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Tuberculosis in Infancy.Twins under the Age of One with Different Forms of the Disease

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Abstract:- Infancy is a period of diminished natural immunity and lack of specific immunity. It is also time of close contact with family members. This facilitates the transmission of the infection of tuberculosis, if someone of the family members is ill. We present twins under the age of one with two different forms of tuberculosis : severe paratracheal lymphadenitis and hematogenous - disseminated tuberculosis. The age and the degree of the involvement made the diagnosis and treatment a difficult process.

Keywords:- *Tuberculosis, Infants, Hematogenous - Disseminated Tuberculosis.*

I. INTRODUCTION

Tuberculosis /TB/ is a disease so old as the human history. However it is very relevant today. Tuberculosis incidence in the WHO European Region increased sharply from 1990 onwards and decreased after the peak in 1999. The trend is also true for our country.

At the same time 55 337 new TB cases occurred in the countries of the European Union and European Economic Area (EU/EEA) in 2017, equivalent to 10,7 cases per 100000 population. 4,4% of all TB casses were children under 15 years, corresponding to a notification rate of 2,9 per 100000 population (17).

Bulgaria and Hong Kong were the first in the world with introducing specific immune prophylaxis by using oral BCG vaccine in 1951. Since 1957 Bulgarian BCG vaccine has been produced and administered (11). All newborns are immunized after 48 hours of birth. After a negative tuberculin sample of Mantoux immunization was repeated when children reached 6-7 and 10-11 years of age.

Tuberculin skin testing /TST/ is made with the use of 5E Bulgarian PPD tuberculin before vaccination as well as for all people who were in contact with a tuberculosis patient (12, 20).This laid the groundwork for limiting the spread of TB (11) . After decades of successfully containing the disease it has once again become a problem for the medical community in our country. The number of new cases is not so important /1603in 2016 or 22,4 per 100 000/ but their concetration in certain regions and groups of people.

The presence of hidden disease among adults with late diagnosis and insufficient treatment creates the conditions for more and more children to become infected. They are an example for endemic tuberculosis (3,4, 14). Despite the low rate of bacillosis, childhood tuberculosis is one of the forms of spreading of the disease (8).

The new TB cases in children under 15 years in 2015 are 140 . This is 7,1 % among all TB cases in Bulgaria and Rate 13,8 per 100 000 /6,3 per 100000 for the EU/ (17).

The case of the two twins is interesting as it shows the manifestations of two different forms of TB developped from the children at the same time.

II. CASE PRESENTATION

The children were born in a family, in which the father was with recently diagnosed TB, a bacilliter. They are boys, from a pathologically pregnant mother, full-term pregnancy, by an operative mechanism, with a good postnatal adaptation. Without BCG vaccination. The remaining immunizations up to the 4 month are in compliance with the immunization calendar.

❖ *Pationt N1*
M.T.H./N 40365-2015

➢ *Patient Information*
A four-month-old infant born 2200.0. A month before the hospitalization he suffered from dry unproductive cough. Fever appears up to 39o C. Does not respond to treatment with ceftazidime - 5 days, amikacin - 4 days and symptomatic medications. After lung radiographs and epidemiological evidence of contact with tuberculosis, it is directed to a diagnostic refinement.

➢ *Clinical Findings*
He is hospitalized with intoxication but without dyspnoea and temperature. Symmetrical chest, vesicular breathing two sided, free of wheezing. During the course of the observation, a broncho-obstructive syndrome occurs. Rhythmic and clear heartbeat. Abdomen - soft, without organomegaly.

Laboratory analysis shows anemia, hemoglobin /Hb/ - 95g / l, Leucytosis - 28.6 G / l: neutrophils /Neutr/ - 44.9%, lymphocytes /Lymph/ - 48.8%, mononuclear cells /Mo/ - 6.3%, erythrocyte sedimentation rate /ESR/ - 20mm/h. Total protein, albumin and ionogram - the norm. Minimal impaired liver function tests, normal within a month. Normal blood clotting status. The investigated nasal and throat probs are negative.

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➢ *Diagnostic Focus And Assessment*

The close contact with a tuberculosis patient, a bacilliter, suggests exclusion of a specific disease. TST with 5E PPD is 12mm at the 72nd hour but with retaining pigmentation on Day 7. Mycobacterium tuberculosis is isolated once in direct microscopy and three times in culture from stomach washes.

