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**PARANEOPLASTIC SYNDROMES IN LUNG
CANCER
~CLINICAL AND EPIDEMIOLOGICAL
RESEARCH~**

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SIBIU 2012

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THE SYNTESIS OF THE GENERAL PART

BRIEF HISTORICAL OF THE PULMONARY CANCER

The pulmonary primitive cancer includes the cases of cancer that develops, in a primitive process, regularly from the bronchic glandular epithelium, invading further the pulmonary parenchyma. It is the most important and frequent form of pulmonary tumour, representing over 90% of the primitive malignant and benign tumours.[5,53]

Some authors (especially the bronchology ones) consider that, the correct name would be *bronhogen* or *bronhogenic cancer* (Lemoine). The majority of them use the name of *pulmonary* or *bronchopulmonary cancer*, that doesn't exclude the idea of the bronchogenic origin predominance, reflects better the co-affection bronchial and parenchymatous and is not incorrectly from the anatomic point of view, because the bronchias are part of the lungs. Also, correctly is the name of *carcinoma*. [5,54]

Rarely met and mistaken, in the antiquity, with tuberculosis and with other consumptive pulmonary diseases, the lung cancer was pointed out for the first time, without being individualised, in the XVIth century, by Paracelsus and by Agricola as *male metallorum*, at the mine workers from Schneeberg (1531) and from St. Joachimstal (1556). The diagnosis was put retrospectively, much more lately, by Hesse and Härting (1879). Meantime Bayle (1810) described it under the name of *cancerous tuberculosis*, considering it as the 6-th form of tuberculosis. The merit of individualisation, as nosologic entity, under the name of the lung's *encephaloid*, it returns, few years later, to Laennec. Stokes (1837) establishes the diagnosis process. Walsche (1843) is the first to give the name of lung *cancer*. Wolf (1895) draws the attention on the association with the tuberculosis. Waldayer specifies, firstly, the epithelial origin of the cancerous tumor.[5]

Untill the end of the XIX century are studied, in detail, the clinical aspects (Stokes, Jaccoud, Darolles, Marchiafanos) and the morphopathological ones (Virchow, Ménetrier). In the first decade of the XX century the radiological aspects of the disease in its manifest stage, correlated with the morphological ones are specified (Letulle, Huguenin, Delarue). Ulteriorly, through the introduction of the new methods of bronchoscopic investigation, cytodiagnosis, biopsic and functional respiratory one becomes possible the diagnosis of the disease in a relatively precocious, operable stage (Adler, Lemoine).[5]

PARANEOPLASTIC MANIFESTATIONS IN THE BRONCHOPULMONARY CANCER

SHORT HISTORICAL

The first rapport of a paraneoplastic syndrome, was done by Trousseau in 1825, that described the growing incidence of the venous thrombosis at the patients with cancer; since then, it has been proved with, a big frequency, the existent relationship between tumours and the particular paraneoplastic tumours.[114,162]

In 1928, was described, for the first time, by Brown, the Cushing syndrome, in a hirsute patient with diabetes mellitus, arterial hypertension and adrenal hyperplasia, that also had small cells pulmonary cancer.[20,64,71]

In 1942, Guichard described leukaemias that were observed in some cancers and called them paraneoplasia. In 1957, Schwartz and Bartter described a syndrome that consists from hyponatremia of dilution and renal loss of sodium, at two patients with bronchopulmonary cancers. The name of paraneoplastic syndromes was given by Bouden in 1962.[79]

The area of paraneoplastic syndromes expended during time in more and more domains from all the chapters of the medical pathology.

DEFINITION. GENERALITIES.

