

CLINICAL, RADIOLOGICAL AND EPIDEMIOLOGICAL CONSIDERATIONS IN BACTERIOLOGICALLY UNCONFIRMED PULMONARY TUBERCULOSIS

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Abstract: Pulmonary tuberculosis, with its numerous clinical-radiological and progressive aspects, puts some real difficulties in finding the causing agent (*M.tuberculosis*), despite all the progress that has been made in the field of laboratory techniques in the last years. Because of the bacteriological confirmation's absence, the anamnesis, the clinical and radiological examination, the patient's epidemiological and biological data contributes to give a good diagnosis. The study examines the features of 108 patients hospitalized, having the diagnosis of pulmonary TB, clinically unconfirmed (code: A160), at the Pneumophthysiology Hospital in Mihăești, Vâlcea, between 01.01.2006 and 31.12.2008. The study illustrates the data related with the signs and symptoms of the disease recorded at admission, the aspect and location of the pulmonary modifications, the epidemiological impact of this type of patients on the contractions in the pest hole of tuberculosis. Symptomatology was dominated by cough, with or without expectoration, in 85% of the cases and there were also recorded a „tuberculous impregnation syndrome“ (loss of appetite with weight loss, night sweats, asthenia). 70% of the patients claimed that the duration of symptoms until hospitalization varied between two and four weeks. The pulmonary X-ray findings included nodular infiltrative-type of changes, for 74% of the patients, caseous-cavity lesions in 23% of the cases, miliaria in 3% and pleurisy associated with lung changes in 4% of the cases. The distribution of lesions prevailed in the upper lobes (93%), and the right upper lobe represented 72% of sites. The pulmonary radiological examination of the people who came into contact with the patients of the study group, proved to be normal for 73 (86%) of the ones examined, in eight cases there were found disabling type changes and in four cases the lesions were infiltrative-nodular type. Two patients diagnosed with nodular infiltrative changes, were received treatment for TB. Tuberculin skin testing (TST) of the children involved, pointed out a positive reaction, diameter of 10-14mm, in five cases (18%) and nine children (33%) had a hyperergic reaction, (diameter of induration > 15 mm). Bacteriologically unconfirmed pulmonary tuberculosis was clinically expressed by cough with or without expectoration and the tuberculous impregnation syndrome, the duration of these events being of about 2-4 weeks. Infiltrative nodular pulmonary lesions located at the upper lobes were the ones that prevailed. Detection of new cases of the disease on the adults involved, of *M. tuberculosis* infection in children from the pest hole draws attention upon the potential source of infection for this category of patients.

Cuvinte cheie: tuberculoza pulmonară, modificări radiologice, contacti, test la tuberculină

Rezumat: Tuberculoza pulmonară (TB), cu multiplele ei forme clinico-radiologice și evolutive, pune uneori reale dificultăți în identificarea agentului cauzal (*M.tuberculosis*), cu toate progresele în tehnici de laborator din ultimii ani. În absența confirmării bacteriologice, la susținerea diagnosticului contribuie anamneza, examenul clinic și radiologic, datele epidemiologice și biologice ale pacientului. Studiul analizează particularitățile a 108 bolnavi internați, cu diagnosticul de tuberculoză pulmonară neconfirmată bacteriologic (cod: A160), în Spitalul de Pneumoftiziologie din Mihăești județul Vâlcea, în perioada 01.01.2006-31.12.2008. Sunt prezentate datele legate de semnele și simptomele bolii la internare, aspectul și localizarea modificărilor pulmonare, impactului epidemiologic al acestui tip de pacienți asupra contactilor în focarul de tuberculoză. Simptomatologia a fost dominată de tuse, cu sau fără expectorație, în 85% dintre cazuri și un sindrom de impregnare bacilară (inapetență cu scădere ponderală, transpirații, astenie). 70% dintre pacienți au raportat o durată a simptomelor până la internare între două și patru săptămâni. Tabloul radiologic pulmonar a cuprins modificări de tip infiltrativ-nodular la 74% dintre bolnavi, leziuni cazeos-cavitare în 23% dintre cazuri, miliaria în 3% iar pleurezia asociată modificărilor pulmonare s-a întâlnit în 4% dintre cazuri. Distribuția leziunilor a fost majoritară în lobi superiorii (93%) iar lobul superior drept a reprezentat 72% dintre localizări. Examenul radiologic pulmonar, al persoanelor contacte cu pacienții lotului studiat, a fost în limite normale la 73 (86%) dintre examinați, în opt cazuri (9%) s-au găsit modificări de tip sechelar iar

