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The Assessment of Primitive or Metastatic Malignant Pulmonary Tumors in Children

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Rezumat

Evaluarea tumorilor pulmonare maligne primitive și metastatice la copil

Introducere: Scopul studiului nostru este de a evalua tumorile maligne pulmonare la copii, primitive și metastatice. Prezența tumorilor pulmonare la nou-născuți și copil reprezintă un punct de interes din partea specialiștilor în chirurgia pediatrică, chirurgia toracică și genetică, din cauza procentului de mortalitate crescut. EUROCARE-study comunică o rată de supraviețuire la peste 5 ani de sub 10% pentru tumorile primitive și sub 15% pentru metastazele pulmonare.
Material și Metodă: Am efectuat un studiu retrospectiv care a analizat 11 copii cu tumori pulmonare primitive maligne și metastatice, internați în Clinica de Chirurgie Pediatrică "Prof. Dr. Al. Pesamosca" a Spitalului Clinic de Urgențe pentru Copii "Maria Curie Sklodowska", București. Pacienții care au fost analizați și la care s-a intervenit chirurgical în studiu, au fost operați de Prof. Dr. Al. Pesamosca și autori în perioada 1985-2011. Lotul studiat a cuprins 4 tumori primitive și 7 secundare: s-au operat 8 pacienți, iar 2 cu tumori primitive au decedat înainte de a fi operați. Incidența tumorilor primitive pulmonare este mai mare pentru fete, 3:1, iar tumorile metastatice pulmonare sunt diagnosticate mai frecvent la baieti, 6:1.
Rezultate: Pacienții cu tumori pulmonare primitive au fost diagnosticați tardiv. Aceștia au avut vârsta cuprinsă între 1-6 ani; 3 au fost operați, dintre care 2 au decedat, iar 1 operat supraviețuiește. Cei 7 pacienți cu tumori pulmonare metastatice au fost de asemenea tardiv diagnosticați, probabil ca o consecință a detectării tardive a tumorii de origine.
Concluzii: Deși toate afecțiunile maligne impun un diagnostic și tratament precoce, realizarea acestui obiectiv, în cazul tumorilor pulmonare maligne la copii, rămâne o dorință care animă pe toți practicienii. Tumorile primitive sunt diagnosticate având ca principală formă de manifestare infecțiile bronhopulmonare, iar tumorile pulmonare metastatice sunt de obicei asimptomatice și se diagnostichează prin monitorizarea pacienților cu o altă localizare tumorală primară. Rezultatele chimioterapiei, radioterapiei și chirurgicale ale tumorilor maligne primitive sau metastazelor la copii rămân nesatisfăcătoare din cauza diagnosticului tardiv și metodelor de tratament limitate. Actualmente ingineria genetică a identificat oncogenele responsabile de explozia blastică pulmonară și rezultate mult mai bune s-ar putea obține prin chirurgia genetică.

Cuvinte cheie: tumori pulmonare primitive, tumori pulmonare secundare, metastaze, copii, toracoscopie, bronhoscopie, citodiagnostic

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Abstract

Background: The purpose of our study is to assess primitive and secondary malignant pulmonary tumors in children. The presence of lung tumors in newborns and infants is a point of interest to specialists in pediatric surgery, thoracic surgery and genetics due to the high death rate. The 5-years survival rate

communicated by EUROCARE-study is less than 10% for primitive tumors and less than 15% in lung metastases.
Materials and Method: We performed a retrospective study which analysed 11 children with pulmonary primary or metastatic tumors admitted in the Pediatric Surgery Department "Prof. Dr. Al. Pesamosca" of the Emergency Clinical Hospital for Children "Maria Sklodowska Curie", Bucharest. The analysed and operated patients underwent surgery by Prof. Dr. Al. Pesamosca and the authors during the period of 1985-2011. In our series there where 4 primitive lung tumors and 7 secondary ones: 8 underwent surgery and 2 died before being operated on. The incidence of primitive pulmonary lung malignancies is higher for females, 3 to 1, and secondary ones are more frequent in males, 6 to 1.
Results: Patients with primitive pulmonary malignancies were late diagnosed. Their age ranged between 1 to 6 years; 3 were operated on, out of which 2 died, and 1 operated still survives. The 7 patients with secondary pulmonary malignancies were late diagnosed, too, probably as a consequence of a late diagnosis of the origin tumor.
Conclusions: Even if all malignancies require an early diagnosis and treatment, this aim regarding malignant lung tumors is still a desideratum animating all practitioners. Primitive tumors are diagnosed presenting the main clinical manifestation a bronchopulmonary infection. Secondary lung malignancies are usually asymptomatic and are diagnosed when monitoring a patient for a malignancy with another origin. Chemotherapy, radiotherapy and surgery of malignant primitive tumors or metastatic ones in children remain unsatisfactory because of the late diagnosis and the limited methods of treatment. Nowadays genetics identified the responsible oncogenes for pulmonary blastic explosion and better results could be obtained by genetic surgery.