The paraneoplastic syndromes are non-especific clinical and biological on-especific manifestations that appear at the patients with malignant neoplasias. Those disorders are not caused by the direct, local, mechanical action of the tumour on the organ or tissue where it develops, as it is not in a direct rapport with the local action of the metastasis of the primitive tumour. Those manifestations may precede the symptomatology of the tumour, may appear concomitantly with it or after its apparition. Usually, those syndromes disappear with the removal of the tumour and reappear in case of recidive or metastasis.[53,78]

The paraneoplastic syndromes associated to the bronchopulmonary cancer, are numerous and extremely varied. They are produced through the secretion of ectopic hormones by the tumoral tissue. The producing of ectopic hormones or their precursors, that are peptides, is characteristic for all the cancer types but, in the bronchopulmonary cancer the incidence of the clinical manifestations, correlated with the secretion of ectopic hormones, is relatively raised. It appears

that, the clinical syndromes may appear, only if the neoplastic tissue is capable to metabolise the polypeptides that are precursors, in bioactive hormones.[53]

Those syndromes are non-specific, the same clinical panel may be observed in different malignant tumours with histological aspect and a varied place, so it may appear also in benign tumours or in the non-tumoral affections.

From the clinical and biological point of view, the syndromes are varied and may be described in three categories:

1. The well-shaped clinical and biological syndromes that appear during every evolutive phase of a malignant tumour (pre-clinical phase, clinical phase) and that represents, actually, real paraneoplastic syndromes.
2. Biological syndromes that have no clinical manifestation and that are due to the presence of the substances secreted by the tumour.
3. Syndromes and symptoms that appear especially in the final phase of the disease (ponderal loss, prolonged febrile states, itchiness). They were named parathias and may be observed, also, in other diseases, not only in the malignant tumours.[56]

The second category of the biological modifications, without clinical expression, is important, especially, in establishing the diagnosis and in the pursuance of the evolution of the disease.

The paraneoplastic manifestations appear frequently in the bronchopulmonary cancer with small cells and rarely in the epidermoid carcinoma and adenocarcinoma, but there isn't an ectopic hormone secretion strictly specific for a certain histological type.[53]

INCIDENCE

Generally, the paraneoplastic syndromes have a great importance, because they are present in almost 15% of the patients with the diagnosis of cancer, and till 70% from the patients with bronchopulmonary cancer may present one of these syndromes during the disease's evolution.[71,114]

Their incidence is different in accordance with the present clinical signs, the most frequently were described in the endocrino-metabolic syndromes (approximatively 12% from the patients).[53]

THE SYNTHESIS OF THE SPECIAL PART

THE MOTIVATION OF THE SUBJECT

Given the growing prevalence of the bronchopulmonary cancer, that represents the first cause of decease through cancer in Europa and USA, the implicitly growth of the paraneoplastic syndromes is possible.

In the speciality literature there are a few substantial studies published, regarding these syndromes, but in our country there is no large study to evidentiate, at least, their incidence among the patients with pulmonary neoplasias.

The paraneoplastic syndrome, may be several times, the initial element that determines the patient to present at the physician, or it may be the first sign of recurrence at the patients diagnosed with bronchopulmonary cancer and treated for this affection. Moreover, these syndromes may mimic the metastatic disease, and if are not detected, may lead to a palliative treatment instead of a curative treatment.

Recognising them is important in establishing a precocious diagnosis. The symptoms may appear with the clinical exteriorization of the tumour or in any other moment of its evolution. In these conditions, the paraneoplastic syndrome may dominate the clinical scene and the neoplasia may be ignored, determining this way diagnosis and treatment mistakes. When the syndrome appears during the evolution of a cancer already known, it may be erroneately interpreted as being in connection with a metastasis, that may determine serious errors. Paraneoplastic syndromes may appear also in the final phase of the cancers, when it represents often the direct cause of the patient death and when, their recognising, would permit the application of a correctly symptomatic treatment, that could prolong the survival of the patient or at least would diminish the patient's sufferences, that represents, in the incurable diseases, an important gain.

That is why I consider that, the thesis may bring important data regarding the characteristics of those syndromes and may constitute a point of departure in the organisation of larger studies with the aim of precocious diagnosis and of the evaluation of their incidence at the patients with neoplastic pathology.