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în patru cazuri (5%) leziunile au fost de tip infiltrativ nodular. Dintre pacienții depistați cu modificări infiltrativ nodulare, doi au fost diagnosticați, declarați și tratați pentru TB. Testarea la tuberculină (IDR) a copiilor contacți a evidențiat o reacție pozitivă, diametrul 10-14mm, în cinci cazuri (18%), iar 9 copii (33%) au prezentat reacție hiperergică (diametrul indurației > de 15 mm). Tuberculoza pulmonară neconfirmată bacteriologic s-a exprimat clinic, predominant prin tuse cu sau fără expectorație și „sindromul de impregnare bacilară”, durată manifestărilor fiind de două-patru săptămâni. Leziunile pulmonare infiltrativ-nodulare localizate la nivelul lobilor superiori au predominat. Depistarea unor cazuri noi de boală la contacții adulți, a infecției cu *M. tuberculosis* la copiii din focar, atrage atenția asupra potențialului de sursă de infecție a acestor categorii de bolnavi.

INTRODUCTION

For most patients with pulmonary TB in our country a diagnosis can be established by sputum examination (microscopy and culture), highlighting the etiologic agent, *M. tuberculosis*. There is a percentage of 20-25% (7) of the cases recorded, without bacteriological confirmation, the diagnosis being supported, according to *The National TB Control Programme* (6) by anamnestic, clinical-radiological and epidemiological data.

THE AIM OF THE STUDY

I considered the approach of some clinical-radiological aspects connected with negative pulmonary TB to be necessary so that the results obtained should be useful in routine practice when choosing the best ways to approach patients with negative sputum at the bacteriological examination. I have also evaluated the epidemiological impact of these patients on the people exposed in the pest hole of tuberculosis.

MATERIAL AND METHOD

This is a retrospective study conducted on 108 patients living in Ramnicu Valcea hospitalized between 01.01.2006 and 31.12.2008 diagnosed with bacteriologically unconfirmed pulmonary tuberculosis, (code: A160), at Pneumophthysiology Hospital in Mihăești, Vâlcea.

What was recorded from the patients' clinical observation sheets and files for epidemiological investigations: patients' data, symptoms and clinical signs at the admission, duration of symptoms, associated diseases, radiological pulmonary test results at the admission, results of radiological examinations performed on the adults exposed, tuberculin skin test values (TST) for the children exposed in the pest hole.

RESULTS

Among the study group of 108 patients, 29 were women (27%) and 79 men, (73%), aged around 17- 76 years old, the average age was of 46,48 years for women and 50,59 years for men. In what concerns the living environment, 70 men, (64,8%), were living in the countryside and 38, (35,1%) in the city.

In terms of real treatment history, 88 patients, (81%) were new cases and 20 patients, (19%) were relapse cases. Symptoms presented by patients in the group studied at the admission were mostly: cough with or without expectoration, in 85% of cases, followed by loss of appetite and of the weight, (48%), chest pain, (29%), night sweats, (28%), asthenia, (21%), haemoptysis (20%), fever, (>38.5°C), in 10% of the cases (Table 1).

One aspect of the clinical manifestations, was the chronicity (duration) of symptoms expressed in weeks, reported by patients as the period between the onset of the disease and the hospitalization. According to the anamnesis recorded in the observation sheets, 70% of the study group reported an average duration of symptoms between two and four weeks until

hospitalization.

