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Solitary peripheral pulmonary lesions of malignant etiology: features

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Peripheral lung cancer makes a large proportion of solitary peripheral pulmonary lesions (SPPL), so their early discovery and diagnosis are crucial, especially because of their asymptomatic development. The paper reviews clinical and radiological features of malignant SPPLs, and the applications of potential diagnostic procedures. Our study included a hundred of patients with a SPPL observed after X-ray examination of chest. All the examined patients underwent a complete diagnostic procedure including bronchoscopy and transthoracic aspiration biopsy. Of the total of 100 SPPLs included in this examination, 70% were malignant of which the most frequent was adenocarcinoma (67.1%), followed by squamous cell carcinoma (24.3%), small-cell lung cancer (4.3%) and metastatic lesions (4.3%). Malignant SPPLs usually affected persons between 50 to 59 years of age, more frequently males; most of them were smokers, and developed no symptoms. SPPLs were commonly localized in the right lung, and appeared in the size of 3 to 3.9 cm. Bronchoscopy revealed the etiology of SPPLs in a small number of cases, unlike transthoracic aspiration biopsy, which disclosed the etiology of 64% of these lesions. Transthoracic aspiration biopsy is doubtlessly a method of choice in preoperative diagnostics of SPPL, and achieves a high level of specificity, sensitivity and accuracy. Thoracotomy is also a method of choice when other diagnostic procedures fail to provide a definite diagnosis of SPPL.

KEY WORDS: *Coin Lesion, Pulmonary; Lung Neoplasms+diagnosis; Biopsy, Needle*

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INTRODUCTION

There is certain diversity in the literature concerning the reported frequency of malignant lesions in the form of solitary peripheral pulmonary nodes, but there is a doubtless concordance on a constant increase in their number and an increasing involvement of younger ages and females. As a great percent of these solitary peripheral pulmonary lesions is a peripheral lung cancer, their early discovery and accurate diagnosis are particularly important because they develop without symptoms.

The relevance of the early discovery, diagnosing and treatment of these lesions is even better understood taking into account the fact that lung cancer is nowadays the leading death-causing malignancy in the world, and in some countries even the malignancy with the highest incidence and mortality rates among males (1). Peripheral lung cancer is radiologically presented by a round or oval shadow with a relatively distinct edge and no site predilection, although the involvement of the upper lobes seems to be more frequent, greatly ranging in size and rarely accompanied by calcification (2).

Some carcinomas such as breast, cervix of the uterus, ovarian, kidney or skin cancer, and sarcomas frequently have solitary metastases that make 3-5% of all solitary lung lesions. They are radiologically manifested as clearly distinct round shadows with a regular or wavy edge, of 3-6 cm in size, more frequently involving the lower lobes of the lungs; solitary metastases are distinguished from a primary peripheral lung cancer by their more regularly round shape (2).

It should be pointed out that a SPPL cannot be classified as malignant or benign either on the basis of a patient's age or according to the radiological features of the peripheral lung lesion (its size, edges, cavitation, homogeneity). However, if the mutual comparison of chest X-ray findings over a two-year period reveals no enlargement of the respective SPPL, it can be qualified, with great certainty, as benign (1), but the calcification within the lesion could not be accepted as an absolute sign of its benign nature. Although a great number of authors have attempted to define SPPL evaluation criteria, there is no doubt that the true nature of the lesion cannot be defined unless a histologic sample analysis is performed.

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The aim of our study was to review clinical and radiological features of malignant solitary peripheral pulmonary lesions and to define the most effective diagnostic procedure with these lesions.

MATERIALS AND METHODS

The investigation was conducted at the Institute of Lung Diseases in Sremska Kamenica, Yugoslavia. It included hundred of patients with a solitary peripheral pulmonary lesion (SPPL) observed on their chest X-ray findings. It involved a roundish or oval, dense and homogenous mass, less transparent, with smooth edges, well distinct from the surrounding tissue, up to 6 cm in its diameter, with no hilar adenopathy, consecutive atelectasis or pneumonitis.

All patients underwent a complete diagnostic regimen, including history taking, clinical examination, standard laboratory analyses and chest X-ray screening (a standard posterior-anterior and profile screening). Sputum analyses included bacteriological essays, cytological essays and sputum study for TB, either by smear (Ziehl-Neelsen staining) or by culture (Lowenstein-Jensen medium). Each patient was submitted to bronchoscopy (B) and transthoracic needle biopsy (TNB).

