Spontaneous expectoration of pulmonary metastases in a child with osteogenic sarcoma.

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Abbreviations

OGS	Osteogenic Sarcoma
ED	Emergency Department
MRI	Magnetic Resonance imaging
CT	Computed tomography
MAP	Methotrexate, doxorubicin, cisplatin
IE	Ifosfamide, etoposide
FDG	Fluorodeoxyglucose
RECIST	Response evaluation criteria in solid tumors
ECOG	Eastern cooperative oncology group
L-MTP-PE	Liposomal muramyl tripeptide phosphatidyl ethanolamine
SPIND	Single patient investigational new drug
FDA	Food and Drug administration
IRB	Institutional review board

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Spontaneous expectoration of pulmonary metastases in a child with osteogenic sarcoma.

To the editor: Pulmonary metastases from solid tumors can be parenchymal (peripheral) or endobronchial (central) (1). Endobronchial metastases are rare events, most frequently reported with breast, colorectal, kidney, stomach and prostate primaries (2). Occasionally, endobronchial metastases present with spontaneous expectoration of the metastatic tissue (1). Although there are few reports of spontaneous expectoration of the tumor tissue in adult literature, there is no such case reported in pediatric literature. We report a case of spontaneous expectoration of metastatic osteogenic sarcoma (OGS) tissue in a child.

A 9 year old female presented to the ED with pain and swelling of the right thigh after a fall in soccer field. X-ray of the leg showed a mass lesion on right lower femur, which was confirmed with a MRI leg. CT chest showed numerous bilateral pulmonary metastases, but bone scan was negative for bone metastases. Biopsy of the primary lesion was consistent with OGS. She was treated with methotrexate, doxorubicin, cisplatin (MAP) + zoledronic acid with addition of ifosfamide and etoposide (IE) following local control (rotationplasty). Her pulmonary lesions were not resectable due to high number of lesions and concern about the capacity of the residual lung tissue after resection of all the metastatic nodules. At completion of standard chemotherapy, her CT scan showed multiple residual pulmonary lesions with minimal FDG avidity in some of the pulmonary nodules, overall stable disease (RECIST 1.1), (ECOG performance score 1). Due to persistent pulmonary disease, she received maintenance sorafenib, everolimus and zoledronic acid. At 22 months from diagnosis, routine imaging showed new FDG-avid pulmonary lesions and increased FDG-avidity in older lesions, suggesting progressive disease. One week later, she presented to the hospital for respiratory distress secondary to complete collapse of right lung from a new metastatic lesion in the right main stem bronchus (Fig 1A, 1B, 1C), (ECOG performance score 3). She received targeted

3000 cGy local radiation and her respiratory distress improved significantly. Post-radiation CT scan showed partial opening of right main stem bronchus (Fig 1D, 1E). Her chemotherapy was changed to gemcitabine and docetaxel. At 27 months from diagnosis, she expectorated a piece of necrotic tissue with degenerate cells and intermixed arborizing matrix (osteoid), consistent with post radiation necrotic changes in the tumor tissue (Fig 2). Post expectoration CT scan showed complete opening of the right main stem bronchus (Fig 1F, 1G, 1H), resolution of the intrabronchial metastasis and she returned to her baseline activity level (ECOG performance score 1). She continued to have other metastatic lesion in pulmonary parenchyma. At 30 months from diagnosis, she had disease progression when routine imaging documented development of new liver metastasis, which was treated with heat ablation. Systemic chemotherapy was changed to high dose methotrexate followed by liposomal muramyl tripeptide phosphatidyl ethanolamine (L-MTP-PE) as Single Patient Investigational New Drug (SPIND) after FDA and IRB approval (Fig 3).

At 34 months, patient developed back and abdominal pain and spontaneously expectorated pieces of tissue two times in an interval of two weeks. Pathologic evaluation of one of these specimens was again consistent with metastatic OGS making a total of three episodes of expectoration of tissue from metastatic OGS. Subsequently, L-MTP-PE was discontinued and she pursued alternative treatment options.

Expectoration of tumor tissue is a very rare event with only 30 reported cases in the literature (3), predominantly from metastatic cancers and only a few primary lung cancers. Most common metastatic cancers presenting as expectoration were renal cell carcinoma (4-7), colon cancer (8-9) and fibrosarcomas (10-11) while common lung primary cancers presenting with expectoration include squamous cell carcinoma, small cell lung cancer, bronchogenic carcinoids and primary sarcoma of lungs (12-16). Expectoration of the primary lung cancer occurs because of exfoliation of free tumor fragments in the airway. But endobronchial

metastases expectorate by releasing tissue into the airway after treatment related ulceration and necrosis (5).

Although endobronchial metastases are rare, they can cause airway obstruction and should be considered in the setting of acute worsening of the respiratory status. Local control with endoscopic surgery, radiation therapy, chemotherapy can relieve the airway obstruction and improve symptoms, and should be considered.

Conflict of interest

Authors of this case report have no conflict of interest to report.

