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COMPARATIVE ANALYSIS OF CYTOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSTIC TESTS IN BRONCHOPULMONARY CANCER

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Abstract

A comparative analysis of cytological and histopathological diagnostic tests in bronchopulmonary cancer was thus undertaken, based on 6 years of cases at hospital level. Samples collected from 150 patients were under analysis, with 4 samples being eventually excluded. In the remaining 146 patients, the biological material was evaluated both from a cytological and histopathological standpoint, 67.12% of patients being male, 69.17% being aged between 51 and 70 and 67.12% coming from an urban environment. 68 samples were proved to be malignant (46.57%) in a cytological exam and 82 (56.15%) in a histopathological exam. The histopathological exam also presented the following types of tumors: NSCLC squamous carcinoma (64.63%), NSCLC-adenocarcinoma (29.27%), SCLC carcinoma (3.66%) and NSCLC-"NOS" carcinoma (2.44%). Cytology has a sensitivity of 87.80%, specificity of 96.87%, positive predictive value of 97.29% and negative predictive value of 86.11%. The accuracy of a cytological examination compared to a histopathological one is of 91.78% while diagnostic concordance values are at 85.33%. The cytological testing is relatively safe, more accessible, less costly and faster, allowing for a quick diagnosis.

Key words: cytological examination, histopathological examination, sensitivity, specificity, accuracy

INTRODUCTION

Bronchopulmonary cancer (BPC) is one of the most important and frequent malignant tumors accounting for 90% of pulmonary tumors. In the last years it has been observed to have the most increased incidence rate of all neoplasms (Parkin DM et al, 2002, Parkin DM 2004). In 2012, in the European Union, the incidence of pulmonary cancer was of 52.2‰ people, while the mortality rate was of 48.752‰ people (Suster S, 2013). When a diagnosis is reached in a therapeutically-useful timeframe, the average survival time is of 6-18 months, with 20% of patients living more than a year (Eldrige L. 2016). There are different methods and techniques used for early diagnosis (WebMD 2015, Travis WD et al 1995). Not all of these techniques can be used in one patient, but combining several techniques leads to a correct diagnosis. One of the most utilized examinations is bronchoscopy, which allows for histopathological testing to be done on harvested material and thus establish a clear diagnosis (Lung protocol

2015). The cytological exam allows for the examination of biological material from areas which are inaccessible for harvesting material for a histopathological examination. Allowing for a fast diagnostic approach and being easily accessible, the cytological examination is a useful method in diagnosing BPC. In sputum cytological examination, the test is diagnostic in 70-80% of cases, with a sensitivity of around 90% (Galbenu P. 2010, De Villaine S. et al 1996). A cytological examination undertaken on biological material harvested through a bronchial brushing, studies show a sensitivity of around 85% (Ahmad M. et al 2004, Sackett M. et al 2010).

Our study aims to determine the validity, predictive value and diagnostic accuracy of bronchopulmonary cancer through cytological examination of biological material harvested through bronchial brushing comparatively to a histopathological examination of bioptic bronchial specimens.

MATERIAL AND METHOD

The study was undertaken in the anatomical pathology laboratory of the Clinical Emergency County Hospital in Oradea between 2009 and 2014. Samples harvested from 150 patients were analyzed. Samples in four patients obtained through bronchial brushing or bronchial biopsy were considered unsuitable both qualitatively and quantitatively, being subsequently excluded from the study. In the remaining 146 patients, the harvested material was examined through cytological and histopathological testing.

Specimen harvesting was undertaken through bronchoscopy, utilizing a Storz flexible bronchoscope. Only the visible biological materials harvested through bronchial brushing and endobronchial biopsies were selected for the study.

The bronchial brushing cytological exam was done in the following manner: the specimen was collected by brushing the suspected area under direct visualization or, without visualization, inserting the brush into smaller bronchi leading to the area where the lesion is located. The smears from the brush were immediately fixed in 70% ethyl alcohol for preservation of cellular features, which is crucial for accurate cytological evaluation. The material was processed in the anatomical pathology laboratory of the same hospital.

For the material obtained through brushing, conventionally colored Babes-Papanicolau smears were used. Biotic fragments (obtained through bronchoscopy) were fixed in 10% concentration formaldehyde for 12-24 hours and histologically processed through inclusion in paraffin. Sectioning was undertaken at a thickness of 4 microns (using a Microm HM325 machine). The discs with histopathological materials were colored through

the Haematoxylin & Eosin stain technique. Microscopic examination was undertaken using Nikon Eclipse E200 and E600 microscopes, and the photographs were taken using a Nikon Coolpix 4500 device.

For the comparison of diagnostic histopathological and cytological tests in pulmonary cancer we have considered as a defined standard the histopathological test, which means that this test correctly identifies the presence or absence of the disease in a patient from a studied population. The cytological diagnostic test offers the possibility to determine the presence or absence of the disease in studied patients. The parameters used in diagnostic testing were validity (sensitivity, specificity), predictive value (positive and negative) and accuracy.

