

Pulmonary metastasectomy – general issues

Metastazectomia pulmonară – aspecte generale

Ciprian Bolca,
Ioan Jentimir,
Georgiana Fotache,
Tudor Mateescu,
Cristian Paleru,
Ioan Cordoș

Thoracic Surgery Division,
"Marius Nasta"
Institute of Pneumology,
Bucharest, Romania

Correspondence:
Ciprian Bolca
"Marius Nasta" Institute of
Pneumology
90 Sos. Viiilor, 5th district,
Bucharest, 050159, Romania
e-mail: bolcaciption@gmail.com

Abstract

Pulmonary metastasectomy has been widely accepted by thoracic surgeons and is applied to the treatment of a variety of histologies, but the evidence that the patient may benefit from lung metastasectomy is not yet elucidated and the best way of integrating oncologic therapies (induction or adjuvant chemotherapy or radiotherapy) with surgical resection are still unknown. When there is no good clinical alternative, the resection of pulmonary metastases can give some patients long-lasting disease free intervals. Patients should be carefully selected on the basis of clinical staging with defined prognostic indicators. In order to obtain suitable results the management of these patients should be based on a multidisciplinary team decision.

Keywords: pulmonary metastasectomy, oncologic therapy, multidisciplinary team

Rezumat

Metastazectomia pulmonară este o procedură practică pe scară largă de chirurgii toracici pentru controlul determinărilor secundare pulmonare ale diverselor tipuri de tumori primitive. Dovezile științifice referitoare la rezultatele acestor intervenții chirurgicale și integrarea lor în contextul mai larg al managementului oncologic al acestor pacienți nu sunt încă foarte clare, dar acolo unde nu există o alternativă de tratament mai potrivită, aceste intervenții pot asigura un control mai bun al maladiei neoplazice, aparent și cu beneficii de supraviețuire. Pentru obținerea unor rezultate adecvate strategia de tratament se bazează pe selectarea cu foarte mare atenție a pacienților, iar deciziile cele mai potrivite sunt luate în cadrul unor comisii pluridisciplinare.

Cuvinte-cheie: metastazectomie pulmonară, tratament oncologic, echipă multidisciplinară

Introduction

Pulmonary metastasectomy is a simple term which describes a great variety of surgical procedures, performed for the purpose of removing the metastases at the level of the pulmonary parenchyma, under certain conditions, for the purpose of prolonging survival of the patients or even healing them. Such surgical procedures have been performed for a long period of time (several decades) but a consensus has not been reached regarding the application strategy of this form of treatment. In the last few years, these procedures have been taken into consideration as part of the customized treatment of neoplastic diseases, but the results are still uncertain and difficult to quantify in the context in which there is a multitude of factors which influences them.

We do not pretend to clarify all unclear aspects regarding these cases, but through this article we wish to draw attention to this pathology, because in everyday practice we encounter a large number of patients who would have probably benefited at a given time during their evolution of these surgical procedures and to whom the surgical timing has been lost.

We know from the beginning that the patients in our care have systemic neoplastic diseases - stage IV - and the surgical treatment in such cases represents salvage surgery, which tries to remove the macroscopic tumour tissue, which cannot even be eliminated with the latest chemotherapy regimens; the role of the systemic ecological treatment is however extremely important for the attempt to sterilize the microscopic outbreaks which cannot be removed by the surgeon.

Diagnosis

The term "oligometastatic" was first mentioned in 1995¹ and referred to a subset of patients with disseminated neoplastic disease, but in which the number of secondary determinations was low, initially established arbitrarily five metastases. Subsequently, by extrapolation, this term has begun to be used within the interdisciplinary groups for the establishment of the therapeutic protocol in cases of patients, which were still regarded as having a curative potential for the advanced neoplastic disease under discussion. In this context, the situations also referred to by the subject of the article shall be regarded as an oligometastatic neoplastic disease.