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Legends

Figure1. A, B, C: Occlusion of right main stem bronchus with endobronchial metastatic lesion, presenting with respiratory distress D, E: Partial opening of the right main stem bronchus post radiation with resolved atelectasis F, G, H: Complete opening of the right main stem bronchus post expectoration of tumor tissue following radiation and chemotherapy.

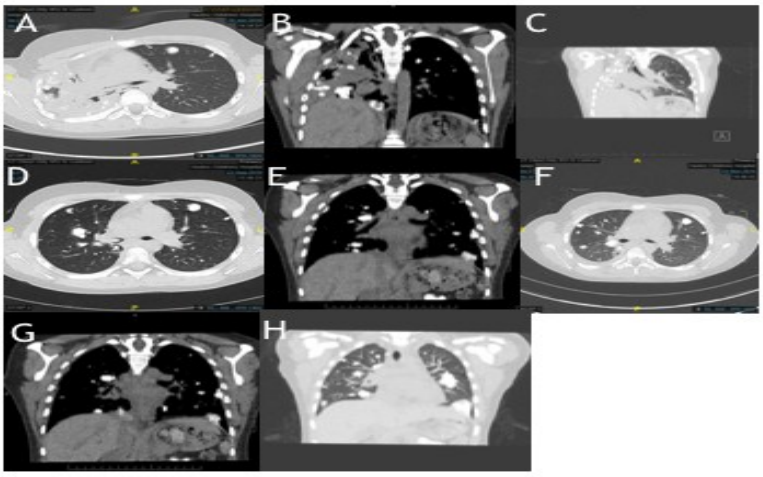


Figure2. A: Low power image demonstrates a very vascular lesion with moderate cellularity and an attenuated epithelial lining at the top (arrow) B: A medium power image: a more cellular area with associated vascularity and the epithelial lining at the top. Islands of bone (arrows) are noted. C: This high power image: a focus with tightly packed tumor cells that are more atypical and associated with bone formation. Two mitotic figures (arrows) are noted.

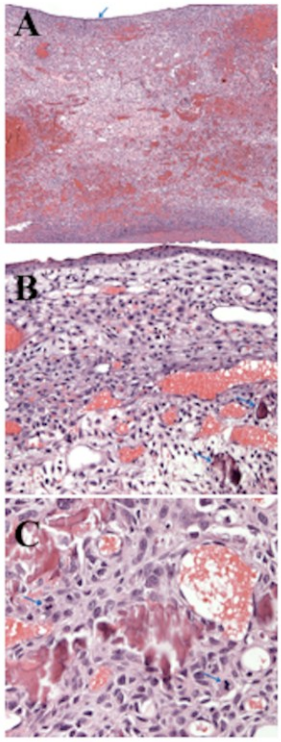
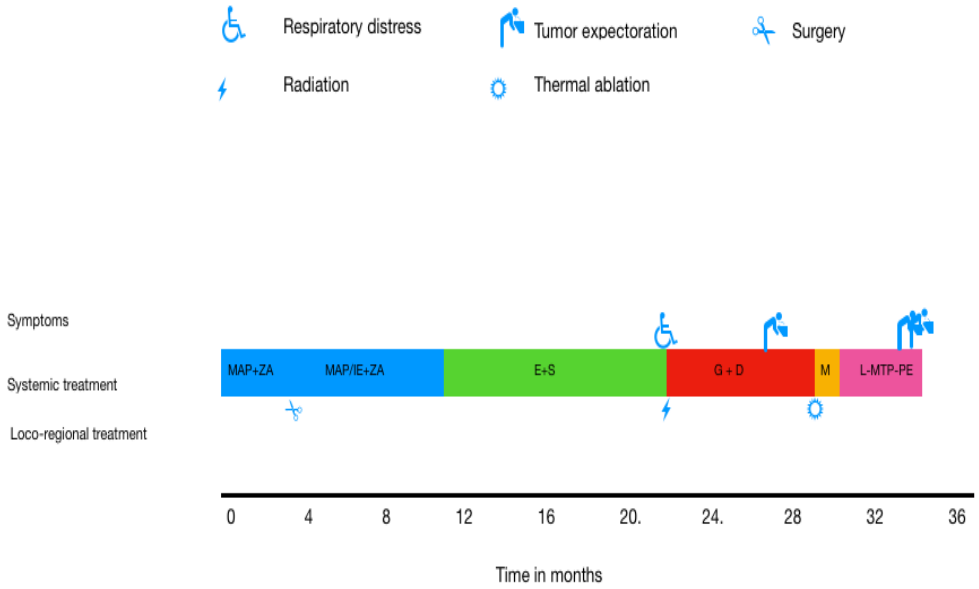


Figure3: A summary of tumor directed treatments received by the patient with time line.



Abbreviations: MAP: methotrexate doxorubicin cisplatin; IE: ifosfamide etoposide; ZA: zoledronic acid; E: everolimus; S: sorafenib; G: gemcitabine; D: docetaxel; M: methotrexate; L-MTP-PE: liposomal muramyl tripeptide phosphatidyl ethanolamine;