Key words: primitive lung tumor, secondary lung tumor, metastasis, children, thoracoscopy, bronchoscopy, cytodiagnosis

Introduction

Pulmonary tumors in children have a much lower frequency than in adults. This is a result of the obvious absence of a series of factors that have a direct impact, such as: chromate inhalation, asbestos powders, tar pavements, radioactive substances, smoking etc. Metastatic lung tumors are relatively common in children and also comprise a spectrum of neoplasia distinct from that of the adult population.

The investigations performed in different countries are enlightening with concern to the adult, but do not point out special environmental conditions that affect the fetus, new born or small child.

The presence of pulmonary tumors in children requires the perfect understanding of the relation between malignant tumors and heredity by studying the familial aggregation of tumors and its concordance in twins.

Until 1982, Goffman and Mulvihill, studying the environment-heredity interaction, acknowledged 13 specific genetic mutations leading to malignant tumors if associated with environment stimulation factors (UV exposure in a patient having xeroderma pigmentosum determines skin cancer). Genetic-mesologic interactions were not identified during the pulmonary oncogenesis (1).

Nowadays the stage of cancer knowledge and the increasing number of cases of malignant pathologies in children, being the cause of death of all afflicted patients, resurrects a particular interest in clinicians and researchers, offering a wide-open study and research field (2).

Materials and Method

In this study we analysed 11 children suffering from primary or metastatic pulmonary tumors admitted to the Pediatric Surgery Department "Prof. Dr. Al. Pesamosca" of the Emergency Clinical Hospital for Children "M.S. Curie" Bucharest.

This paper includes aspects concerning symptoms and clinical, laboratory and imagistic explorations of the pulmonary primary or metastatic tumors (see *Table 1*).

The patients, a group of 11 patients with pulmonary primitive or metastatic tumors (see *Table 2*), were admitted and treated differently in relation to the cellular type of the tumors and the evolution stage assessed, using the 2004 revised OMS classification. The age of the patients ranged between 6 months and 18 years. The postoperative follow-up period ranged from 8 months to 9 years.

Periodic evaluations were performed every 6 months and included clinical and imagistic investigations. Some patients underwent cytodiagnosis and tumoral marker identification.

Our study included 11 patients with primitive and metastatic pulmonary tumors, out of which 8 have been operated on.

Results

In the studied group we observed equal frequency among the sexes. The incidence of primitive pulmonary tumors is higher for girls 2/1, and metastatic lung tumors are more often diagnosed in boys, 3/2 (3).

Concerning the age cohort, the highest frequency of pulmonary tumors was encountered at 1 to 6 years of age (see *Table 3*). This age group included the children that had congenital primitive lung tumors that were diagnosed at the age of 2 years and 2 months, and 5 years, respectively.

The follow-up did not exceed 2 years in 4 of the 7 patients having metastatic lung tumors. Only 2 patients

Table 1. *Pulmonary primitive or secondary tumors*

Pulmonary primitive tumors	4	36,3%
Pulmonary metastatic tumors	7	63,7%
Total	11	100%

Table 2. *Our study group of 11 cases*

Cases	Gender	Age	Affected lung	Diagnosis Complications	Treatment	Results	Survival period
Case 1	F	2 years 2 months	Right	Carcinoid tumor Cardio-respiratory failure	Medical	Death	3 days after admittance
Case 2	F	15 years	Left	Leiomyosarcoma Cardio-respiratory failure	Tumor resection Radiotherapy Chemotherapy	Death	8 months
Case 3	M	4 years	Bilateral metastasis	LAL Bilateral Communicating hydrocele	Testicular biopsy Chemotherapy	Good	Periodical observation. Healed.
Case 4	M	6 months	Right	Pleuropulmonay blastoma Congential heart disease Right collarbone fracture	Medical	Death	Immediately after admittance
Case 5	M	1 year 10 months	Bilateral metastasis	Abdominal neuroblastoma	Excision Radiotherapy Chemotherapy	Death	11 months
Case 6	M	3 years 5 months	Bilateral metastasis	Presacral teratocarcinoma	Excision	Death	1 year
Case 7	F	15 years	Right metastasis	Right 5th rib reticulosarcoma	Full excision Radiotherapy Chemotherapy	Death	9 months
Case 8	F	5 years	Right	Right lung inferior lobe plasmocytoma	Right lung lobectomy	Very goo	2 years follow-up
Case 9	M	9 years	Right middle lobe metastasis	4th-5th ribs Ewing sarcoma Antero-basal right pleuresia	Lateral and partially the medial segments of the middle lobe resection, Chest wall reconstruction chimiotherapy	Good	2 years follow-up
Case 10	M	17 years	Left superior lobe metastasis	2nd-4th left rib Ewing sarcoma	Superior lingula and inferior lingula of the superior left lobe resection, Chest wall reconstruction chimiotherapy	Good	1.5 year follow-up
Case 11	M	18 years	Right superior lobe metastasis	Left Tibial parosteal osteosarcoma	Metastasis resection chimiotherapy	Fair	8 month follow-up

survived for a period of more than 3.5 years. In 3 patients with primitive pulmonary tumors the survival period did not exceed 1 year. The patient with plasmocytoma completely recovered after surgery.