In terms of the severity of the condition, cellular and humoral immunity has been investigated. Data on lymphocytosis with relative T-cell deficiency is detected against the background of an active specific process. Enhanced CD4 / CD8 index. Natural Killer cells /NK cells/ at a lower limit. Elevated B-lymphocytes. Immunoglobulins - at the norm. Phagocytic Activity Assay - Normal Oxidative Blast (90-100%).

Ultrasound: liver, gallbladder, pancreas and spleen - without patologic signs, kidneys at normal place, without drainage disturbances.

Radiographies present meny patopogical findings. Fig.1 and Fig.2

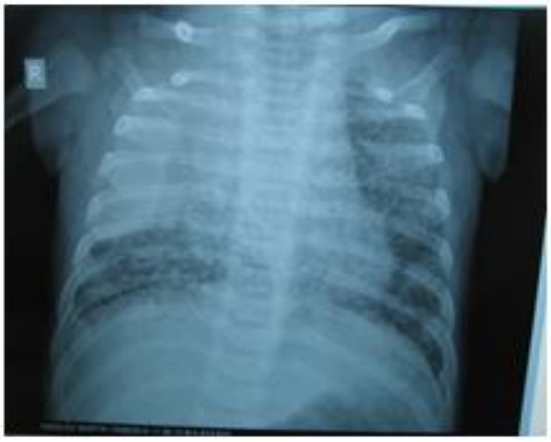

Fig. 1:- Frontal chest X-ray: Right upper and middle pulmonary fields reveal inhomogeneous shading with unclear boundaries, a dense shadow on the right side

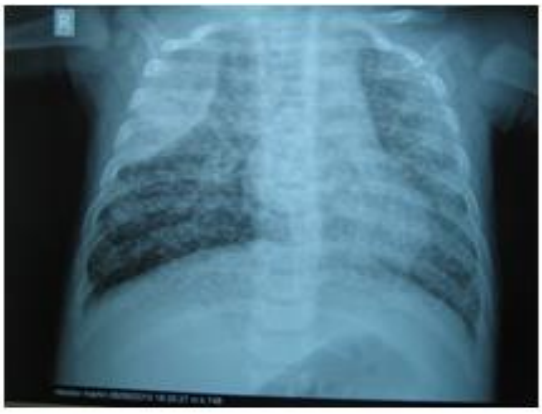

Fig. 2:- Chest X-rey two months later: Nodular shadows symmetrically located in the interstitium persist, mostly apical in the two lung halves. The dense shadow has diminished in size.

Fibro-bronchoscopy (FBS) in view of the persistent pulmonary evidence shows atelectasis in right upper lobe as a result of endobronchial changes in right upper bronchus. To the right, the mouth of the upper bronchus is partially narrowed by a yellowish formation that hangs over the mouth of the bronchus.

Computer tomography with contrast shows athelectasis with airborne bronchogram of right upper lobe, segmental stenosis of upper bronchus. Enlarged axillary, hylex and mediastenal lymph nodes. Fig. 3 and Fig 4

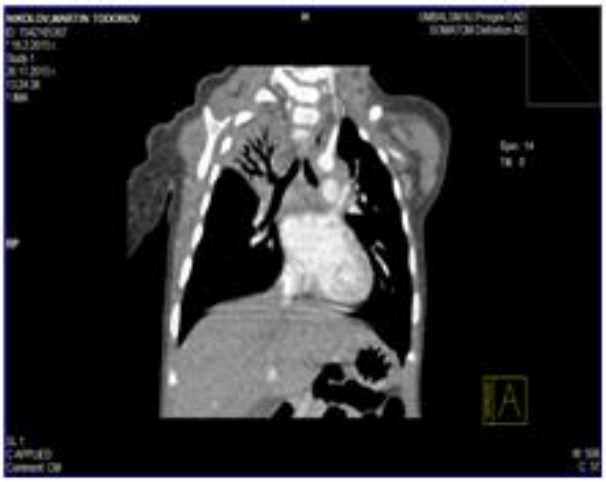

Fig. 3:- CT scan: Athelectasis with airborne bronchogram of right upper lobe, segmental stenosis of upper bronchus.