Bronchoscopy was performed either by a rigid bronchoscope (Friedl's Narcosa bronchoscope) or by a flexible one (Olympus), equipped by sampling tools (Stors's forceps for sampling the bronchial mucus, a catheter for catheter biopsy, a forceps for a peripheral biopsy of the lungs). Transthoracic needle biopsy (TNB) was performed by a Rotex II needle; it was either X-ray (with an electronic amplifier) or CT guided to obtain an accurate location of the lesion and a precise directing of the needle in the course of the intervention itself. Thoracotomy was performed in 91 patients. The cytological analysis of the sputum and TNB samples was performed by May-Grunwald-Giemsa (MGG) staining, while the histologic samples obtained by bronchoscopy or thoracotomy were stained by hematoxylin-eosin (HE) as a basic staining method and by alcian-blue PAS stain.

RESULTS

The study revealed that of 100 (100%) solitary peripheral pulmonary lesions, 70 (70%) were malignant tumors, 19 (19%) tuberculous lesions, 6 (6%) benign tumors, 2 (2%) hydatid diseases, 2 (2%) chronic pneumonias and 1 (1%) fungal infection (aspergilloma).

Among malignancies, the most common was adenoarcinoma of the lungs in 47 (67.1%) cases, then epidermoid lung cancer in 17 (24.3%), small-cell lung cancer in 55 (4.3%) and metastatic cancer in 3 (4.3%) cases (Figure 1).

The following analysis was based on the study of 70 malignant solitary peripheral pulmonary lesions.

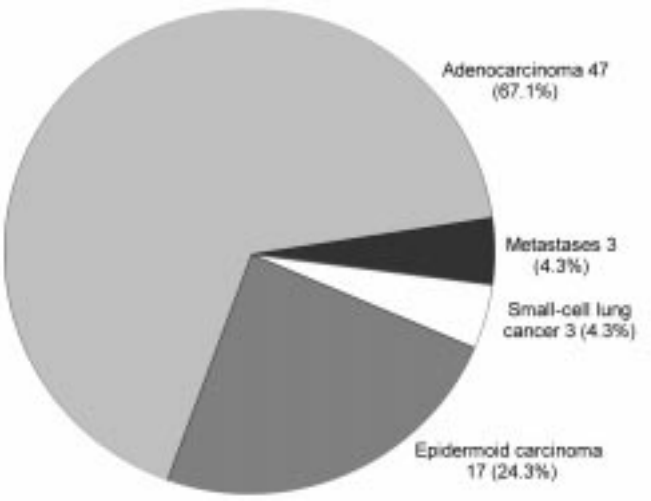

Figure 1. Malignant solitary peripheral pulmonary lesions

The majority of patients (31, 44.3%) with malignant solitary peripheral lung nodes were from 50 to 59 years of age; the groups from 40 to 49 and over 60 years of age were slightly less frequently but almost evenly affected (Figure 2).

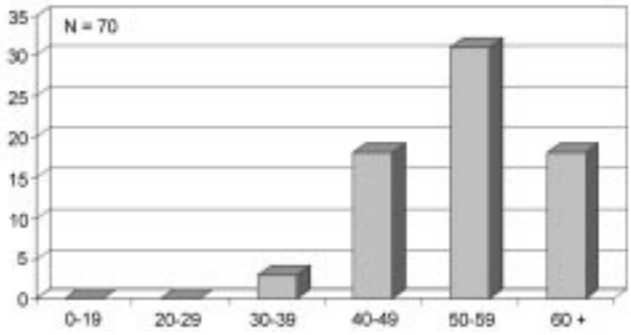

Figure 2. Patients: Age classification

The male : female ratio was found to be 4.8:1. Fifty-eight (82.9%) malignant SPPLs were found in males.

Considering the family history of the analyzed patients, we noticed that six patients with a confirmed lung malignancy had one of the parents, usually father, affected by lung cancer, too.

The analysis of former diseases in the examined patients revealed that three of them already had an extrapulmonary malignancy surgically treated a few years ago, and now developed pulmonary metastases. It was a breast cancer, a leyomyosarcoma of the uterus and a urinary bladder carcinoma, respectively.