A. Primitive tumors

Malignant broncho-pulmonary tumors are dominant by frequency: 95% related to the histopathologic statistics data and 80-85% after R Filler. H. Wellons and co-workers have reviewed the literature finding 56 reported cases in children, adding 2 new ones (4).

Primary broncho-pulmonary malignant tumor in children develops either in the bronchial epithelium, in most cases (carcinoid tumor, mucoepidermoid carcinoma), or in the lung parenchyma, less frequently (pleuropulmonary blastoma type I, II or III, spindle cell sarcoma, squamous cell carcinoma).

Table 3. *Our study's age cohort*

Age	No. children	Primitive lung tumors	Metastatic lung tumors
0 - 1 years	1	1	-
1 - 6 years	5	2	3
6 - 12 years	1	-	1
12 - 18 years	4	1	3

There have been 291 cases with primitive pulmonary tumors described in the literature until 1993 (5). To these cases Megan K. Dishop and Suprya Kuruwilla added 25 more, out of which 14 have been operated on (2). Literature gathered data present the described histologic types (see *Table 4*). The most frequent histologic types are pleuro-pulmonary blastoma, carcinoid tumor, bronchogenic carcinoma and mucoepideroid carcinoma.

Pleuropulmonary blastoma is a primitive lung tumor which appears exclusively in children. In adults the biphasic pulmonary blastoma type develops. In contrast to the adult-type biphasic pulmonary blastoma, pleuropulmonary blastoma is a polyphenotypic mesenchymal malignancy without an epithelial component (2). Pleuropulmonary blastoma is subclassified based on the spectrum of gross morphology: pure cystic lesions (type I), solid and cystic lesions (type II), and pure solid lesions (type III) (6). Symptoms in this histologic type, especially in children, are extremely severe and induce respiratory failure in a short period of time: the tumor is located in

Table 4. *Pulmonary primitive malignant tumors in children described in the literature*

Tumor type	Number of cases	
	in the literature	our cases (Maria S. Curie Hospital Bucharest)
Pleuropulmonary blastoma	71	1
Carcinoid tumor	51	1
Bronchogenic carcinoma	51	
Mucoepideroid carcinoma	41	
Bronchopulmonary fibrosarcoma	29	
"Bronchial adenoma" not specified	27	
Rhabdomyosarcoma	12	
Leiomyosarcoma	12	1
Other sarcoma	5	
Adenoid cystic carcinoma	4	
Hemangiopericytoma	4	
Plasmocitoma	4	1
Lymphoma	3	
Immature teratoma	3	
Total	316	4

Table 5. *The anatomopathological classification of malignant pulmonary tumors (OMS 2004) (4,5)*

Squamous cell carcinoma (epidermoid)	Papilar carcinoma Clear cell carcinoma Small cell carcinoma Basaloid carcinoma
Small cell carcinoma (microcelular)	Combined small cell carcinoma
Adenocarcinoma	Mixted adenocarcinoma Acinar adenocarcionoma Papilar adenocarcinoma Bronchoalveolar adenocarcinoma Non mucinous Mucinoous Combined Mucipar solid adenocarcinom Fetal adenocarcinom Mucinous carcinoma Mucinous cyst adenocarcinoma Sygnet ring adenocarcinoma Clear cell adenocarcinoma
Big cells adenocarcinoma (macrocelular)	Big cell neuroendocrine carcinoma Combined big cell neuroendocrine carcinoma Basaloid carcinoma Limfoepiteliom like carcinoma Clear cell carcinoma Rhabdoid big cell carcinoma
Adenosquamous adenocarcinoma	
Sarcomatoid carcinoma	Pleomorphic carcinoma Fusiforme cell carcinoma Gigantic cell carcinoma Carcino-sarcoma Blastoma carcinoma
Carcinoid	Typical carcinoma Atypical carcinoma
Salivary gland tumor	Mucoepidermoid carcinoma Cystic adenocarcinoma Mioepitelial-epitelial carcinoma
Preinvasive lesions	Squamous in situ carcinoma A-typical adenomatous carcinoma Diffuse idiopathic pulmonary hyperplasic neuroendocrine tumor

the margins, rarely centrally, inducing massive atelectasis with the retraction of the thoracic wall resulting in a rapidly developing cardio-respiratory failure which predates the surgical act.

The carcinoid tumor presents a low grade of local aggressiveness and a diminished potential of metastasis. The younger the child is, the higher the tumoral aggressiveness. The extrinsic obstruction induced by the tumoral development is frequently associated with infected bronchopneumonitis, being a possible cause of death. Our presented patient was 2 years and 2 months old and he died 3 days after admittance due to a cardio-respiratory failure non-responsive to treatment. This type of tumor may appear in about 85% of the cases. They may arise from the lobar bronchi (75%), mainstem bronchi (10%), or within the lung parenchyma (15%) (7).

