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ЛІНГВІСТИЧНИЙ НАВЧАЛЬНО-МЕТОДИЧНИЙ ЦЕНТР**

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# THE PLACE OF BCG-OSTEITIS WITHIN DISEASES OF BONE SYSTEM IN CHILDREN OF PRESCHOOL AGE

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**Introduction.** The epidemiological situation of tuberculosis in Ukraine does not tend to improve.

**Background.** In Europe extra pulmonary tuberculosis is 97% and in Ukraine - 3%. But affection of the bones among children of preschool age began to increase. This generates some diagnostic difficulties.

The goal of the work is to share research with pediatricians, pediatric surgeons and orthopedists with features of tuberculosisosteitis and its diagnosis in preschool age groups.

**Materials and methods.** The article presents the analysis, diagnosis and treatment of 67 children under 6 years.

**Results.** Tuberculosis etiology was observed in 30 (44.8%) children. The vast majority of tuberculousosteitis was diagnosed at age of 3 in 83.3% cases, lesion of the femur was observed in most cases - in 12 (40%).

**Keywords:** osteomyelitis in children, BCG-osteitis.

**Introduction.** The epidemiological situation with tuberculosis around the world every year becomes worse [1, 2, 3, 4, 5, 6, 7, 9, 10]. Every year 8-10 million new cases are being diagnosed. More than 3 million patients die [3]. Ukraine has reached a certain stabilization of the infectious disease [2, 3, 4]. In our country in general the rate of extrapulmonary forms of tuberculosis is 3 % [3, 5, 6]. In 40-45 % of cases the osteoarticular processes are observed[5]. It is believed that

osteoarticular tuberculosis has a tendency to increase in numbers. [4, 5].

Recently the cases of tuberculous lesions of skeleton apparatus have started to occur in young children [2, 3, 4, 6, 7, 8]. Osteitis, which can be associated with vaccination against tuberculosis is disclosed in 75 % of these patients [3, 7, 9]. Though the first case of BCG osteomyelitis was described over 40 years ago phthisiatricians and immunologists refer this pathology to serious complications of vaccination, the causes of which, until recently, remained unclear [1, 6, 7]. According to an international survey, the estimated rate of osteitis/osteomyelitis is 1–700/1,000,000 vaccinated newborns or infants with different strain-derived BCG. Russian authors on their territory found 0.3 of osteitis per 100 thousand of vaccinated with BCG [1]. In the case of other sources 21.1 per 100 thousand vaccinated [5]. In Western Europe (Denmark, Germany, Finland, Sweden, Czech Republic), the frequency of BCG-osteitis in 70-90 years was 73.0 cases per 100,000 vaccinated children [6, 8, 9, 12]. For publication [4], their frequency was 22 per 100 thousand of vaccinated.

Total number of publications concerning this complication is limited. In view of this problem diagnostics of BCG-osteitis at this time remains unsolved. This situation is explained by the peculiarities of the disease, the difficulty of pathogen detection and its identification. While it is clear that, the selection of standard bacteriological mycobacterium from the affected area of the bone is the most reliable method for confirmation of tuberculosis etiology [1, 5]. However, the mycobacterium in BCG-osteitis is found in to European research only in 56 % - 67 % of cases [7, 8, 12]. Russian researchers diagnose it only in 24 - 50%, depending on atypical form of the pathogen and technical capabilities of the laboratory [1]. Publications in reference to bacteriological nature of osteitis are absent in Ukraine. Thus, formally given the above mentioned,

including microbiological testing data, the frequency of postvaccinal osteitis can be underestimated and cannot be treated etiopathogenetically. Thus, BCG disease etiology cannot be excluded by the negative results of bacteriological studies [7, 12]. In such situations the cytological and histological verification methods are of great importance [2, 3, 5, 9]. There were publications concerning molecular-genetic techniques for verification of such processes [7, 13]. But not all laboratories are able to perform such studies [12, 13].

Urgency of the problem is determined by innovation and imperfect knowledge of BCG-osteitis, and factors, mentioned above as well as the lack of adequate number of publications on the subject.

The goal of the work was to investigate the incidence and clinical course of inflammatory diseases of the skeletal system in children of Slobozhansky part of Sumy region, draw attention of wide medical community to the problem of the existence and features of BCG-osteitis. To study the possible connection of specific osteitis with BCG vaccination and to establish possible factors that can contribute to the development of such complications.