Table no. 1. Clinical symptoms of the patients at the hospitalization

Symptoms and clinical signs at admission	Absolute frequency (no.)	Relative frequency(%)
Dry cough	28	26
Cough + mucous/ muco-purulent expectoration	64	60
Haemoptysis	22	20
Fever	11	10
Nocturnal sweats	30	28
Dyspnea on exertion	20	19
Chest pain	31	29
Loss of appetite and of weight	52	48
Physical fatigue	23	21

The most common diseases associated with tuberculosis (comorbidities) were: chronic hepatitis, gastric and duodenal ulcer, diabetes, neuro-psychiatric diseases, renal failure and chronic alcoholism, seen in 32% of the patients in the study group. At the hospitalization, the pulmonary radiological picture was polymorphic, with infiltrative- nodular type lesions, seen in 74% of cases, caseous-cavity lesions in 23% of cases, miliaria in 3% of cases and pleurisy associated to lung changes, in 4% of the cases. If we are to compare it with radiological changes according to gender, it appears that infiltrative, nodular lesions were predominant both in women (73%) and in men, (75%). Caseous-cavity aspects were found in equal percentages (23%) while pleurisy associated with lung parenchyma measurements was found only in men (Table 2).

Table no. 2. The aspect of pulmonary radiological changes according to the gender

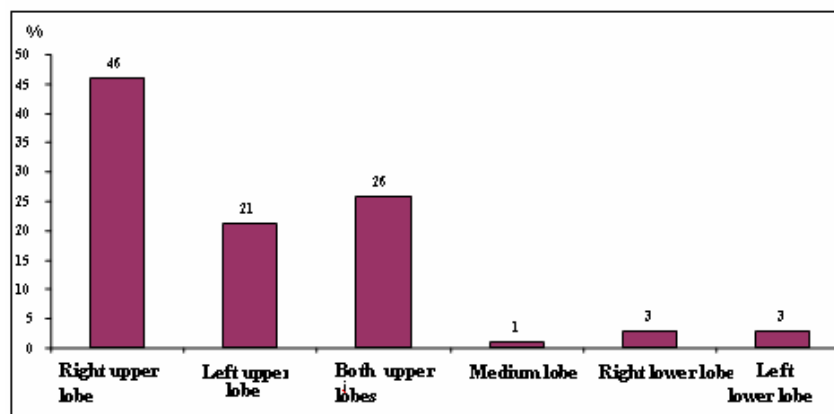
Radiological modification	WOMEN		MEN	
	Number	Percentage (%)	Number	Percentage (%)
Infiltrative, nodular aspect	21	73	59	75
Caseous-cavity aspect	7	23	18	23
Pulmonary and pleural lesions	0	0	(4)	(5)
Miliaria	1	4	2	2
TOTAL	29	100	79	100

Cavity type lesions were met more frequently in patients with relapse and associated diseases. The distribution of lesions showed a predominant localization in the upper lobes, (93% of the patients), the right upper lobe being affected in greater proportion- 72% than the left upper lobe- 48% and radiological changes in the lower lobes were found in 3% of the

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patients. (Figure1).

Figure no. 1. Distribution of pulmonary radiological changes



Epidemiological impact of patients on the exposed people in the pest hole has been evaluated according to the results of tests carried out under 67 epidemiological surveys. Of the exposed persons, there were 87 adults and 27 children, aged 5-15, examined radiologically, by tuberculin skin testing. Pulmonary radiological aspects common to the people exposed, domiciliary or non-domiciliary, with the patients enrolled in the research group were described as nodular infiltrative-type lesions (5% of patients), disabling fibrotic (9%) and normal aspects in 86% of cases. (Figure2). The interpretation of skin test (TST) showed that 10 children (37%) had a response < than 9 mm, five children (18%) had an induration diameter of 10-14 mm, 9 of them, (33%) had a response > than 15 mm, (hyperergia) and in three cases, (12%), the reaction was negative. (Figure3).

Figure no. 2. Pulmonary radiological aspect-people exposed

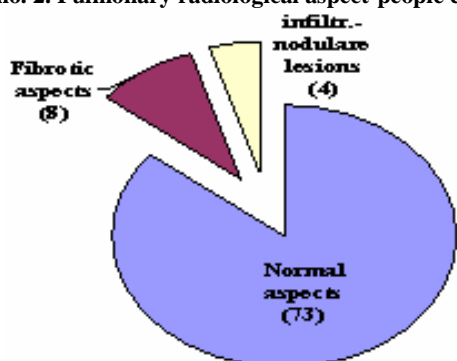
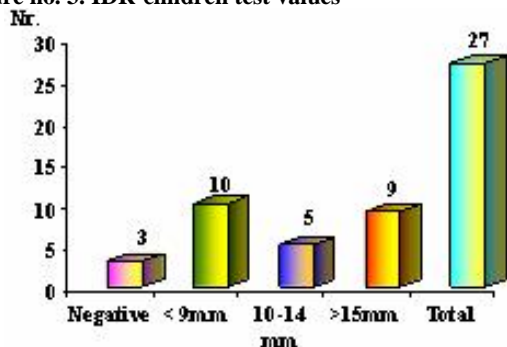