Leiomyosarcoma in older children shows aggressive local invasion, metastasis and poor prognosis (2).

Plasmocytoma is exceptional in children. In the literature, out of the 320 primitive lung tumors in children, including our 4 presented cases, too, only 5 are mentioned. The 3-year-old patient in our series was admitted with the diagnosis of infra-hilar lung tumor. Bronchoscopy showed a right main bronchia almost totally obstructed by extrinsic compression, without parietal infiltration. Out of the post-stenosis area there flowed a purulent secretion paced to the breathing rhythm. CT-scan showed areas of hypertransparency in the center of the formation (probably a necrosis process). Surgery was performed (Prof. Dr. Al. Pesamosca) by a thoracotomy in the 6th left intercostal space. After the lysis of the adhesions between the tumor and parietal pleura, a tumor the size of a fetal head was found, developed in the right lower lung lobe. Tumor removal from the chest wall was performed together with the lateral endothoracic fascia which adhered intimately to the tumor. Right lower lobe lobectomy was performed, removing the tumor entirely, with the adhesions to the endothoracic fascia and to the diaphragmatic dome. The postoperative evolution was uncomplicated. Macroscopic examination of the excised tumor presented copious amounts of blood-like fluid and large bronchial fistulas were individualized.

Histopathology revealed fibro-conjunctive tissue strips arranged in large, irregular bands, peppered with islands of mature and immature plasma cells, less lymphocytes and histiocytes, sometimes with xanthomas.

Because of the multitude of histological forms and the necessity to correlate a histological type with a certain prognosis, OMS revised in 2004 the histological classification of malignant lung tumors from 1999 (see *Table 5*). When a solitary lung nodule appears, it is most frequently a pulmonary tumor (8). The percentage of malignant nodules is between 10% and 70% of all malignant and benign ones (9), and most of the solitary malignant pulmonary nodules are in fact primitive lung cancers (10).

B. Metastatic tumors

Secondary tumors appear as a metastasis of a pulmonary neoplasm or of another organ. They are more frequent in case of sarcoma and carcinoma and less frequent in neuroblastoma, nephroblastoma and acute lymphoblastic leukaemia (LAL) (13, 14).

Dishop & Kuruwilla communicated in 2008 a number of 162 cases of secondary pulmonary tumors, being metastases of various primitive histological tumor types. In our study we met 7 cases of secondary tumors (see *Table 6*).

Neuroblastoma occurs at a median age of 2 years, ganglioneuroblastoma at a median age of 5.5 years and ganglioneuroma usually occurs after 10 years of age (15).

Askin tumor is a Ewing sarcoma or primitive neuroectodermal tumor that arises from the chest wall, sometimes from a rib and rarely from lung parenchyma. Ewing sarcoma may occur in any age group, but the usual age at presentation is 15 years. This tumor is often represented by a large chest wall mass with an intrathoracic or extrathoracic component or both. The rapid growth of these tumors induces invasion and destruction of adjacent structures, including muscle, ribs, pleura and lung parenchyma (*Fig. 1*). CT-scan or MRI may not be able to distinguish between lung compression and invasion. Tumor extension into the pleura and pleural effusions occur frequently. Rib destruction is not uncommon and the tumor rarely contains calcification. Necrosis and hemorrhage make the tumor to appear heterogeneous on CT and MRI. The prognosis of patients with Askin tumor is poor and depends on tumor extension at diagnosis and tumor resectability after chemotherapy (16). Our case series presents 4 cases of Askin tumor. We practiced en bloc oncologic resection (lobe and thoracic wall) followed by thoracic wall reconstruction (*Fig. 2*).

Table 6. *Secondary pulmonary tumors in literature*

Secondary tumoral type	Dishop & Kuruwilla (2008)	Our cases (Maria S. Curie Hospital, Bucharest)
Acute Lymphoblastic Leukemia	1	1
Ewing sarcoma (EWS) / Primitive neuroectodermal tumor (PNET)	13	3
Germ cell tumor	6	1
Neuroblastoma	6	1
Osteosarcoma	5	1

Discussions

For every tumor, from the moment of the cytological beginning to that of the clinical manifestation one, there is a non-symptomatic period, appreciated to be 3 to 12 months after the radiological diagnosis (17).

