THE DIFFICULTIES OF DETECTION OF EXTRAPULMONARY TUBERCULOSIS AMONG CHILDREN WITH THE CONCOMITANT PATHOLOGY

Zoriana Piskur
MD, Assistant of the department of pulmonology and tuberculosis
Danylo Halytsky Lviv National Medical University

UKRAINE

Introduction. In Ukraine the incidence of tuberculosis (TB) among children in 2015 and 2016 was 8.8 per 100 thousand population. Among the total number of patients with TB, the proportion of extrapulmonary TB in children was 1.88 % and 1.98 %, respectively [1]. Detection and differential diagnostics of this disease is difficult [2, 3] especially at the presence of concomitant pathology [4, 5].

The aim: to assess the impact of concomitant pathology on the course and the detection of TB among children.

Materials and methods. The data from 330 case histories of children who were hospitalized in Lviv Anti-TB Dispensary because of TB from 1988 to 2017 was retrospectively analyzed. The children were divided into the following groups: the first (1st) group – extrapulmonary tuberculosis (EPTB) with concomitant pathology (CP) (n=49); the second (2nd) group – EPTB without CP (n=112); the third (3rd) group – pulmonary tuberculosis (PTB) with CP (n=63); the fourth (4th) group – PTN without CP (n=106). The statistical processing of materials was performed using the computer program Statistica 8.0. The reliability of the difference between the two relative indicators was assessed using the Fisher test with the Metropolis algorithm. The difference in \( p<0.05 \) was considered statistically significant.

Results. The young children (Table 1) were more often observed in the 1st group (53.0%), 27.0% of them were under one year of age. The children aged 4-7 years old predominated in the 3rd (38.1%) and 4th (34.0%) groups; the children aged 8-14 years old – in the 2nd group (49.1%). It was found that the average age of children in the 1st group was significantly lower than the average age of children in the 2nd (5.34±0.69 vs. 7.21±0.42; \( p<0.05 \)) and 4th (5.34±0.69 vs. 7.03±0.40; \( p<0.01 \)) groups.

| Age          | Group | The 1st group (n=49) | The 2nd group (n=112) | The 3rd group (n=63) | The 4th group (n=106) |
|--------------|-------|----------------------|-----------------------|----------------------|-----------------------|
|              | number | %                    | number %               | number                | number %               |
| 0-3 years old| 26     | 53.0                 | 29                    | 25.9                 | 19                    | 30.2                 | 31                    | 29.2                 |
| 4-7 years old| 7      | 14.3                 | 28                    | 25.0                 | 24                    | 38.1                 | 36                    | 34.0                 |
| 8-14 years old| 16     | 32.7                 | 55                    | 49.1                 | 20                    | 31.7                 | 39                    | 36.8                 |
| The average age (M±m) years | 5.34±0.69*,** | 7.21±0.42* | 6.41±0.48 | 7.03±0.40** |

Notes. * - the difference is significant between the average age of the 1st relative to 2nd, \( p<0.05 \); ** - the difference is significant between the average age of the 1st relative to 4th, \( p<0.01 \).

Girls predominated in the 4th group – 57.5% (in the 1st – 40.8%, in the 2nd – 43.7%, in the 3rd – 47.6%), the number of boys did not differ significantly (in the 1st – 59.2%, in the 2nd – 56.3%, in the 3rd – 52.4 %, in the 4th – 42.5 %). The children from urban (the
At the analysis of CP among children of the 1st group was found somewhat more often diseases of the hematopoietic system (16.3% vs. 6.3%; p>0.05), the vast majority of iron deficiency anemia (87.5%) as well as diseases of the digestive system (10.2% vs. 4.8%; p>0.05): gastritis, gastroduodenitis, cholecystitis, enterocolitis. It was found that in this group protein and mineral metabolism disorders were observed somewhat more often (10.2% vs. 1.6%; p<0.05), namely the malnutrition of the second stage was found in 3 (60.0%) children and in one case - cachexia and rickets. The pathology of the endocrine system was also more common among the children of the 1st group (8.2% vs. 3.2%; p>0.05). It was found that the children of the 3rd group were significantly more likely to have infectious and parasitic diseases (41.3% vs. 22.4%; p<0.05), and respiratory diseases (14.3% vs. 2.0%; p<0.05). In addition, only this group was diagnosed with diseases of eyes (6.3%) and ears (1.6%). Among infectious and parasitic diseases among the children of the 3rd group most often were found ascariasis (42.3%), enterobiosis (23.1%), in one case – a combination of them, and in 7.7% - trichofacillosis; among diseases of the respiratory system it was found bronchitis (55.6%). It should be noted that the pathology of the immune system was represented by HIV infection in two children of the 1st group and one child of the 3rd one.