**Materials and methods.** 67 children, treated in the surgical department of Sumy Regional Children's Clinical Hospital and Sumy Regional Clinical TB Dispensary were examined. The age of patients ranged from 8 months to 6 years. All hospitalized patients were diagnosed with inflammatory diseases of the skeletal system. In all cases studied "TB" history of family and close circle, enquired information about vaccinations, analyzed the results of tuberculin tests in dynamics. During examination, patients showed BCG vaccination scar on the left shoulder. Clinical, biochemical and microbiological study of material obtained from osteobiopsy and surgical operations were completed. Traditional X-ray and ultrasound was also performed.

Results and discussion. The largest number of pediatric patients - 38 (56.7 %) live in eastern Sumy region of Ukraine. This region is considered the most polluted by industrial waste and emissions of public and private transport. [4]

Patients' age: under 1 year - 20 (29.9 %) children, 1-2 years - 18 (26.9 %), 2-3 years - 12 (17.9 %), 3-4 years - 7 (10.5 %), 4-5 years - 8 (11.9 %), 5-6 years - 2 (2.9 %) - (Table 1).

Table 1

Distribution of patients by age of children

Osteomyelitis type		Tuberculous	Nonspecific	Total
Up to 1 year	Absolute #	7	13	20
	Relative #	23,3%	35,1%	29,9%
1-2 years	Absolute	12	6	18
	Relative	40,0%	16,2%	26,9%
2-3 years	Absolute	6	6	12
	Relative	20,0%	16,2%	17,9%
3-4 years	Absolute	1	6	7
	Relative	3,3%	16,2%	10,4%
4-5 years	Absolute	2	6	8
	Relative	6,7%	16,2%	11,9%
5-6 years	Absolute	2	0	2
	Relative	6,7%	0	3,0%

The table shows that the vast majority of patients with inflammatory diseases of the bones were younger than 3 years: with tuberculous osteitis - 25 (83.3 %) with non-specific osteomyelitis - 25 (67.7 %) children. Frequency of tuberculosis osteomyelitis was 1.2 times greater ( $P > 0.05$ ). Among patients of 1 year osteomyelitis of non-specific etiology dominated - 35.1 % of children and tuberculous osteitis occurred in 23.3 %, which is less than 1.5 times ( $P < 0.05$ ). At the age of 1-2 years, patients with tuberculosis osteomyelitis was 12 (40 %), and patients with osteomyelitis of non-specific origin - 6 (16.2 %), which is less than 2-fold ( $P < 0.05$ ). In the age group of 2 - 3 years osteitis tuberculosis etiology occurred in 6 (20 %) children, and non-specific etiology - in 6 (16.2 %), which is less than 1.2 times. So the difference in the frequency of specific and non-specific osteitis 1 year was in favor of non-specific - 1.5 times and 2 times the difference in favor of specific osteitis, which occurred at the age of 1-2 years, with a probability indicates the prevalence of osteo-tuberculosis 2 years. In the age group of 2-3 years, there has been some difference in the incidence of osteitis in favor of specific, but it was not accurate - in 1.2 times ( $P > 0.05$ ). That is, in this age "alignment" frequency osteomyelitis their etiology was recorded.

No significant differences in the incidence of osteomyelitis by gender of affected children have been identified. Osteomyelitis occurred among boys 53.7% , girls - at 46.3 %, which is less than 1.2 times ( $P > 0.05$ ).

Children with inflammation of the bone - 45 (67.2 %) patients were the residents of the city. However, among patients with tuberculosis osteomyelitis in urban areas 21 children (70% ), and the villagers were 9 (30 %), which is 2.3 times more likely ( $P < 0.05$ ). The nonspecific osteomyelitis among children who live in cities is 24 (64.9%); in the villages - 13 (35.1 %), i.e. 1.9 times more ( $P < 0.05$ ) in favor of the cities.

Localization process has been established - (Table 2). Most illnesses struck long bones of the lower limb has been studied- 49 (73.1 %). Thus, tuberculosis hip inflammation occurred among 40 % of children and hematogenous osteomyelitis - in 40.5 %. Tuberculosis and non-specific etiology occurred in 36.7 % and 29.7 %. Shoulder tuberculosis origin is 13.3 %, and non-specific - 10.8 %. The bones of the forearm were affected by tuberculosis in 13.3 % of cases. The patients with non-specific hematogenous osteomyelitis were not. Overall affection of the bones of the upper extremities was observed in 12 cases (17.9 %) less than the disease of the lower extremities in 4.1 -fold ( $P < 0.05$ ). The affection of tubular bones was diagnosed in 2.8 % of cases, and in flat bones - in 15.3 % cases which is 5.5 times more frequent for flat bones. However, specific and non-specific osteomyelitis short tubular and flat bones struck with the same frequency ( $P > 0.05$ ).