By the origin of development, either from the muscular layer of the bronchial wall or from pulmonary tissue, lung tumors may be: endobronchial, pulmonary or mixed, "iceberg" type. Endobronchial and "iceberg" forms determine the following types of lesions:

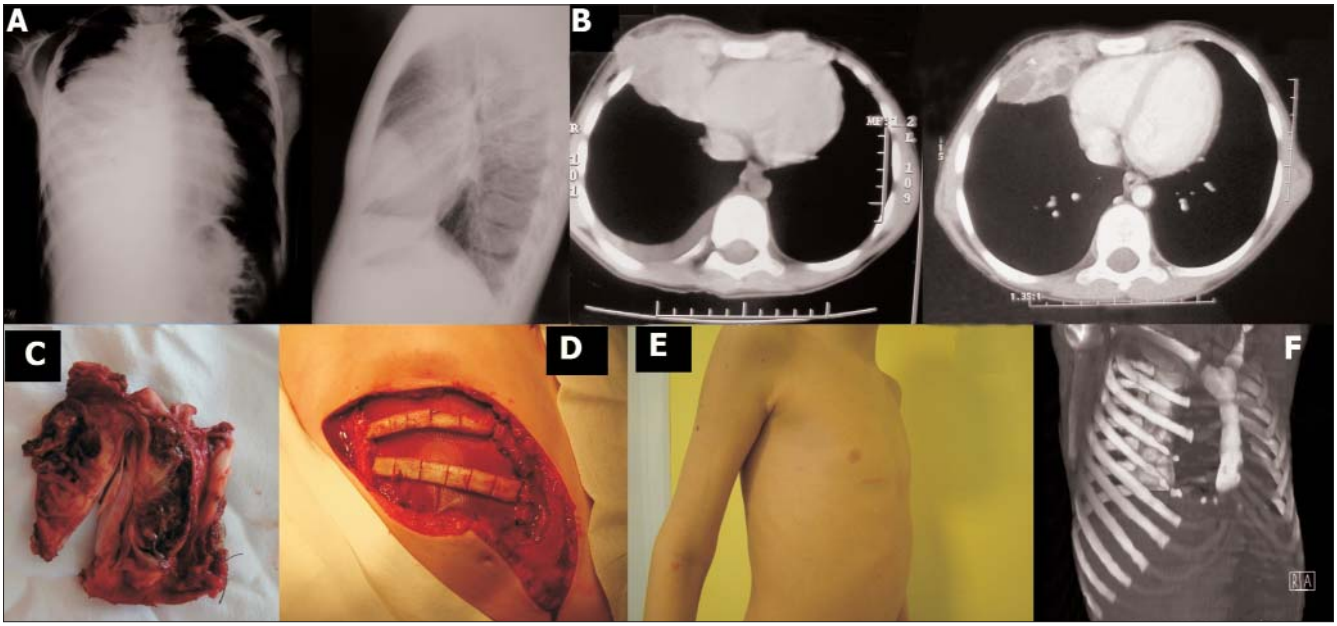

Figure 1. ***(A)*** *Chest X-rays show a tumoral mass, quite well contoured, with a subcostal intensity, extended in the middle right lobe, adjacent to the chest wall, more obvious in the sagittal incidence.* ***(B)*** *CT-scan shows very clear the tumor which destroys the 4th-5th anterior right rib arches, extending in the chest wall muscles to the subcutaneous tissue. After chemotherapy the tumoral mass diminished in volume and the pulmonary extension, even if decreased, is still present.* ***(C)*** *En bloc resection of the tumor includes the anterior arches of 4th-5th right ribs, the lung metastasis with the lateral and partially the medial segments of the middle lobe. D. Chest wall reconstruction with rib allografts after Burnei's procedure. E. Clinical appearance 2 years after surgery. F. CT-3D chest wall reconstruction showing the rib allograft integration*