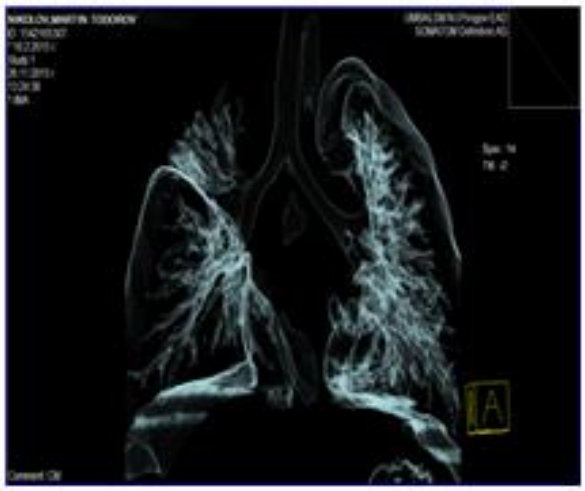

Fig. 4:- CT scan: Athelectasis with airborne bronchogram of right upper lobe, segmental stenosis of upper bronchus.

Control X-ray demonstrates significant resorption around the primary hearth with relative intake of interstitial changes. Persistence of granulomatous changes in the paratraheal lymph nodes and right thymus lobe hyperplasia. Fig. 5 and Fig. 6.

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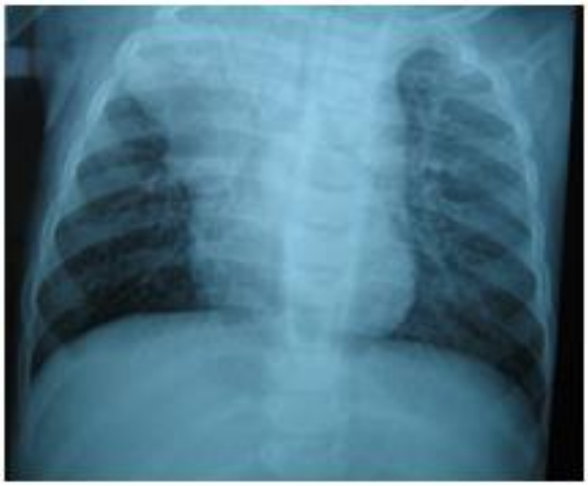

Fig. 5:- Frontal X-ray: Significant resorption around the primary hearth with relative intake of interstitial changes.

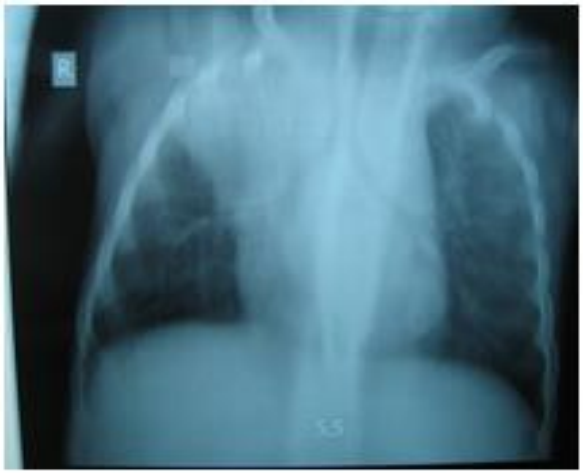

Fig. 6:- Median tomogram: Persistence of granulomatous changes in the paratraheal lymph nodes and right thymus lobe hyperplasia

➢ *Therapeutic Focus and Assessment*

The epidemiological data, clinical and laboratory findings, the radiographic morphological changes give ground to assume the presence of subacute haematogenous-disseminated tuberculosis of the lungs with bacillosis. Treatment with streptomycin for 40 days, replaced with pyrazinamide for 6 months, followed by ethambutol; tubocin and rimicide throughout the course of treatment. Due to deterioration in the second month of treatment with fever and respiratory failure, another month of streptomycine was performed. There were episodes of bronchial obstruction during which inhalation with ventolin, O2 therapy and systemic corticosteroid was included.

Stabilization in his emotional tone and development are registered. The child is treated with rimicid, tubocin and ethambutol up to the 12 month after the beginning.

❖ *Pationt N2*

E.T.N./40240-2015

➢ *Patient Information*

A four-month-old infant born T-2150.0. Two weeks with cough and fever. Due to being unaffected by the treatment with ceftriaxone and amikacin and epidemiological contact data, he is directed to the hospital.

➢ *Clinical Findings*

He is hospitalized without dyspnoea. Symmetrical chest, vesicular breathlessness without wheezing. Rhythmic and clear heartbeat. Other organs and systems - without pathological abnormalities.

Anemic syndrome with possible iron deficiency (Hb - 97g / l, Er - 5,1T / l) and inflammatory activity – Leucocytosis -19.8 G / l: Neutr - 32.3%, Lymph - 61.0%, Mo-6.7%; ESR - 35mm. The investigated nasal and throat secretions are negative.