Figure no. 3. IDR-children test values



Patients with obvious clinical and radiological signs of pulmonary TB but repeated negative sputum investigations are a common clinical problem in specialty practice. In these cases, the diagnosis is usually supported in the first stage, by clinical anamnestic and radiological pulmonary findings, but it is known that these have a high sensitivity and a low specificity (5).

The symptoms of pulmonary TB in adults are generally, cough, with or without expectoration, along with the "syndrome of tuberculous impregnation" (2) (4) which installs insidiously, progressively, events that become revealing if they exceed three weeks and don't remit under non-specific treatment. In the study group, 85% of patients presented cough syndrome, chronic infection was seen in 70% of cases and the symptoms in most patients lasted between 2-4 weeks.

Pulmonary radiological examination is essential for the diagnosis, monitoring and evaluation of negative TB patients' treatment, the aspect and the location of pulmonary changes depending on: individual reactivity, the evolutionary stage of disease, associated diseases. The radiological changes that were predominantly found were the nodular-infiltrative type ones in both sexes (over 73%), fact which probably expresses the specific alveolitis (3), processes most frequently met in the early stages of these illnesses. The distribution of lesions showed an upper lobe predominant impairment (93% of patients), literature showing that the favorite location of tuberculosis in the lung is in the superior lobes (2). Cavity type lesions were more frequently met in patients with disease relapse and associated diseases (diabetes, chronic hepatitis, ulcer), explained by their particular reactivity.

Until recently, negative tuberculosis was not considered as having significant contribution to the secondary transmission of disease, the confirmation of the link between microscopy negative sources and the cases supposed to have been disordered by them, is difficult, but studies on population, carried out by means of genetic testing, estimated that patients with negative TB can contribute with at least 17% to the disease's incidence in the community (1). Among the adult patients diagnosed at the radiologic examination of the people exposed, with nodular infiltrative changes, two were diagnosed and treated for pulmonary TB.

In children, it is known that the sensitivity and specificity of the tuberculin skin test are variable, correlated with regional prevalence of tuberculosis, mass BCG vaccination and infection with atypical mycobacteria which may induce cross-reactions (8). Strong positive reactions of IDR (induration diameter greater than 15 mm) suggesting a possible infection with *M. tuberculosis* and an increased risk of development of lesions, were seen in nine (33%) of the children exposed,

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examined in epidemiological investigations. Children are more susceptible to tuberculosis and the risk of the progression of the infection in a severe disease is higher, compared to adults (9).

CONCLUSIONS

Pulmonary tuberculosis remains a major public health issue in Romania and the current percentage of bacteriologically unconfirmed cases shows that the results of the microbiological investigation are still insufficient. Bacteriologically unconfirmed tuberculosis or few bacilli eliminator (microscopically negative) is accepted in the World Health Organization (W.H.O) but the case's evaluation based on other criteria (epidemiological, biological, clinical and radiological) lacks the diagnosis' "Gold standard", that is the etiologic confirmation.

Cough, with or without expectoration, accompanied by tuberculous impregnation syndrome, manifested over a period of at least two weeks, was the dominant element in the symptomatic array of patients in the study group. Pulmonary radiological examination, by the polymorphic appearance of lesions and the distribution predominant in the upper lobes was the essential investigation in supporting the diagnosis.

Patients with chronic diseases associated with TB showed extensive, evolved (cavity) lesions more frequently, with possible epidemiological implications, in response to the treatment.

Bacteriologically unconfirmed tuberculosis can be a source of infection for the community, the epidemiological investigations carried out in the pest holes of the patients investigated proving two new cases of the disease, the percentage of children exposed estimated to be infected with M.tuberculosis, being of 51%.

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