THE AIM OF THE PAPER

The paper proposed to evaluate the incidence of the paraneoplastic syndromes in the patients diagnosed with lung neoplasm in our geographical area, at the moment of diagnosis and during the disease evolution.

Another objective was the study of the characteristics of these paraneoplastic syndromes in accordance with the histologic and evolutive type of the pulmonary neoplasia.

MATERIAL AND METHOD

We have realised a prospective study, including the patients diagnosed with bronchopulmonary cancer, with or without treatment, and patients that presented with the symptomatology of a paraneoplastic syndrome diagnosed further with this cancer.

The lot was selected from the patients admitted consequently in the Oncology, Medical I, Medical II, Neurology, Nephrology, Hematology Clinics of the Clinical County Emergency Hospital Sibiu and the patients diagnosed at the Pneumophthysiology Hospital Sibiu and guided towards the Oncology Clinic for speciality treatment.

The data were gathered from the observation files and also from the anamnesis and from the objective examination of the patients.

The following examinations were done:

- The objective examination in detail, insisting on some characteristic modifications for the paraneoplastic syndromes (hippocratic fingers, hypertrophic osteoarthropathy, full moon face, the evaluation of the nutrition score, etc);
- Laboratory examination:
 1. Complete hemoleucograme, leukocytic formula and erithroid morphology in case of modification of the hemoleucograme, sideremia;
 2. Na, K, Ca, Mg, P;
 3. Astrup;
 4. Seric alkaline phosphatasis, creatine phosphokinase, LDH, TGO, TGP, glicemia;
 5. CIC, C3, IgA, IgM, IgG, crioglobulin, Rheumatoid factor, Anti-nuclear antibodies;
 6. Inflammatory probes: VSH, Fibrinogen, PCR;

7. Seric ureea, seric creatinine, uric acid, proteinuria, urine summary exam, urinary sediment, calciuria, phosphaturia, urinary Na.
 8. Complete lipids panel;
 9. Determining the plasmatic cortisole and the urinary 17-ketosteroids;
 10. Determining the parathormone (PTH);
- Bone radiographies in case of pains or modifications of the osteoarticular system;
 - Abdominal ecographies to evidentiate the possible hepatic metastasis, tumour of the suprarenal gland; ecographies of the cervical region at the cases diagnosed with hypercalcemias, ecographies of other regions in accordance with this symptomatology;
 - Electroencephalograms, electromiographies at the patients with neurologic symptomatology;

The data were centralised, processed and analysed, followed by the formulation of the study's conclusions.

RESULTS

In the present paper were taken in discussion all the patients diagnosed with lung cancer or treated for this affection, during 1st of January 2007 – 31st December 2009, among them were selected the patients that presented in a moment or another a form of paraneoplasia.

During the 3 years of study were diagnosed with lung cancer a number of 242 of patients: 80 (33,05%) in 2007, 72 (29,75%) in 2008 and 90 (37,19%) in 2009.

Table no.1 – The repartition on years of study of the patients with bronchopulmonary cancer

The year of study	2007	2008	2009
The number of patients	80 (33,05%)	72 (29,75%)	90 (37,19%)
Total no. of patients	242		

From the total amount of 242 patients 207 (85,53%) were men and only 35 (14,47%) were women.

Table no.2 - The repartition on sex ratio of the patients with bronchopulmonary neoplasm

Total no. of patients	242
Men	207 (85,53%)
Women	35 (14,47%)

Analysing the selected patients, is observed that, the majority of them are from the urban environment, 124 (51,23%) of the patients, while 118 (48,77%) of the patients were from the rural environment, the females being represented in a percentage of 98,2% as coming from the urban environment.

In a great proportion of cases, in 204 (84,29%) patients, was established that, the diagnosis of bronchopulmonary cancer has a direct connection with smoking, those patients being ex- or at present smokers. 38 (15,71%) of the patients diagnosed with this affection were non-smokers. The average number of cigarettes smoked daily was of 20, during 20-40 years.