➢ *Diagnostic Focus And Assessment*

Close contact with tuberculosis patients and lack of scarring from BCG is a reason to provide TST with a 5E PPD, positive - 17 mm at the 72nd hour. Stomach washes are negative for Mycobacterium tuberculosis in direct microscopy and culture. In terms of the severity of the disease, cellular and humoral immunity has been investigated. There is a slight decrease in total T-lymphocytes at the expense of their suppressor-cytotoxic subpopulation. B-lymphocytes are elevated. NK cells are in limits in percentage terms and elevated in absolute numbers.

On frontal X-ray, two enlarged pulmonary hilluses, normal pulmonary pattern, and thymus hyperplasia are established. Fig.7.

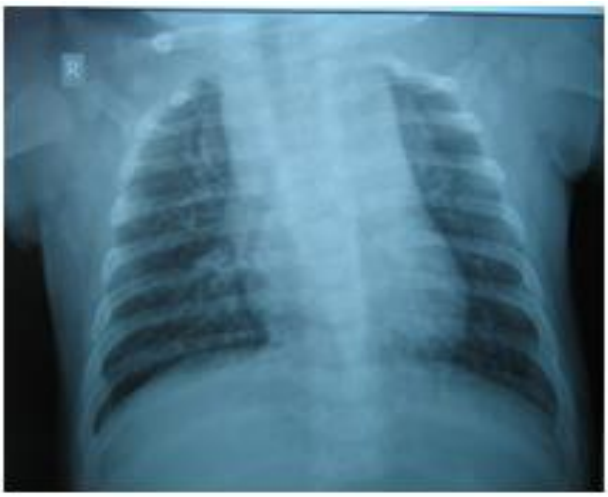

Fig. 7:- Frontal X-ray: Two enlarged pulmonary hilluses .

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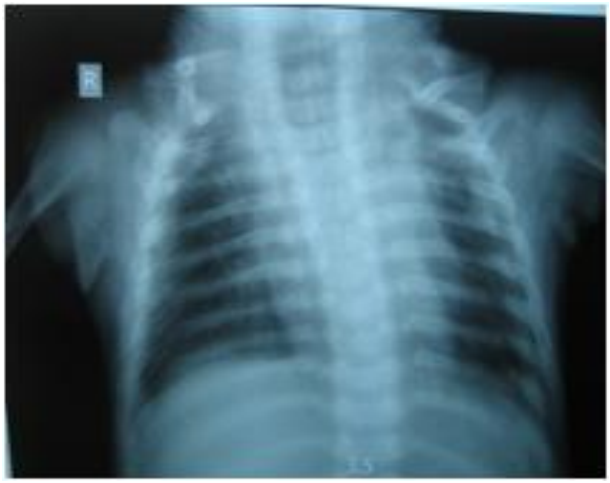

Fig. 8:- .Median tomogram: Data on granulomatously performed lymph nodes left=

On a median tomogram - data on granulomatously performed lymph nodes left. Fig.8. The observed changes are even better outlined on the tomogram a month later. Fig. 9.

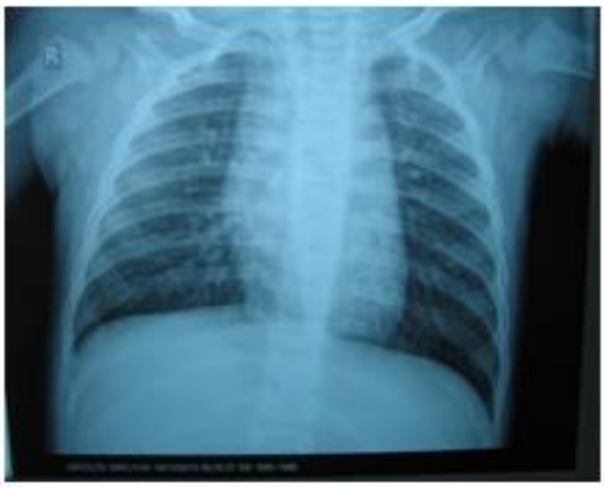

Fig. 9:- Median tomogram:The observed changes are even better outlined

Epidemiological data, clinical status, specific X-ray morphological features supported by the positive tuberculin prob suggest the diagnose TB of the perytracheal lymph node without bacillosis.

➢ *Therapeutic Focus And Assessment*

Treatment with streptomycin for 33 days, substituted with pyrazinamide, rimicide and tubocin, is performed throughout the six-month stay in the clinic. The control chast X-ray shows resorption of the observed granulomatously altered lymph nodes. Fig. 10.

