung metastases may spontaneously evolve towards necrosis or ossification [23]. Radiotherapy [19] is contraindicated due to the risk of induced malignancy.

Mortality associated with GCT lung metastasis ranges from 0 to 40% according to the series: for 69 cases compiled from the literature [4,5,16,19,21], there were six deaths: i.e., 9% mortality. Death may be caused directly, as in the present case of respiratory distress, or by massive hemoptysis, or else indirectly via chemotherapy side-effects such as sepsis associated with agranulocytosis, or epistaxis with associated coagulation disorder [4]. In conclusion, chest X-ray should be performed as of the onset of GCT, whatever the aspect, location or patient’s age. Prognosis in case of lung metastasis is reserved: where surgery is not feasible, chemotherapy does not always succeed in preventing unfavorable evolution. The present case confirms the possibility of GCT occurring in a child before growth cartilage closure.

Conflict of interest statement

None.

References