The best represented age group was comprised between 50-59 years, the diagnosis being established at 93 patients, followed by the age group of 60-69 years, the diagnosis being established at 89 de patients. The younger patient was 38 years old, and the older one was 85 years, the average age was of 60,83 years.

Table no. 3 - The repartition of the patients with bronchopulmonary cancer in accordance with the age group

Age category	35-39 years	40-49 years	50-59 years	60-69 years	70-79 years	80-89 years
Number of patients	2 (0,82%)	15 (6,19%)	93 (38,42%)	89 (36,77%)	39 (16,11%)	4 (1,65%)

The histopathologic diagnosis was established at 181 patients as:

- Epidermoid carcinoma – 80 patients (33,05%);
- Small cells carcinoma – 43 patients (17,76%);

- Adenocarcinoma – 49 patients (20,24%);
- Big cells carcinoma – 8 patients (3,3%);
- Pericytoma – 1 patient (0,41%).

From various reasons 61 patients hadn't a histopathologic diagnosis of the lung cancer (old age, concomitant cardiac affections, the diagnosis of the neoplasia was done in an advanced phase, etc.).

We have tried to find a correlation between the histopathologic type of cancer and the cigarettes consumption. This could be done so: in the case of the epidermoid carcinoma 79 patients declared being ex- or at present smokers, 41 of the patients diagnosed with small cells declared ex- or present smokers, in the case of the adenocarcinoma 33 patients never smoked, 21 among them are women, and in the case of the big cells carcinoma all being ex- or present smokers. Among the patients at which it couldn't be determined the histopathologic type, only 2 were non-smokers.

Table no. 4 – The repartition of the smoker patients in accordance with the histopathologic type of the lung cancer

Histopathologic type	Smoker patients
Epidermoid carcinom	79
Small cell carcinoma	41
Adenocarcinoma	16
Big cell carcinoma	8
Undetermined histopathologic type	59

PARANEOPLASTIC SYNDROMES

An important percentage of the patients 110 (45,45% from the total of the lung cancer), presented before, at the moment of diagnosis or during the disease evolution, a certain type of a paraneoplastic syndrome. Several times were evidenced, at the same patient, two or more types of paraneoplastic syndromes (digital hypocratism associated with pulmonary hypertrophic osteoarthropathie, with hypercalcemia or with rheumatismal paraneoplastic syndromes, migratory trombophlebitis associated with rheumatismal syndromes; the majority of the paraneoplastic syndromes have associated one type or several types of hematologic paraneoplastic syndromes, etc).

HEMATOLOGIC MANIFESTATION

The main clinical and biological parameters characteristic to the paraneoplastic syndromes were pursued. The hematologic paraneoplasias occupy an important place, during the study evidentiating several paraneoplasias.

Table no.5 – The main hematologic syndromes evidentiating at the moment of diagnosis of lung cancer

Hematologic syndromes	Number of patients
Anemic syndromes	21 (19,09%)
Poliglobulias	6 (5,45%)
Trombocytosis	23 (20,9%)
Monocytosis	21 (19,09%)
Granulocytosis	19 (17,27%)
Eosinophilias	2 (1,81%)

HYPERCALCEMIA

In 29 of the patients with bronchopulmonary cancer (11,98% from the total of the bronchopulmonary cancer and 26,36% from the total of the paraneoplasias), in a certain moment of the disease, was evidenced a certain degree of hypercalcemia. In the case of this syndrome a correlation with the histopathologic type of the lung cancer was made. So, 23 (79,31%) patients diagnosed with hypercalcemia were also diagnosed with epidermoid carcinoma, a patient (3,44%) had a big cells carcinoma, another one adenocarcinoma (3,44%), and the other 4 (13,79%) hadn't a histopathologic diagnosis of the lung neoplasm.