Regarding the occupation of the examined patients, malignant SPPLs were most frequently found in civil engineering workers (18.6%) and in farmers (17%).

Of the total of 70 patients with malignant SPPLs, 64 (91.4%) were smokers.

Thirty-two (45.7%) patients developed clinical symptoms, while 38 (54.3%) had no symptoms at all and for sure would not have

come to see the doctor if they had not been discovered by chance on X-ray screening of the population.

Of the total of 70 patients with a malignant SPPL, 32 (45.7%) patients were presented by symptoms, usually a few concurrent ones; among the symptoms, thoracic pain was most common, then cough. Other symptoms produced by the organs involved by dissemination of the malignant process were also registered, such as hemiparesis, bone pains and headache.

The clinical examination resulted in practically normal findings; in two patients only auscultation revealed the signs of bronchoobstruction, the accompanied chronic obstructive pulmonary disease, which was confirmed by lung function test findings. Mallet fingers and the signs of hemiparesis were noticed in two patients respectively.

The most common localization of the malignant SPPL was the right lung, involved in 42 (60%) patients, or more precisely the right upper lobe, which was affected in 29 (41.4) patients.

The majority of SPPLs, that is 7% of them, ranged from 3 to 3.9 cm in size (Figure 3); the mean size of all SPPLs was 3.22 cm; the mean size of the malignant ones was 3.39 cm and the mean size of tuberculous lesions was 2.46 cm.

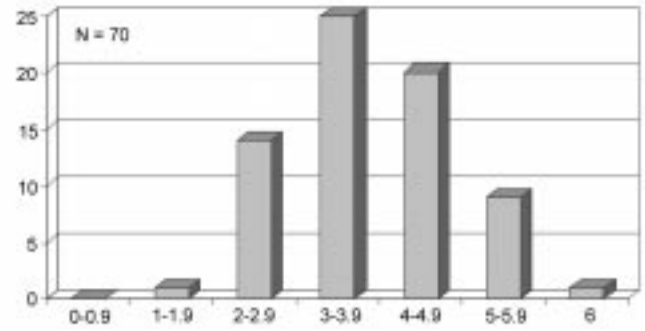

Figure 3. Chest X-ray: size of the shadow

Calcification was noticed in 7 (10%) malignant solitary peripheral pulmonary nodes, with four of them localized in the center of the lesion and three at its periphery.

The cytological sputum analysis enlightened the etiology of the disease in five (7.1%) patients, confirming three epidermoid carcinomas, one adenocarcinoma and one small-cell lung cancer, respectively. Those were peripheral, round shadows in the diameter of 4x4cm and 5x5 cm.

On bronchoscopy, all one hundred examined patients with a solitary peripheral pulmonary lesion seen on the chest X-ray had a normal endoscopic finding; catheter biopsy enlightened the etiology of the SPPL in two patients (one adenocarcinoma and one epidermoid lung cancer). In both patients the shadow was measured to be 5x5 cm in diameter. The diagnosis was confirmed by TNB in both patients.

Transthoracic needle biopsy (TNB) enlightened the etiology of SPPL in 64% of the examined patients (Figure 4); the method was established to have the sensitivity of 82%, specificity of 100% and accuracy of 87%. Regarding complications, 19% of the patients submitted to TNB developed a partial pneumothorax, which was adequately treated; other complications were not registered.

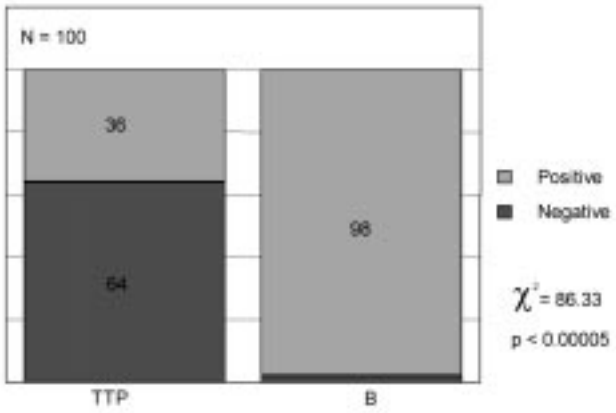

Figure 4. Transthoracic needle aspiration vs bronchoscopy

Of the total of 100 examined patients with SPPL, thoracotomy was performed in 91; nine patients were not thoracotomized. In one of those nine patients, transthoracic needle biopsy confirmed the diagnosis of granulomatous inflammation; an antituberculous treatment was initiated requiring no surgery. In other eight patients transthoracic needle biopsy provided the diagnosis of a malignancy, but thoracotomy was abandoned due to dissemination of the malignant disease or to patients' bad cardiorespiratory condition.