The basic mechanisms for the metastatic spreading of the various types of tumours are only superficially known, and the clinical incidence of isolated pulmonary metastases (determinations only at the level of the pulmonary parenchyma) varies greatly according to the location and type of the primitive tumour. Studies carried out on large autopsy series have shown that the lung is the second location as far as the frequency of the distant dissemination is concerned, in case of patients who died due to neoplasms (29%) and also that the lungs represent the only metastatic localization in 20% of the cases.²

Detection of pulmonary metastases is closely connected to the long-term tracking of the patient, after the initial management of the primitive tumour. Their presence may be totally asymptomatic or it may mimic all the symptoms of the primitive pulmonary tumours, from which they also need to be carefully differentiated in the case of unique metastasis. Obviously, most frequently,

pulmonary lesions are detected by means of classical chest X-ray. However, the discovery of this kind of lesions involves modern imaging techniques (CT, MRI, PET) in order to clearly establish the extent of the disease.

Why do we mention imaging investigations? Because the important aspects regarding the surgical tactics depend on the correct assessment of the lesions, the first generation of CT scanners identified the vast majority of lesions, but not all; thoracotomy and palpation of the lung have been (and still are, according to the authors) the basic approach of this pathology. In up to 25% of the cases, more metastatic lesions were being identified by systematic palpation than those identified by means of imaging³.

Subsequently, along with the rapid development of CT devices and the emergence of spiral imaging acquisition, numerous non-metastatic pulmonary nodules have been identified; thus, surgical procedures have been resized regarding time and scale, sometimes not justified. The emergence and use of the PET examination have hardly clarified this issue, the false negative or false positive results being widely known, depending on the size and associated pathology of the patients.

We shall discuss in a subsequent article the aspects regarding the actual surgical approach of pulmonary metastases. Until then it is worth mentioning that a more elaborate imaging investigation of patients who are suspected to be suffering from a metastatic disease is of a vital importance because (with a few exceptions which shall be subsequently mentioned) the pulmonary metastases have a surgical indication when the **primary tumour is controlled** (or controllable), meaning there are no signs of local recurrence and **there are no other metastases** except the pulmonary ones.

The clinical staging of these patients raises a series of questions. As previously mentioned, there is a certain possibility of some false positive imaging results, the eye of the radiologist and/or clinician being in this regard of vital importance, especially for nodules of small dimensions. Many times, a small, unique lesion, without imaging characteristics of malignancy, is better tracked for a period of time (3 - 6 months) and surgically removed at the first possible changes, rather than subject the patient to a useless thoracic surgical procedure.

Once again, it is very important to differentiate a unique metastatic nodule from a primitive pulmonary tumour. The cases when we are faced with such a situation are rare, but these patients require a complete battery of pneumological investigations because both the expected surgical procedure as well as the subsequent oncology treatment is very different. Such aspects are to be taken into consideration, especially when there is a history of initial primitive tumours directly linked to smoking (urothelial neoplasms or high respiratory tract). Obtaining histopathological or preoperative cytological information in these cases may greatly improve the surgical approach. As a curiosity, when we meet a unique epidermoid pulmonary lesion and we have a history of squamous cell carcinoma of the high aerodigestive tract, meaning that

immunohistochemistry shall not be able to establish the differential diagnosis between a pulmonary primitive or a secondary determination, the surgical procedure shall be performed as for a squamous lung cancer, survival being superior in this way, the conclusion being that in case of heavy smokers we encounter more frequently a second primitive lung cancer than a metastasis⁴.

Other aspects which shall be established by the diagnosis stage of the management of these patients are linked to the number of lesions and the unilateral or bilateral localization, important elements of prognosis in the surgery of pulmonary metastases. It has been proven based on retrospective series that a unique metastasis has a better prognosis than multiple metastases and the unilateral localization is superior in terms of survival to bilateral localization. These data have become more obvious after the publication of larger series of cases which have taken into consideration the treatment of secondary pulmonary determinations spread from a single type of primitive tumour⁵. It should be mentioned that the number of pulmonary metastases does not represent a surgical contraindication as long as **complete resection** is possible, this also being the most important prognostic factor in this type of surgery. Obviously, the surgical approach regarding access to the thoracic cavity, as well as the planned resection shall be in accordance with the localization of the lesions and their dimensions.