THE SCHWARTZ-BARTTER SYNDROME

5 patients (4,54% from the total of the paraneoplasias, 2,06% from the total of the bronchopulmonary cancers) presented, in a moment or another of the evolution of the pulmonary neoplasia, values of the serum Na <130 mmol/l, but not smaller than 115 mmol/l, fact that determined the continuation of the investigations. It was determined the plasmatic osmolarity that was decreased (<280 mOsm/l), it was determined the natriuresis and urinary osmolarity that were increased (natriuresis of 20mEq/l, urinary osmolarity of 500mmol/), all those being increased in all 5 cases.

Those modifications accompanied by a clinical panel consisting from anorexia, queasy, eructations, physical astenia associated with the renal, hepatic, suprarenal and thyroid functions that were normal, concluded that it is a Schwartz-Bartter syndrome associated to the pulmonary neoplasia.

All the cases were associated to the small cells pulmonary cancer (11,62%).

THE ECTOPIC SECRETION OF ACTH – THE CUSHING SYNDROME

This syndrome was evidenced in 27 patients, representing 11,15% of the total amount of lung cancer and 24,54% from the whole paraneoplasias.

GYNECOMASTIA

7 patients (2,89% from the total of the lung cancer and 6,36% from the total of the paraneoplasias), were diagnosed with gynecomastia uni or bilateral, 3 of them having this

modification since the diagnosis of the malignant affection, at the others patients, it appeared during the disease's evolution.

In 5 patients this sign was accompanied by clubbing of the digits, in this case we may speak about the digital hypocratism-gynecomastia syndrome (2,06% of the total of lung cancer and 4,54% from the total of the paraneoplasias).

ACANTHOSIS NIGRICANS

Only one patient (representing 0,41% from the total of the lung cancer and 0,9% from the total of the paraneoplasias) was diagnosed with *Acantosis Nigricans*. At this paraneoplasia the patient associates also hypocratic fingers.

Fig. no.1 – Patient S.E. (Personal archive)



OSTHEO-ARTICULAR MANIFESTATIONS

1. Digital hypocratism

Had an increased incidence in the studied population, 68 (28,09% from the patients with bronchopulmonary cancer and 61,81% from the paraneoplasias) patients having this sign. 3 (1,23%) patients presented digital hypocratism at the moment of diagnosis of the lung cancer, at the rest of the patients (26,85%) this sign appears during the disease's evolution. This type of paraneoplastic syndrome appeared concomitantly with other types of paraneoplastic syndromes, its single presence being rare.

2. Hypertrophic pulmonary osteoarthropathy

Hypertrophic pulmonary osteoarthropathy in its complete form, was present at 11 patients (4,54% from the total of the lung cancer and 10% from the total of the paraneoplasias) 2 patients presenting at the doctor, for the rheumatoid syndrome manifested through pains and joint inflammations, simetric at the radiocarpal, knee or ankles articulations. In 9 patients this manifestation appeared in a moment or another of the evolution of the pulmonary neoplasia.

3. Rheumatismal paraneoplastic syndromes

22 patients, representing 9,09% from the total of the lung cancer and 20% from the total of the paraneoplasias, were diagnosed also with a rheumatoid paraneoplastic syndrome.

9 patients (3,71% from the total of the bronchopulmonary cancer and 8,18% from the total of the paraneoplasias) presented at the doctor with an polyarthralgia syndrome, and the biologic probes effectuated evidentiated an important inflamatory syndrome, in 5 patients being present also the rheumatoid factor, but with absent antinuclear antibodies.

13 patients (5,37% from the total of those with pulmonary cancer, 11,8% from the total of those with paraneoplasias) had polyarthralgias during the disease evolution, at a certain moment from the diagnosis of the neoplasia, more or less distant.

NEUROLOGICAL MANIFESTATIONS

5 types of neurological syndromes were evidenced in 14 patients, representing 5,78% from the total of the lung cancer and 12,72% from the total of the paraneoplasias.

The diagnosis was established such as: a case of limbic encephalitis (0,41%), a case of subacute cerebellar degeneration (0,41%) that also presented a sensitive motor polyneuropathy, a case of left femoral mononeuropathy (0,41%), 2 cases with myasthenic syndrome (0,82%), at 9 patients being diagnosed a sensitive motor polyneuropathy (3,71%).