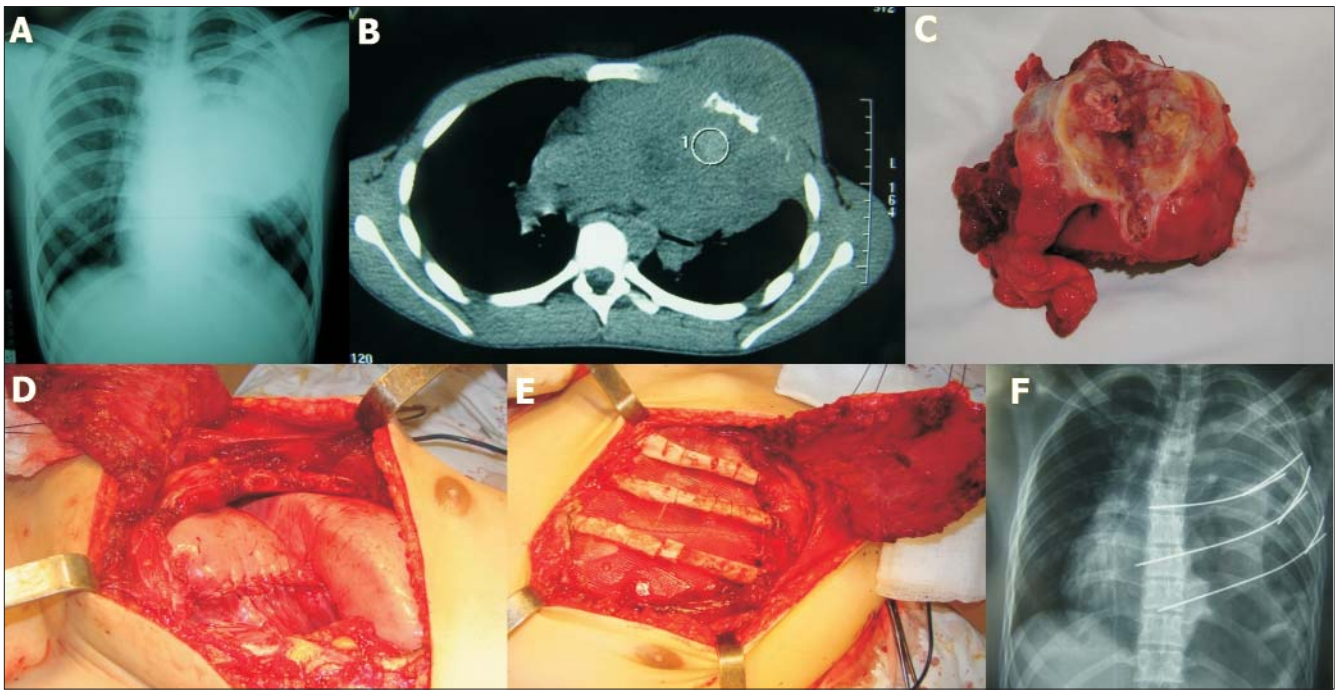

Figure 2. *(A) X-rays exam of a Ewing sarcoma of the 2th-4th left ribs invading the inferior segments of the upper left lobe. (B) CT-scan presents the lung invasion by the tumor. It extends outside the chest wall.* ***(C)*** *The excised block included the tumoral mass with 3 ribs and the anterior segment, the superior lingula and inferior lingula of the superior left lobe.* ***(D)*** *The extended excision of the chest wall requires reconstruction to avoid lung hernia. E., F. Intraoperative image and X-rays exam after Burnei's reconstruction with rib allografts on a metallic splint*

1. Incomplete bronchial obstruction is signalized by a sibilant rhonchus and more rarely by crackle sounds that we are able to listen in a limited area of the thoracic surface; when the bronchia remains permeable, only during inspiration we may detect localized emphysema, manifested by means of a pulmonary hypersonority ;
2. Complete bronchial obstruction that produces atelectasis of a pulmonary segment or lobe;
3. Pleural involvement that determines a serofibrinous or a serohaematic exudate;
4. The infection of the subsiding tumoral pulmonary territory manifested by a pneumonia; this may be the first symptom of a lung tumor;
5. Signs of compression over mediastinal anatomic components may appear later in time.

Lung tumors in children present invariably, sooner or later according to age, as first symptoms, the clinical signs of a pulmonary infection as a complication of the tumor evolution (18). Recent progress in perfecting the routine exams, using radioisotopes and the study of "like" substances, reduces appreciably the asymptomatic period and improves the treatment outcome.

In new born and small children pulmonary infections are severe from the beginning and evolve dramatically to cardio-respiratory failure. Observing a single case belonging to this age period in our study highlighted the setting of the cardio-respiratory failure at 30 hours after birth. The patient also had a non-cyanogenic cardiac disease and a collarbone fracture due to a difficult delivery.

Children aged 1 to 6 years have a better immunological arsenal. That is why the pulmonary infections are found as a functional respiratory syndrome during a basal pneumonia or asthma. The characteristic of these infections and the orientation towards the diagnosis resides in recurrence after a well-established treatment.

Preadolescents and adolescents present inconstant and non-specific symptoms such as: asthenia, fever, mucous purulent expectoration, haemoptysis and thoracic pain. Two cases in our analysis had metastatic tumors with the general condition in progressive decline induced by the neoplastic impregnation of the main illness that induced a late respiratory insufficiency.

All our secondary lung tumors cases were asymptomatic: 7 out of 7 (see *Table 7*). The majority of tumors involving the respiratory system are metastatic ones and primary lung tumors are even more rarely encountered. Approximately 75% of primary lung tumors are malignant, the most frequent being adenoma, bronchogenic carcinoma, and pleuropulmonary blastoma. Due to the rarity of these malignancies, and the usually nonspecific clinical symptoms, they are often not considered in the differential diagnosis in children presenting with persistent pneumonia, coughing, and atelectasis. This often results in delayed definitive treatment and, usually, a worse prognosis (19). In the moment of their radiological detection, the patients had no clinical evidence, only one case suffered from recurrent respiratory infections.

Radiological exploration has an essential role in the detection and diagnosis of pulmonary tumors due to the nonspecific symptoms or their complete absence during the

Table 7. *Pulmonary symptoms*

Symptoms	No. children	Age group	Tumor type	Percentage %
Severe pulmonary infections	1	0 - 1 years	primitive	9%
Pulmonary infections	3	1 - 6 years	primitive	27,3%
Asymptomatic	7	6 - 18 years	metastatic	63,7%

initial phases or even in more advanced ones. Some pulmonary tumors in children are discovered accidentally during a radiological exam for acute respiratory infections.