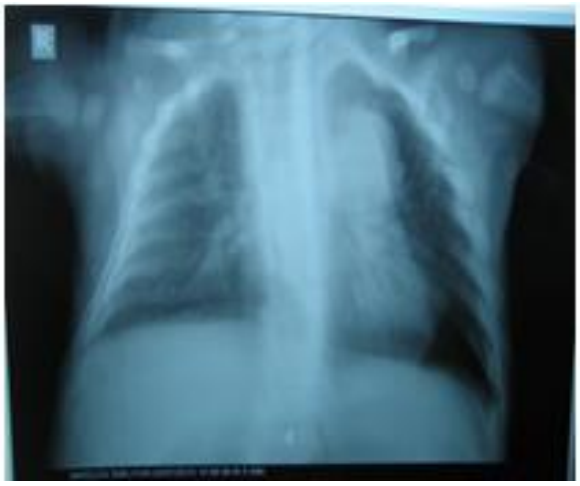

Fig. 10:- Control chest X-ray: Resorption of the observed granulomatously altered lymph nodes.

Home treatment with rimicide, tubocin and ethambutol.

III. DISCUSSION

The cases that were presented illustrate the importance of the problem of TB, focusing on the impact on children in breastfeeding age and early childhood.

Obviously,TB is a disease to be considered on the first day after birth. In both twins the severity of the disease explains the wide differential diagnosis: sepsis, foreign body in bronchus, staphylococcus pneumonia, etc. The anemic syndrome in combination with leucocytosis that is seen in both children can be observed with any severe bacterial infections. The FBS rejects the presence of a foreign body in bronchus in the first case, which could be presented with a similar clinical picture: broncho-obstructive syndrome, X-ray data for atelectasis. In the absence of vaccination, the positive TST is susceptible to disease (2).The diagnosis is based on a history of close contact with a bacilliter, the clinical course of the disease – unresponsive to conventional antibiotic treatment, with positive TSTwith PPD tuberculine and distinctive X-ray morphological changes and confirmed by bacteriology(1, 7).

Close contact with adults with an inadequately diagnosed or incorrectly treated TB infection threatens the child's organism from the first days after birth.

The risk of disease progression is extremely high in children under the age of one (11). Without prophylaxis, which is seen in both cases, 30-40% of them develop pulmonary TB, 20% disseminated form or tuberculous meningitis, after which the survivors most often remain with permanent mental, motor and sensory impairments (11,18). Mortality in this age group remains higher in the years with chemotherapy as well.

The patient's response depends on individual features of his immune system, which performs complex interaction with the tuberculous bacteria and predetermines the form of the disease.

Parallel observation of breastfed infants demonstrate the complex interaction of the micro / macro-organism and the importance of the individual's specific features for the development of the disease (6). Despite being raised in the same way, the first child develops hematogenous disseminated TB, while the second child suffers a primary form of tuberculosis involving the paratracheal group of lymph nodes.

Hematogen-dissemineted tuberculosis is a disease of the immature immune system as well as immunocompromised children: congenital immune deficiency, HIV infected and severely malnourished children. Insufficient cell-mediated immune response cannot distinguish the disease in a regional lymph node.

The bronchadenitis also leads to specific complications - exobronchial obstruction with segmented or lobar collapse and distal air resorbtion as seen in the first case; development of granulomatous tissue in the bronchial wall with breakthrough, leakage of caseosa and intraluminal involvement. Aspiration of caseinous matter may lead to transient parenchymal consolidation in a weak hypersensitivity response or to expanded segmentation type pneumonia or cavity formation.

In the development of TB the initial stage (4-6 weeks) during which the cell mediated immunity is performed is very important. Hemocultures during this period can be positive. Thus, in the early proliferative phase of the process there may be hidden dissemination before activation of cellular immunity, as in the case of the first child. Most authors say that in children up to the age of three, or in immunocompromised patients, there should be no major difference between latent infection and illness, as the infection often advances at a very fast pace (2,6).

In both case studies timely diagnosis and adequate active and prolonged tuberculostatic treatment helped control the process and prevent possible further complications.

IV. CONCLUSIONS

The multiple matifestations of tuberculosis continue to be a challenge for physicians treating patients in all age groups. When dealing with patients in breastfeed infancy particular attention is required to stop its rapid progression. Diagnozing the disease is particularly challenging in children up to the age of one as it is difficult to differentiate the condition due to the fact that it is closely related to the unstable state of the immune system. .

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