THROMBOPHLEBITIS

At 3 (1,23% from the whole patients with pulmonary cancer, 2,72% from the whole of the paraneoplasias) of the patients diagnosed with bronchopulmonary cancer was observed the presence of a thrombophlebitis.

Two patients presented, to the general practitioner, with the suspicion of a *thrombophlebitis*, proved, further, clinically and ecographically. A patient was diagnosed with thrombophlebitis on the axillary and left brachial vein, the another patient with thrombophlebitis of the right popliteal vein. During the period of hospitalisation for this affection, the radiologic examination revealed bronchopulmonary cancer, other investigations being made to support this diagnosis. The third patient was diagnosed with thrombophlebitis further to the diagnosis of the pulmonary neoplasia.

POLYMYOSITIS - DERMATOMYOSITIS

Polymyositis – Dermatomyositis was present, as a form of onset of the bronchopulmonary cancer, in only one case (0,41% from the total of the bronchopulmonary cancer and 0,9% from the total of the paraneoplasias).

NEPHROTIC SYNDROME

The nephrotic syndrome, as a paraneoplastic syndrome associated to the lung cancer, was present in only one patient (0,41% from the total lung cancer and 0,9% from the total of the paraneoplasias).

FEVER

From the 242 patients, associated to the respiratory symptoms or after case to other symptoms, 27 had as a debut symptom the subfebrility, with temperatures comprised between 37,2-37,5 °C, while 8 of them had fever, with temperatures comprised between 37,6-38,9°C. The infectious, inflammatory causes of the febrile process were excluded, this symptomatology being interpreted as a paraneoplasia. During the disease evolution other 102 patients presented with increased body temperature, and were evaluated, but the paraneoplastic etiology couldn't be asserted with certainty.

ANOREXIA as a symptom of debut was evidenced at 24 patients, accusing, at the first moment of presentation at the general practitioner, the lack of appetite, one of the symptoms for which they presented at the doctor being this one. Ulterior, during the disease evolution, other 38 patients reported the apparition of the anorexia, at a variable distance from the administration of the chemotherapy treatment.

CACHEXIA. At the moment of the first medical consultation all the patients were calculated the body mass index after the formula: $BMI=W/H^2$; where W = body weight in kilograms, H = height in meters. From the 242 patients 28 had the $BMI=25 \text{ kg/m}^2$, those being framed in various degrees of obesity or superweight, 185 had $BMI=20-24,9 \text{ kg/m}^2$, 7 had a BMI between $18,6-19,9 \text{ kg/m}^2$, and 22 of them had BMI of $18,5 \text{ kg/m}^2$.

Table no.6 – The repartition of the patients in accordance with the nutritional status

Nutritional Status	Number of patients
BMI>25 kg/m²	28
BMI=20-24,9 kg/m²	185
BMI=18,6-19,9 kg/m²	7
BMI <18,5 kg/m²	22

CONCLUSIONS

1. The bronchopulmonary cancer remains, still, the privilege of males, with a rapport between men/ women of 5,9/1.
2. The most frequent apparition of the bronchopulmonary cancer was in smokers than in non-smokers, with a rapport smokers/non-smokers of 5,3/1.
3. The incidence of the pulmonary neoplasm is slightly increased in the human environment (51,23%).
4. It is observed an increased incidence, of the bronchopulmonary cancer, in the young aged people, the age category that is most affected is situated between 50-59 years (38,42%).
5. The epidermoid carcinoma, that is tobacco dependent, is the most frequent hystopathologic type in 33,05% of the cases (n=80).
6. The prevalent localization of the bronchopulmonary cancer, in the studied lote was in the right lung, in 64,04% of the cases (n=155).
7. It was evidentiated an increased incidence, of 45,45% (n=110), of the paraneoplastic syndromes. The paraneoplastic syndromes were diagnosed previously to the moment of the cancer diagnosis, or during the evolution of the pulmonary neoplasm.
8. The incidence of the paraneoplastic syndromes that preceded the bronchopulmonary cancer diagnosis was of 12,8% (n=31).
9. The most frequent paraneoplastic hematologic syndrome was the monocytosis, in 16,1% (n=39) of the cases.
10. The presence of the monocytosis in an important number of cases diagnosed with bronchopulmonary cancer, pleads for the its paraneoplastic character.
11. There weren't observed severe anemic syndromes, except the ones after the initiation of the specific oncologic therapy, but those weren't catalogued as paraneoplastic.
12. The thrombocytosis was diagnosed in an important number of cases, 12,8% (n=31), the values of the thrombocytes weren't surpassing 1.000.000/mm³.
13. Next to the hematologic syndromes, the paraneoplastic endocrine syndromes, are evidentiated in an important number of cases (69 patients), representing 28,51% from the total amount of bronchopulmonary cancer.