Data resulting from these calculations was grouped according to different criteria in order to be interpreted statistically. The results were represented through tables and graphs. We have obtained the approval of patients included in the study and the ethical committee of the hospital. There is no conflict of interest with any pharmaceutical or histological technical companies.

RESULTS AND DISCUSSION

146 patients suspected of BPC were included in our study, 98 of which (67.12%) were male and 48 (32.88%) were female, leading to a male-female ratio of approximately 2:1. The average age where suspicion of BPC arises was situated between 51 and 70 (including a total of 101 patients – 69.17%). The following incidence group had an age of over 71 (28 patients – 19.18%). Patients aged under 50 were only 17 in number, or 11.64% (Table 1).

Table 1

Distribution by age groups of the number of taken biopsies

No.	Age group (years)	No. of taken biopsies	Distribution in percent	Cytological exam Nr. cases of BPC	Histopat. exam Nr. Cases of BPC
1	≤ 50	17	11,64%	3	5
2	51-70	101	69,17%	49	57
3	≥71	28	19,18%	16	20
	Total	**146**	**100%**	**68**	**82**

Analyzing the environment from which patients hail from, we have observed that 99 (67.81%) of them live in an urban environment and 47 (32.19%) live in a rural environment.

From a cytological standpoint, 68 samples were malignant, with squamous carcinoma leading with 45 cases followed by primary adenocarcinoma (21 cases) and 2 cases of NOS carcinoma (Figure 1).

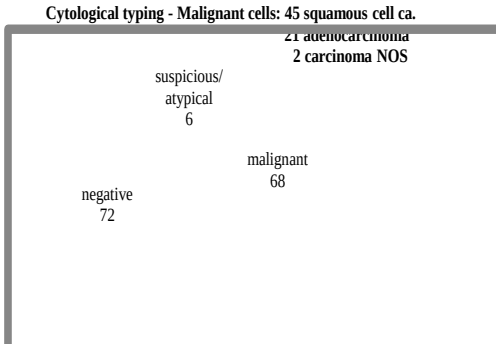

Fig. 1. Distribution of the number of samples obtained in a cytological exam

In a histopathological examination, 82 samples (56.16%) were malignant and 64 (43.83%) were negative. Malignant tumors were classified as squamous carcinoma (53 cases), adenocarcinoma (24 cases), NOS carcinoma (2 cases) and small cell carcinoma (3 cases). Negative samples showed specific and non-specific chronic inflammation (5 specific, 59 non-specific) (Figure 2).

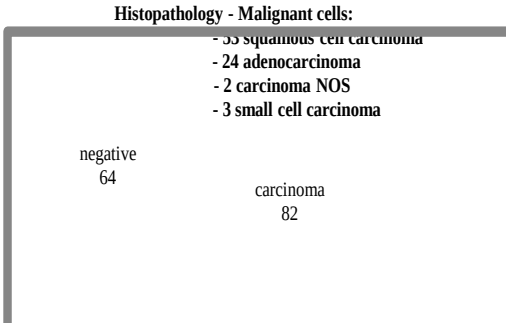

Fig. 2. Distribution of the number of samples obtained in a histopathological exam

In a cytological exam 68 samples were malignant and 6 samples were suspect. The 6 suspect samples were proven to be malignant in a histopathological setting, being included in the True positive group (TP). From the 68 malignant samples, two were proven to be negative in a histopathological exam, presenting with dysplastic alterations and being included in the False positive group (FP). The total samples included in the True positive (TP) group were 72 (66 malignant in cytology and 6 suspects in cytology and malignant in histopathology). 72 samples were negative in a cytological exam, 10 of which were proven to be malignant in a histopathological exam. The 10 samples were considered to be False negatives (FN). The 62 cytological samples which remained negative even

after a histopathological examination were considered True negatives (TN) (Table 2, Table 3).

Table 2

Number of cases based on sample types obtained in a cytological and histopathological examination

Diagnostic categories	Cytological (No. of cases)	Histopathological (No. of cases)
Malignant	68 (**66**+2)	82 (**66**+10+6)
Negative	72 (**62**+10)	64 (**62**+2)
Suspicious/Atypical	6	-
Inadequate	4	4

Table 3

2x2 contingency table with the number of samples obtained in a cytological and histopathological examination

Cytological exam.	Histopathological exam.		Total
	+	-	
+	72	2	Positive
-	10	62	Negative
Total	Sick	Non-sick	Total

Cytology has a sensitivity of 87.80%, specificity of 96.87%, positive predictive value of 97.29% and negative predictive value of 86.11%. The accuracy of a cytological diagnosis compared to a histopathological one is of 91.78% (Figure 3).