In the structure of the clinical forms of the EPTB in the 1st and 2nd groups, the TB of the peripheral lymphatic nodes (LN) was more often observed (32.7% vs. 33.0%). The tuberculous meningitis and the TB of the central nervous system (CNS) (18.4% vs. 23.2%), the TB of bones and joints (14.3% vs. 25.0%), and the TB of eyes (6.1% vs. 8.0%) were observed somewhat less frequently (p>0.05) among children from the 1st group. At the same time, the proportion of the TB of another localization was slightly higher in the 1st group (14.3% vs. 7.1%; p>0.05). The above may indicate a mistaken attribution of EP localization of TB to the manifestations of CP. The complications of the EPTB were developed among 24.5% of the children from the 1st group and 27.7% of the children from the 2nd one.

In 83.7% children of the 1st group and 71.4% children of the 2nd one, EPTB was combined with of the TB of the respiratory organs. Figure 1 shows the structure of the clinical forms of the PTB.

![Bar chart showing the proportion of clinical forms of the pulmonary tuberculosis in different groups.](image)

**Fig. 1. The structure of clinical forms of the pulmonary tuberculosis.**

In the 2nd group compared to the 4th one, the proportion of TB of intrathoracic
LN was significantly higher (67.5% vs. 51.9%; p<0.05), and the primary tuberculosis complex was significantly lower (25.0% vs. 48.1%; p<0.01), it was also lower in the 1st group compared to 3rd one (31.7% vs. 52.4%; p<0.05). However, in 29.3% of the children of the 1st group and 6.2% of children of the 2nd one, miliary PTB was noted, in one child of the 1st group and in one child of the 2nd group TB of pleura and focal TB were observed, respectively.

It was established that among children of the 1st compared to the 3rd one, the proportion of the PTB detected in the phase of infiltration was significantly lower (39.0% vs. 73.0%; p<0.01), and detected in the phase of infiltration, seeding and decay was significantly higher (46.3% vs. 12.7%; p<0.001), this indicator was also higher in the 2nd group compared to the 4th one (21.3% vs. 7.5%; p<0.01). The phase of compaction of the children of the studied groups did not differ significantly (p>0.05).

At the same time, bilateral lesions were detected significantly more frequently among the children of the 1st group compared to the 3rd one (58.5% vs. 14.3%; p<0.001), in the 2nd group compared to the 4th one (33.7% vs. 13.2%; p<0.001), and in the 1st group compared to the 2nd one (58.5% vs. 33.7%; p<0.05). The complications of the PTB were noted in 22.0% of the 1st group, in 3.8% of the 2nd group, and in 17.5% of the 3rd group.

At the beginning of the disease, the Mantoux test was significantly less frequently performed among the children of 1st group compared to the 3rd one (75.5% vs. 95.2%; p<0.01) and slightly less often among the children of the 2nd group compared to the 4th one (84.8% vs. 92.5%; p>0.05). Importantly, in the 1st group compared to the 3rd one, the percentage of negative results of the Mantoux test was significantly higher (18.9% vs. 3.3%; p<0.05) (Figure 2). It was found that the average number of non-specialized medical institutions, which before hospitalization in a specialized hospital were children in, was significantly greater (p<0.001) in the 1st group compared to the 3rd one (1.45±0.14 vs. 0.49±0.08) and in the 2nd group compared to the 4th one (1.35±0.09 vs. 0.43±0.06). It was established that from the children of the 1st and the 2nd groups (28.6% and 27.7%) compared to the 3rd and the 4th (7.9% and 5.7%), were slightly more often in two non-specialized medical institutions and 14.2% of the children of the 1st group were in three and four institutions. It indicates that children with extrapulmonary localization of a specific process and in the presence of CP are in more somatic medical institutions that children with PTB.