14. Hypercalcemia is the most important paraneoplastic endocrine symptom, being diagnosed at 11,98% of the patients (n=29).
15. 23 patients, representing 79,31% from the total of the hypercalcemias, were diagnosed with epidermoid carcinoma.
16. There were also diagnosed rare paraneoplastic pathologies, described in the specialty literature: hyperthyroidia, acanthosis nigricans, nephrotic syndrome, each being represented by a case (0,41% from the total of the bronchopulmonary cancer).
17. The predominant histopathologic type associated with the ectopic secretion of ACTH, is the small cells carcinoma, being observed in 24 patients (82,75% from the total of this paraneoplastic syndrome).
18. In 2,06% of the patients (n=5) was diagnosed the syndrome of digital hypocratism-gynecomastia, syndrome consisting of the association between digital hypocratism and gynecomastia.
19. The most frequent paraneoplastic manifestation is represented by the hypocratic fingers, being observed in 68 patients (28,09%).
20. The predominant histopathologic type, as in the case of the pulmonary hypertrophic osteoarthropathy and of the rheumatoid syndromes, is represented by the epidermoid carcinoma, 8 patients, respectively 14 patients being diagnosed with this histopathologic type.
21. The presence of the venous thrombosis with an atypical localisation, that are resistant to anticoagulants, is obvious in 3 patients (1,23%).
22. The neurologic paraneoplastic syndromes precede, in the majority of the cases, the discovery of the pulmonary tumour, in 10 from 14 patients diagnosed with a neurologic manifestation, the diagnosis of the bronchopulmonary cancer being established further.
23. The most frequent neurologic manifestation is represented by the sensitivo-motor polyneuropathy, being obvious in 9 patients (3,71%).
24. The predominant histopathological type, in the frame of the neurologic manifestations, is the carcinoma with small cells (n=8).
25. The paraneoplastic syndromes are important from the numerical point of view in the diagnosing of the bronchopulmonary cancer.

26. It is observed the association of one or several paraneoplastic syndromes in the same patient.
27. The apparition of some clinical biological manifestations suggestive for a paraneoplastic syndrome, especially at the patients with risk factors for bronchopulmonary cancer, should determine the initiation of investigations.
28. The results of this study confirms the existing data in the literature, according to which the paraneoplastic syndromes appear with an increased incidence among the patients diagnosed with bronchopulmonary cancer.

WHAT NOVELTY BRINGS THIS PAPER

Our study is the first published paper that has as a research theme this pathology in the geographical area of the south of Transilvania.

Interesting data were obtained regarding the correlations between the different histopathological types of the bronchopulmonary cancer and the presence of the paraneoplastic syndromes.

It was evaluated the relationship of the paraneoplastic syndromes with the evolutive moment of the pulmonary neoplasia.

It was proved the importance of knowing the paraneoplastic syndromes associated to the cancers in general and of the bronchopulmonary cancer in particular.

Original contributions are brought through the diagnosis of a new type of a paraneoplastic syndrome, with the evidention of the **monocytosis** in an important percentage of patients pleading for its enframing in the category of paraneoplastic hematologic syndromes.