Table 2

The frequency of osteomyelitis localization process

Osteomyelitis type			Tuberculous	Non specific	Total
Localization process	Thighs	Absolute#	12	15	27
		Relative#	40%	40,5%	40,3%
	Shin	Absolute	11	11	22
		Relative	36,7%	29,7%	32,8%
	Shoulder	Absolute	4	4	8
		Relative	13,3%	10,8%	11,9%
	Forearms	Absolute	4	0	4
		Relative	13,3%	0	5,6%
	Short bones	Absolute	1	1	2
		Relative	3,3%	2,7%	2,8%
	Flat Bones	Absolute	5	6	11
		Relative	16,7%	16,2%	15,3%

As with non-specific osteomyelitis and tuberculosis in the first place of inflammation was femur, the second - tibial - in third case - flat bones, the fourth - shoulder.

It is noteworthy that the bones of the forearm were affected by tuberculousosteitisin 13.3% of cases , while hematogenous localization has not taken place at all, which may have some differential- diagnostic value.

Only on the basis of clinical symptoms and objective data, tubostitis occurred among 3 (10.0%) children. Other pathognomonic objective data among these children have not been obtained. MBT type of BCG based on the results of bacteriological examination was detected in 11 (36.7%) of cases. Histological and cytological study material was obtained during surgery confirmed tuberculosis granulomas elements in 17 (53.3 %) patients.

Most patients with osteomyelitis had a surgery. Thus, the number of children with tuberculousosteitis osteotomy is 23 (76.7%) individuals, which is 3,3 times more frequent than conservative treatment ( $P < 0.05$ ). Non-specific osteomyelitis of osteotomy was found among 27 (72.9 %) patients, which is 2.7 times more frequent than during conservative treatment ( $P < 0.05$ ). Thus, differences in the relative frequency of surgical treatment for tuberculosis (76.7 %) and non-specific osteomyelitis (72.9 %) was not ( $P > 0.05$ ). However, the indications for surgical intervention in osteitis various origins were significantly different. Thus, tuberculosis osteomyelitis origin surgery was carried out after failure of conservative treatment and the eradication of the bone defect. Non-specific osteomyelitis cases surgical treatment has been done urgently in order to reduce the pressure inside the bone.

The essence of the operation tuberculousosteitis was as follows: under intravenous anesthesia intra or extra-articularnecrosequestrectomiawas performed, curettage of the walls of the bone cavity following injection into the cavity of the bone

rifampicin powder followed by simultaneous grafting of bone defects by auto material (muscle or bone). This operation has been performed for 20 patients. In specific osteomyelitis cases post surgical treatment is 16 days, and conservative - 25.5 days, which is more than 1.6 times ( $P < 0.05$ ). Further treatment of tuberculosis osteomyelitis is continued on an outpatient basis for 6 months, and then - preventive courses are taken for 2-3 months a year. After non-specific osteomyelitis treatment after surgery duration lasts for 13.5 days, conservative therapy was done with repeated courses of treatment. Thus, the benefits of surgical treatment of children with osteomyelitis of specific and non-specific origin are obvious.

The problem of diagnosis of BCG-osteitis at this time remains unresolved. In Ukrainian literature no clear statistical data on the dynamics of the disease is found. In our observations the clinical diagnosis was found in 11 (36.7%) cases based on the results of bacteriological examination, 17 (53.3 %) according to histological examination and in 3 cases (10.0 %) - by clinical symptoms. The vast majority of tuberculousosteitis was observed among children under the age of 3 years (83.3 %). It is important to remember that diagnosis of osteomyelitis in this age group is of high probability of tuberculosis etiology of the inflammatory process, with the relevant objective and subjective -objective disease-based tuberculosis history and connection with the BCG vaccination.

#### Conclusion:

1. Over the past 10 years, there were 67 cases of osteomyelitis in preschool age groups in Sumy region. 30 cases had tuberculosis etiology of inflammation (44.8 %).

2. The vast majority of tuberculousosteitis occurs before the age of 3 years (83.3 %).

3. The patients with tuberculosis osteomyelitis should be given surgical treatment for rapid removal of cell tuberculosis

infection, which reduces the number of bed-days: 1.6 times less than with conservative treatment.

Further research: It is necessary to continue accumulating material for clarification of the clinical course of tuberculous osteitis. When this diagnosis is suspected, patients should be immediately consulted by tuberculosis institutions for confirmation or exclusion of BCG-osteitis. In view of the above it is necessary to focus the attention of wide medical community on the existence of BCG-osteitis and the importance of timely verification.

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