In our group study all the primitive lung tumors were discovered while performing a radiological exam in children that had numerous pulmonary infections.

Sometimes the revealed tumoral mass is advanced and is of important dimensions. We came upon this aspect in two cases: a congenital pulmonary tumor in a 2-year-old patient and in the case of a pulmonary plasmocytoma.

Secondary lung tumors were found on the radiological films performed in the case of patients operated for other tumors that could have developed metastatic disseminations or in patients with other tumors and having the symptoms of a functional respiratory syndrome.

Pulmonary radioscopy in big children, correctly performed, may identify opacities with a diameter of 1-2 cm, hyperinflation areas produced by expiratory valve and observed as one part of the diaphragm ascending while the other does not move. The radioscopic dynamic study reveals volume modifications, the extension of the tumor and sometimes may diagnose the tumor observing the growth rhythm and the structural modifications. Enlightening for this point of view is our case of plasmocytoma (case 8) from *Table 2*. In approximately 3 months, the tumor, situated inferiorly to the hilum, extended to the entire inferior lobe. The presence of intermittent lacunar images corroborated with the other data established the diagnosis of inflammatory tumor with necrotic areas. The radiological evolution of the case can be followed in *Fig. 3*.

Pulmonary X-ray becomes the examination of choice. It has revealed subcostal intensive opacities hidden sometimes by the rib; it may also establish, as an objective document together with radioscopy, the dynamics of the pathologic process, by appreciating its dimensions. For this reason the follow-up X-rays have to be performed using the same machine, the same FF distance, the same respiratory phase and as much as possible the same electric constants.

Trans-thoracic ultrasound highlights the presence of pleural liquid and has a better sensitivity than thoracic X-Rays. It is very useful in spotting the encysted pleural effusions and it is necessary in order to perform thoracocentesis, whether exploratory or evacuative.

CT-scan is an analytic procedure valuable for a precise localization of the tumor and in establishing the anatomic relations with nearby tissues. It is necessary to perform a frontal and sagittal CT-scan in case of tumors situated in the central area are in intimate proximity to the mediastinal elements. The axial CT-scan establishes better the proximity of the tumor to the mediastinum and especially to the phrenic nerve, left recurrent nerve, bronchus and trachea.

The bronchogram is preceded by a bronchoscopy, and it detects bronchial modifications in areas where the fibrobronchoscope does not reach. It is better to be performed directed at and only in the afflicted lobe or segment, to avoid summing the images and lead to difficulty of interpretation. Double contrast bronchography highlights small bronchus lesions and the grade of distal bronchiectasis especially, as a consequence of the atelectasis; this information is vital in deciding if the lung can be saved or not.

Cinedensigraphy, scintigraphy and phlebogram are investigations which are available for a limited number of specialists. Cinedensigraphy can differentiate between malignant, benign and inflammatory tumors in comparison to necrotic masses. Pulmonary scintigraphy reveals an area in the lung in which perfusion is disturbed and phlebogram is important to determine the diagnosis of malignant tumors, their operability and the presence of metastases.

Biological samples are not conclusive, but are good for orienting. ESR, proteinogram and immunological tests are useful for the preoperative period, for the therapy conduct and the for follow-up.

Bronchoscopy is performed if the radiological investigations do not reveal the persistence of anomalies, when we suspect the possibility of an obstructive endolumenal lesion (20). In this situation although the CT-scan may help to make a diagnosis, its certainty has to be established by performing a bronchoscopy, which may highlight the following aspects:

1. A pink, friable mass that bleeds abundantly represents a typical aspect of an adenocarcinoma; the biopsy has to be performed carefully and the surgeon has to take all precautions for controlling the hemorrhage.
2. A less vascular mass, better defined, orients the

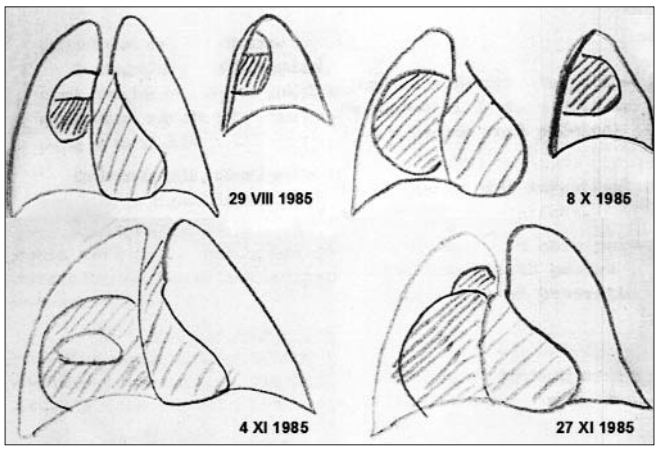

Figure 3. *Radiologic evolution of the case with plasmocytoma (Collection of Prof. Emil Popescu)*

diagnosis towards a mucoepidermoid or a cylindroma type carcinoma;
3. Bronchus infiltration is found in tumors that have an incipient intrabronchial development;
4. The obstruction or the narrowing of the bronchus lumen in large benign or dysembrioplastic tumors; in malignant tumors together with the obstruction we notice mucous-purulent secretions and necrotic tissue.