By correlating the cytological finding of the transthoracic biopsy sample from 91 patients submitted to thoracotomy with the definite histologic finding of the resection sample, we concluded that the cytological essay of the transthoracic biopsy sample provided a positive finding in 55 patients (a malignancy in 51 and granulomatous inflammation in 4 patients - as it was confirmed by a histologic analysis of the resection sample), while a negative, that is a nonspecific finding was obtained from 36 patients. After they had been submitted to thoracotomy and a definite histologic essay, the diagnosis of a malignancy was obtained in 11 patients, pulmonary tuberculosis in 14, chronic pneumonia and hydatid disease in two patients respectively, fungal infection in one, fibroma in two, neurinoma in one and chondroma in three patients (Table 1).

By correlating cytological findings of transthoracic biopsy samples with histologic findings of lung resection samples, we concluded that all positive transthoracic biopsy findings were confirmed by a histologic analysis of the resection samples.

It was also noticed that the number of patients with malignancy that was confirmed by transthoracic needle biopsy exceeded the number of patients in whom the method failed to provide the diag-

nosis. At the same time, this diagnostic method confirmed tuberculous nodes in the minority of cases, the majority of which were, however, diagnosed by a histologic essay of the resection sample.

Table 1. TNB vs. surgery N=91

	SURGERY								TNB
	M	Tbc	HP	HD	A	F	N	C	Total
Malignancies	51								
Granululomatous inflammation		4							
Nonspecific finding	11	14	2	2	1	2	1	3	36
Total	62	18	2	2	1	2	1	3	91

M - Malignant
Tbc - Tuberculosis
HP - Chronic Pneumonia
HD - Hydatid disease
A - Aspergillus
F - Fibroma
N - Neurinoma
C - Chondroma
TNB - Transtoracic needle biopsy

DISCUSSION

Our investigation revealed that malignancies made 70% of all solitary peripheral pulmonary lesions, correlating well to the literature data reporting a constant year-to-year increase in the number of patients affected by peripheral lung cancer. Šušterić (3) (1963) reports 32% of carcinomas involved in his series of examined peripheral solitary nodes. In a similar study Popović M. (4) (1971) reports 35% of carcinomas, commonly epidermoid in type. Vučinić V. (5) (1987) finds 51% of malignant solitary peripheral lung lesions in his examined series. Examining the series of 190 solitary pulmonary nodes, Das et al (6) (1995) confirm 140 lung carcinomas (73.6%), correlating quite well to the data we have obtained in our study.

The majority of our patients with a malignant peripheral solitary lesion in the lungs were from 50 to 59 years of age, that is 44.3%; it is well correlating to the data reported in the literature. None of the patients from our examined group was under the age of 30, correlating to the data reported by authors who had only one case of a malignancy and 79 benign lesions in the examined series of 80 resected peripheral pulmonary nodes from patients at 20 to 29 years of age (7).

In our study 82.9% of all malignant solitary peripheral lung lesions were found in males, correlating well to the reports by Vučinić V. (5), who similarly found 70% of males affected by SPPL.

We found that smokers made the majority of the patients with a malignant SPPL (91.4%).

Only 32 (45.7%), of the patients with a malignant SPPL were presented by symptoms - with thoracic pain and cough as the most common ones, unlike hemoptysis which developed less frequently and not exclusively with lung cancer. These results of ours correlate well to those reported by Vucinic V (5) and Popović M. (4); similarly, Good reports hemoptysis to accompany lung cancer more often, but not necessarily so (7).

Standard chest X-ray screening method is the most simple and efficient in detection a solitary peripheral node, that is a peripheral lung cancer as well.

In the majority of our examined patients (60%) the right lung, or more precisely its upper right lobe, was involved with malignant SPPL. Similar malignant SPPL sites are reported by Jackman and Good (7), while Dedić M (8) reports the left lung as predominantly affected by peripheral lung cancer in his examined series.