Fig. 2. The results of the Mantoux test among children of researched groups.
It was found that both children of the 1st group compared to the 3rd one (83.7% vs. 63.5%; \( p<0.05 \)) and children of the 2nd group compared to the 4th one (92.9% vs. 50.0%; \( p<0.001 \)) were significantly more frequently detected during the application for the medical care. During delivering medical care the children of the 1st group compared to the 3rd one (19.5% vs. 47.5%; \( p<0.01 \)), and the children of the 2nd group compared to the 4th one (10.6% vs. 70.0%; \( p<0.001 \)) significantly less were detected within 2 weeks. At the same time, the 2nd group compared to the 4th one, was significantly more often detected within 6 months (28.8% vs. 1.9%; \( p<0.01 \)). The children of the 1st group compared to the 3rd one, slightly more often were detected within 6 months (19.5% vs. 7.5%; \( p>0.05 \)), but a significant difference in diagnosing within one month (43.9% vs. 45.0%; \( p>0.05 \)) was not detected. In addition, 7.3% and 9.8% of the children of the 1st group were diagnosed before one year and more than one year, respectively. The above indicates that before the diagnosis "Tuberculosis" among children with CP, the specific process lasts longer which leads to the development of complications and generalization in various organs.

Conclusions.
1. It is proved that children of the early age with concomitant pathology significantly more often developed extrapulmonary TB.
2. In the structure of the concomitant pathology among children with the extrapulmonary TB more often were observed iron deficiency anemia, the diseases of the digestive and endocrine systems, the malnutrition of second stage, cachexia and rickets; among children with the pulmonary TB were detected infectious and parasitic diseases, bronchitis.
3. In 83.7% of children with CP, EPTB was combined with a specific process of the respiratory system which was significantly more often bilateral and in the phase of infiltration, seeding and decay. In addition, 29.3% of them had miliary PTB.
4. In the majority (75.5%) of the children with EPTB the Mantoux test was not performed, and in 18.9% of the children negative results of the Mantoux test was detected due to the masking of symptoms of CP due to a combination of specific and nonspecific processes.
5. The combination of CP with EPTB contributed to the stay of children in a large number of non-specialized medical institutions and long-term (from 6 months to more than one year) diagnosing, mostly (83.7%) during the applications for the medical care.

References:
[1] Туберкульоз в Україні (2017). ДУ «Центр громадського здоров’я Міністерства охорони здоров’я України». Аналітично-статистичний довідник. Київ. Вилучено з: https://phc.org.ua/kontrol-zakhvoryvanyan/tuberkuloz/statistika-z-tb/analitichno-statistichni-materialy-z-tb.
[2] Кульчавеня, Е.В., Жукова, И.И. (2017). Внелегочный туберкулез – вопросов больше, чем ответов. Туберкулез и болезни легких, (2), 59-63. Вилучено з: https://doi.org/10.21292/2075-1230-2017-95-2-59-63
[3] Dasho, M. B., Lyshenyuk, C. A., Chulovska, U. B., & Lytvyn, H. О. (2016). Труднощі і помилки диференціальної діагностики при туберкульозному менінгоенцефаліті у дитини 6,5 місяців. Інфекційні хвороби, (2), 87-91. Вилучено з: https://doi.org/10.11603/1681-2727.2016.2.6529
[4] Романова, М.А., Мордик, А.В., Иванова, О.Г., Турцик, А.А., Мерко, Е.А. (2018). Болезни мочеполовой системы у больных туберкулезом детей. Туберкулез и болезни легких, (2), 36-40. Вилучено з: https://doi.org/10.21292/2075-1230-2018-96-2-36-40
[5] Полякова, А.С., Багдарсарян, Т.Р., Степанян, И.Э., Березовский, Ю.С., Романов, В.В., Заргашов, А.Э. (2018). Случай диссеминированного поражения легких при сочетанном заболевании. Туберкулез и болезни легких, (7), 55-59. Вилучено з: https://doi.org/10.21292/2075-1230-2018-96-7-55-59