While interpreting the data, we will take into consideration superimposed processes (inflammation, necrosis) and the completion of knowledge with the anamnestic, radiologic and cytodiagnostic information. Because pediatric bronchoscopy needs a particular equipment and a special knowledge of child anatomy and physiology, it should be performed in a tertiary center. The procedure has to be done by an endoscopist or by an anaesthesiologist with very good experience in children's airway pathology, especially in small babies, because of their particularities. It is mandatory to know the main differences between a child and an adult: the infant's tongue being larger, the epiglottis longer, the larynx softer and the child being a nasal breather until 6 months of age. The correct technique must be well mastered in order to reduce the risks to a minimum. The correct size rigid bronchoscope allows a small leak at 20–25 cm H_2O. Premature infants 1–2 kg in weight require a bronchoscope size 2.5. However, the very high intrapulmonary pressure generated when the telescope is inserted risks barotrauma and prevents adequate gas exchange. Therefore, an apnoeic technique is safer. In infants <1 kg, even the 2.5 bronchoscope is too big, therefore the telescope (OD 2.7 mm) alone may be inserted (21).

Cytodiagnosis represents an investigation process useful only in malignant tumors. In children, retrieving sputum from the profound respiratory ways while expectorating may encounter some difficulties. Useful methods are represented by bronchus aspiration or bronchoscopy. Bronchial lavage is laborious and dangerous in children. Ross established that for the first exam positive results are of approximately 60% and after 5 exams they reach 90% (22).

Markers for pulmonary tumors represent one research objective of malignant tumors. These are substances produced by the neoplasm or associated with it, called "ectopic substances" or "like substances" (their action being similar to that of the endocrine glands). Until now serotonin, kallikrein, estradiol, hypoglycemic factor, gastrin and others were isolated. Kaiser and Filler remarked the presence of serotonin and kallikrein, but not of the characinoid syndrome and recommend the investigation of abnormal serotonin in every case, the measurements being used to establish an adequate treatment (23).

Thoracoscopy as a diagnostic method has to be considered as a convenient alternative to other diagnostic procedures, offering the great advantage of a possible therapeutic act to follow (24). In children, thoracoscopy is useful for biopsy of pulmonary and mediastinal masses, excisions and lobectomies. Lung biopsy has a great efficacy in establishing the stage of a pulmonary or mediastinal tumor or metastatic disease in the paediatric population. Improved technology and decreased morbidity from the thoracoscopic approach allows for a more aggressive approach to obtain tissue for diagnostic purposes in cases of interstitial lung disease and questionable focal lesions (25). There are some limits which must be specified, for example the inability to palpate lesions. The appearance of recurrent disease at port sites as a complication of the procedure has to be considered too. The indications for thoracoscopy (26) in children are:

- Interstitial lung disease in immunocompromised patient;
- Interstitial lung disease in immunocompetent patient;
- Mediastinal masses – biopsy and excision;
- Staging in the initial work-up of tumors;
- Evaluation of residual masses after chemotherapy;
- Evaluation of new masses after treatment of tumors.

In larger patients, a double lumen endotracheal tube is indicated. In infants and smaller children single lung ventilation is obtained by mainstem intubation of the opposite side (27). Over the last years, thoracic video assisted surgery (TVAS) offered the possibility to establish the malignant diagnosis by performing parietal pleural biopsy or by means of a pulmonary biopsy resection (28). Some studies (29) try to enhance the diagnostic sensitivity of this method towards 100% by combining thoracoscopy with fluorescent diagnosis (thoracoscopic fluorescent diagnosis–TFD). At the same time, we have to take into consideration that the introduction into practice of minimally invasive video-endos-copic techniques, telesurgery or robotic surgery influences in a significant way many diagnostic and therapeutic procedures concerning pulmonary tumor pathology (30).

Conclusions

Nowadays pulmonary symptoms allow for a valuable clinician to detect a tumor in 9 to 12 months from its onset. Laboratory investigations may confirm or deny the diagnosis, offering information regarding the primitive or metastatic, benign or malignant, operable or non-operable tumor. Primitive tumors when diagnosed, present as main manifestation a pulmonary infectious process, and secondary tumors evolve usually without symptoms, being discovered when monitoring a patient for a malignant process with another location. Chemotherapy, radiotherapy and surgery of malignant primitive or metastatic tumors in children remain unsatisfactory, especially in small children and preadolescents due to a late diagnosis and to the limited methods of treatment. Genetic surgery will remove in the future the drama of ending a pregnancy due to the possibility of replacing the genes responsible for these tumors.

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