The majority of malignant solitary pulmonary nodes in case of our patients ranged in size from 3 to 3.9 cm; the mean size of the malignant lesions exceeded the mean size of all SPN and the mean size of the tuberculous ones, which were in fact the smallest. Siegelman reports similar sizes of solitary pulmonary nodes in his examined series (9).

Calcification inside the solitary pulmonary node was not found to be more suggestive of a benign lesion, but it can be involved in a malignant solitary node in the lungs as well, and therefore is not considered as an absolute marker of benign nature of the lesion. We registered calcification in 10% of all examined malignant SPPLs. It correlates well to the reports by Popović M. (4) who found calcification in 13% of peripheral lung cancers in his examined series. According to Cummings and associates (10), calcification was registered in 3.7% of the total of 316 examined solitary malignant pulmonary nodes, while Jones et al (11) reported 7% of their peripheral lung cancer series were involved by peripheral calcification, seen on chest CT screening.

The cytological sputum analysis has a minor diagnostic relevance with solitary lung nodes and peripheral lung cancer and can rarely enlighten the etiology of the lesion, but with central lung tumors it plays an important role in establishing the diagnosis. We obtained slightly better results with this method than Popović M. (4) who established the diagnosis by the method in 4% of the total number of examined lung carcinomas and Vučinić V. (5) in only 3%.

In our examined series transthoracic needle biopsy (TNB) enlightened the etiology of the solitary lung node in 64% of patients, correlating well to the literature data. Similarly, Hancko J (1987) (12) reported 60.7% of positive findings, Dubay (1983) (12) 76.5% , while Laiby (12) obtained a positive finding in 50% of his examined series. Our results suggested that transthoracic needle biopsy provided a larger number of positive findings in lung cancer (82.2%) than in benign lung lesions (13.7%). They are well correlated with other authors' experience, who also point out that the number of positive TNB findings in lung cancer exceeds the one in benign lesions. Cummings (10) reports a positive TNB finding in 80-95% of malignant solitary lesions larger than 2cm in diameter or in 50-70% of those smaller than 2cm in diameter. As he reports, in benign peripheral lung lesions TNB provides a positive finding in 13%.

When evaluating the sensitivity, specificity and accuracy of TNB

diagnostic method, we obtained similar results to those reported by other authors. For example, Poe and Tobin report the sensitivity of 90% and specificity of 95% (13).

Regarding complications, pneumothorax developed most frequently, predominantly in patients with severe pulmonary emphysema or those with deeply localized lesions. Doyle (14) reports development of pneumothorax in 20% of his examined series, more often when the node is localized in the anterior segment, 5% of these requiring a surgical draining.

Transthoracic needle biopsy is a simple method characteristic for rare complications and low mortality. It achieves positive findings in a high proportion and enables sampling for a cytological analysis. The results we obtained with this method confirmed that we achieved a satisfactory level regarding the number of positive findings, specificity, and complications.

Bronchoscopy can rarely enlighten the etiology of solitary peripheral pulmonary lesions since their localization makes them hardly reachable by this method and the endoscopic finding is practically always normal.

It is not unusual that despite the application of complex diagnostic methods the etiology of round shadows in the lungs still remains obscure. In such cases explorative thoracotomy emerges as a unique method that can provide a definite diagnosis, giving at the same time a chance for an adequate resection, which is exceptionally important in lung malignancies. Since malignant tumors make a large portion of SPPL, thoracotomy should not be postponed; instead, it is better to perform it early and remove the lesion which is not malignant than do it late when a disseminated malignant process produces both technical and biological inoperability.

CONCLUSION

About 70% of all solitary peripheral pulmonary lesions were malignant in nature, with adenocarcinoma for the most common cancer type (67.1%), followed by epidermoid (24.3%), small-cell (4.3%) and metastatic carcinoma (4.3%).

Males were five times as affected by peripheral lung cancer as females.

Smokers made 91.4% of the examined patients with malignant solitary peripheral pulmonary lesions.

Transthoracic needle biopsy (TNB) was for sure the method of choice in the preoperative diagnostics of SPPL, highly specific, sensitive and accurate.

Thoracotomy was certainly the method of choice in case other diagnostic procedures fail to provide a definite diagnosis of a SPPL.

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