Neoplastic involvement of mediastinal adenopathies is a factor of negative prognosis. The anatomy and physiology of the thoracic lymphatic system, the dissemination ways of neoplastic diseases are just partially known⁶. We cannot always preoperatively establish if the mediastinal and/or hilar adenopathies are involved by malignancy; however, if this suspicion exists, mediastinoscopy and/or EUS/EBUS may be revealing in this regard. Although it should not be taken as an axiom, in general, the great majority of authors recommends abandoning the surgical treatment and continue with specific oncology treatment when the mediastinal implication is proven⁷. It is very important that during the surgical procedure an extended mediastinal lymphadenectomy is performed⁸ for complete resection as well as for the clear establishment of the extension of the disease and the orientation of the subsequent oncology treatment.

The assessment of the patient prior to the surgical procedure shall take into consideration all typical aspects of thoracic surgery. The pulmonary reserve of the patient shall carefully be calculated according to the volume of pulmonary tissue intended to be resected. Bronchoscopy is mandatory, about 2% of these patients having intrabronchial secondary determinations, an aspect that changes the type of surgical resection planned. As a general rule, the performed resections shall be the smallest possible, preferably atypical resections or enucleation with resection limit in the healthy tissue; occasionally, depending on the localization, lobectomies may be considered, the need to perform a pneumonectomy for complete resection being usually a surgical contraindication.

Patient Selection

As previously mentioned, pulmonary metastasectomy shall be taken into consideration in the context of customized treatment of neoplasms to each individual patient. The elements agreed by all authors refer to several criteria for the selection of patients.

- The primary tumour is controlled or controllable
- There are no extrathoracic localizations (with an exception for the colorectal neoplasm which we shall explain later)
- There are no other proven effective methods of treatment
- The general condition of the patient allows the proposed resection
- Complete resection seems possible in compliance with the preoperative investigations

The control of the primary tumour represents a basic element, there are no signs of local recurrence or in case of synchronous metastasis the possibility of its resection is obvious. In certain circumstances, we may start with pulmonary surgery in order to be sure that the complete resection of the metastases is successful, before preparing a mutilating resection of the primitive tumour (for example an enlarged member amputation in case of sarcoma). If pulmonary metastases are associated with a local recurrence, we may consider pulmonary surgery only after its complete control. Worth mentioning is the fact that the disease free interval (DFI), meaning the duration from the treatment of the primary tumour until the emergence of metastases, is a prognosis factor recognised by numerous authors. Practically, the higher the DFI is the better the survival after surgery of the metastases⁹.

A complete restaging is necessary in order to establish the pulmonary localization of secondary determinations. As an exception, in case of colorectal neoplasm, good results have been obtained in combined liver and lung resections for metastatic disease, both synchronous and metachronous¹⁰. Moreover, in case of colorectal neoplasm, the surgical cure of metastasis is considered as possibly having a curative aim (!!!) if complete resection is obtained, obviously associated with specific oncology treatment.

With respect to the pre and postoperative oncology treatment, this is to a large extent linked to the type of primary tumour and the treatment received until the emergence of the pulmonary metastases. For chemosensitive tumours it is better to start the treatment with a first line chemotherapy agent, and eventually second line, if available, and then in case of residual metastatic disease the pulmonary metastasectomy should be considered. In case of more chemoresistant tumours, for example osteosarcoma, the resection surgery of secondary determinations is initially recommended, subsequently supplementing with oncology treatment. Radiotherapy may also be considered when we are dealing with mediastinal lymph node involvement or incomplete resection.

In certain cases, repeated procedures of pulmonary metastasis resection have been described. Such cases are rare and require restoring of the previously men-

tioned staging, but the results are encouraging, the survival rate being superior compared with patients who did not undergo resection¹¹.

Conclusions

When approaching patients with pulmonary metastasis, multiple factors should be taken into consideration which may influence the prognosis of the disease. There are no rules yet regarding this pathology and most likely these patients shall be discussed within the context of the basic neoplastic disease and more rarely in pneumologic context. Following the publication in the last few years of a series of patients more and more consistent, the series grouped according to the type of primary tumour have already given a number of answers; however, for the time being only partial. The lack of prospective studies and the impossibility to randomize the series due to the numerous different elements between patients shall continue to fail in offering clear answers. What is clear is the fact that each patient, to whom resection of pulmonary metastases may be considered, shall be discussed by a multidisciplinary board with a view to decide the appropriate treatment. The results obtained on the published series, with obvious increases of survival in case of resected patients are encouraging. ■

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