Seminars in Pediatric Surgery (2012) 21, 79-87

ELSEVIER

SEMINARS IN PEDIATRIC SURGERY

Surgical treatment of lung metastases in patients with embryonal pediatric solid tumors: an update

Joerg Fuchs, MD,[a] Guido Seitz, MD,[a] Rupert Handgretinger, MD,[b] Juergen Schäfer, MD,[c] Steven W. Warmann, MD[a]

From the [a]Department of Pediatric Surgery and Pediatric Urology, Children's Hospital, University of Tübingen, Tuebingen, Germany;
[b]Department of Pediatric Hematology and Oncology, Children's Hospital, University of Tübingen, Tuebingen, Germany; and
[c]Department of Diagnostic and Interventional Radiology, Children's Hospital, University of Tübingen, Tuebingen, Germany.

KEYWORDS
Lung metastases;
Children;
Diagnostic;
Surgery;
Outcome;
Osteosarcoma;
Wilms tumor;
Hepatoblastoma;
Ewing sarcoma;
Neuroblastoma

Distant metastases regularly occur in children with solid tumors. The most affected organ is the lung. Nearly in all extracranial pediatric solid tumors, the presence of lung metastases is associated with an adverse prognosis for the children. Therefore, the correct treatment of lung metastases is essential and influences the outcome. Despite different national and international trials for pediatric tumor entities, specific surgical aspects or guidelines for lung metastases are usually not addressed thoroughly in these protocols. The aim of this article is to present the diagnostic challenges and principles of surgical treatment by focusing on the influence of surgery on the outcome of children. Special points of interest are discussed that emphasize sarcomas, nephroblastomas, hepatoblastomas, and other tumors. Surgery of lung metastases is safe, has a positive impact on the patients' prognosis, and should be aggressive depending on the tumor entity. An interdisciplinary approach, including pediatric oncology and radiology, is mandatory in any case.

The outcome of children with solid tumors has improved significantly over recent years as the result of many national and international cooperative group treatment protocols. Generally, the stage-independent overall survival rate for nonmetastatic pediatric solid tumors is 75%-90%. Currently, the main challenge is to improve the treatment of children with advanced or recurrent tumors in addition to those with metastatic disease.[1]

Approximately 10%-40% of all children with solid tumors present with lung metastases at the time of diagnosis (Table 1). Despite the advances in chemotherapy, stem cell transplantation, radiation therapy, and immunotherapy, the outcome for these children has not improved significantly. The survival ranges from 20% to 70% and depends on several prognostic factors such as histology and response to chemotherapy. If pulmonary metastases persist after initial chemotherapy, there are several options for local treatment, including surgery, radiotherapy, or the combination of both. Surgery of lung metastases is an important tool given the possible late effects after chemotherapy and/or radiotherapy, including cardiomyopathy, secondary malignancies, breast aplasia, or impairment of pulmonary function.[2-5]

The aim of this review article is to define the role of surgery in the treatment of lung metastases with the main

Address reprint requests and correspondence: Joerg Fuchs, MD, Professor of Pediatric Surgery and Paediatric Urology Department of Pediatric Surgery and Paediatric Urology, Children's Hospital, University of Tübingen, Hoppe, Seyler, Street 3, 72076 Tuebingen, Germany.
E-mail: joerg.fuchs@med.uni-tuebingen.de.

1055-8586/$ -see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1053/j.sempedsurg.2011.10.008

Table 1 Incidence and outcome of children with solid tumors and isolated pulmonary metastases

Tumor entity	Metastases at diagnosis, %*	Availability of independent prognostic factors	Impact of radical surgery for prognosis	Outcome 5-year survival, %*
Nephroblastoma	10	Yes	High	80
Osteosarcoma	15-20	Yes	High	10-40
Rhabdomyosarcoma	30-40	Yes	Low	30
Ewing or PNET	15	Yes	Unclear	30-40
Hepatoblastoma	20	No	High	50
Neuroblastoma	3-4	No	None	35

PNET, primitive neuroectodermal tumor.
*Averaged data based on the literature analyzed in this article.

focus on nephroblastoma, osteosarcoma, and hepatoblastoma. We will highlight the diagnostic challenges, the relevant surgical principles and analyze the therapeutic outcomes.

Methods

The present article summarizes a literature review of the past 5-7 years and assesses the major conclusions on the basis of the authors' own experience. A special emphasis was placed on the presentation of clinical advances as well as challenges of treatment.

Imaging, diagnostic challenges, and labeling of lung metastases

According to the different study protocols, most children with newly diagnosed solid tumors undergo plain chest radiography. There is an ongoing debate regarding the use of plain radiographs vs computed tomography (CT) scans for staging. CT scanning is clearly more sensitive than chest radiography in detecting pulmonary lesions. The detection of lung lesions through CT scanning often results in an upstaging of the patients and has important clinical implications because of the subsequently intensified treatment with greater potential toxicity.[6] Specificity of CT scans is lower than for plain radiographs and lesions are frequently identified which are benign.[7-10] There is also variability among reviewers of CT scans. Central review of thoracic CT scans is often used for staging within current cooperative studies to address this issue.[11]

However, the CT is generally considered the gold standard in diagnosis of pulmonary metastases because it is more sensitive than standard radiographs and essential for judging the response of metastases to chemotherapy/radiotherapy and for successful planning of surgery.

Different techniques exist for performing a thoracic CT scan (eg, single-slice vs multislice high-pitch helical CT) as well as various reconstruction algorithms ranging from the 3-5 to 1-mm slice thickness with high-resolution kernel. To achieve the best technical results, we use both thin-slice maximum intensity projection and multiplanar images (Figure 1).

From the practical point of view, CT scans should be examined prospectively for planning of metastatic resection by the same radiologist and the same surgeon on a workstation in consensus reading. This approach is essential for an exact planning of the surgical approach and management of the lung parenchyma.

Relevant differences have been described between the pre- and intraoperative detection of lung metastases. The analysis from Kayton et al[9] and our own investigations have clearly demonstrated, that even in the era of modern CT scanning, the number of intraoperatively identified lesions often far exceeds the number identified by CT. A discrepancy of up to 30%-40% is often encountered, and the risk of underestimation increases with the number of metastases (Figure 2). The definition of the cut-off point, which describes the exact correlation between the CT findings and the intraoperative detection, ranges between 5 and 10 lesions and depends on the tumor entity and the size of the nodules.[9,12]

Table 2 shows the variety of different benign pathologies that were considered osteosarcoma metastases on preoperative CT scan.[9] PET-CT may help define these lesions, but no prospective studies have assessed its specificity or sensitivity in pediatric tumors. However, some radiologists believe that because of their size, PET scanning is not helpful in assessing small questionable lesions, even if they are tumors.

Small lesions that are not visible on the surface of the lung are a particular challenge. This is frustrating because these are just the lesions a surgeon would prefer to resect thoracoscopically. A possible solution to this problem has been proposed: CT-guided labeling of intraparenchymal metastases with use of the Somatex equipment. The Somatex coil is introduced under CT guidance surrounding the lesion (Figure 3). The success of this technique has been reported in adults, but not in children.[13] The advantage of the Somatex system is a minimal risk of needle dislocation or pneumothorax. Our preliminary experiences with 4 cases show that consecutive thoracoscopic resection is safer and easier and avoids use of a thoracotomy.

Another method to identify pulmonary lesions is with a radionuclide scanner device after preoperative injection of a