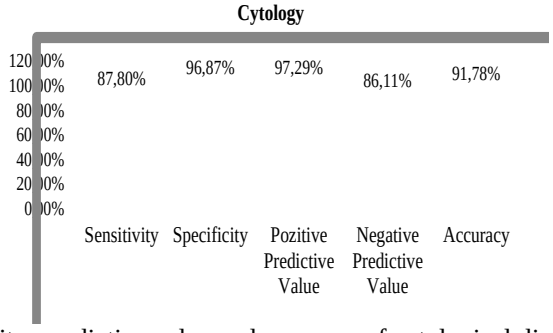

Fig. 3. Validity, predictive value and accuracy of cytological diagnostic test

The concordance of cytology with histopathology, taking into account correctly identified samples in malignant and negative settings is of 128 cases (85.33%).

Bronchopulmonary cancer presents with a high morbidity rate in males in most countries, the male-female ratio of 2:1 found in our study being different from other data in relevant literature, where some studies show a ratio of 8:1 (Ahmad M. et al 2004). The predominance of

bronchopulmonary cancer in males is explained by a multitude of risk factors for this disease: professional factors (industrial polluting agents), social factors (stress) and lifestyle factors (smoking) (Țârlea A. et al 2010).

The high number of cases in the 51-70 age group can be explained by the frequent association of the main cancer factors which need a long time to show clinical symptoms. The fact that BPC strikes three times more in people from an urban setting is a consequence of the higher addressability of patients for an earlier diagnosis of the disease and also due to the high atmospheric pollution in an urban setting, mostly because of fuel combustion smoke.

The frequency of malignant smears of 82.93% obtained in our study in cytology testing undertaken on biological samples is situated within the limit of malignant positivity of previous studies which is between 70 and 90% (Galbenu P. 2010, De Villaine S. et al 1996). If we add the suspect smears we obtained (6 samples) then the total percentage for malignant suspicion in a cytological exam will reach 90.25%, a value which is over the superior limit of previous studies in specialty literature.

Data obtained in the histopathological exams from our study show that squamous NSCLC carcinoma is in first place with 64.63% of cases, a frequency which is over the WHO statistics for our country (40-45%). Adenocarcinoma is in second place with 29.27%, under the WHO statistics for Romania (40%). The frequency of SCLC carcinoma (3.66%) in third place is under the WHO statistics in Romania (10-15%), the same being the case with NSCLC-NOS carcinoma (2.44%) compared to 5-10% nationally. Differentiating between squamous carcinoma and pulmonary adenocarcinoma is achieved through standard morphological criteria (Stang A. et al 2006). In our study from the 74 cytological malignant or suspect samples, only 72 of them were proven to be malignant in a histopathological setting with the 2 negative cases being included in the False positive category, results which are lower than in other studies (Tanwani AK et al 2000). The false interpretation in a cytological setting may be due to a chronic inflammatory process, cellular dysplasia, atypical histiocytes or squamous metaplasia. The presence of intermediate cells does not necessarily reflect a local metaplasia of the examined bronchial epithelium, with these cells maybe travelling from the oral or pharyngeal cavity once the bronchoscope was introduced.

From the 72 negative samples in a cytological exam, 10 samples were proven to be malignant in a histopathological setting, being False negatives and offering a result higher than in other studies (Tanwani AK et al 2000). The false negative results were due to the insufficiency of bioptic material, inflammation or hypocellular aspirate.

The concordance between cytological and histopathological results was situated at 62 samples interpreted negatively in both examinations, results similar to other studies (Rosell A. et al 1998, De Villaine S. et al 1996). The cytological diagnostic value in our study has a sensitivity of 87.80% (correctly identifying patients with the disease), and specificity of 96.87% (correctly identifying patients who do not have the disease), values which are comparable to other studies (Jay SJ et al 1980). The proportion of real positives from the total positives was of 97.29% and the proportion of real negatives from the total negatives was of 86.11%. The accuracy of cytological diagnosis compared to the histopathological diagnosis, meaning the degree in which cytology present the real value of a measured characteristic was of 91.78%, value comparable to other studies (Chaudhary BA et al 1978). The accuracy of techniques used is very important in sustaining a cytological diagnosis.

The concordance of cytological diagnosis compared to the histopathological diagnosis of 85.33% is the result of difficulties encountered in interpreting the cytological sample: chronic inflammatory process, cellular dysplasia, insufficient bioptic material or mucus production. Atypical cells can be identified in the sampled biological material through bronchial brushing, but interpreting cell types is difficult because a cell broken from its tissue environment has the tendency to change morphology. The cytological exam very rarely offers a certain diagnostic value by itself. This type of exploration always needs to be corroborated with other clinical and paraclinical explorations.

From the results obtained in our study we can however state that the cytological examination is still a method which can be recommended as accessible, less costly and allowing for a fast diagnosis.

CONCLUSIONS

Cytology with bioptic material obtained through bronchial brushing has a high sensitivity, specificity and accuracy in diagnosing bronchopulmonary cancer.

The cytological exam is relatively safe while also being accessible, less costly and fast in offering a diagnosis. The obtained results offer almost the same information as the results obtained through a histopathological examination.

Even still, cytological examination rarely offers a diagnosis all by itself and needs to be correlated with other clinical and paraclinical explorations. Samples with suspicion of malignancy in a cytological exam need to be given a histopathological exam as well.

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