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CASE REPORTS

Diagnostic difficulties in an infant with tuberculosis

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ABSTRACT

Tuberculosis (TB) is one of the oldest diseases known in the world. Nowadays, in Romania there is a recrudescence of TB. This is rather due to the rate of unemployment and poor medical surveillance in the pauper population than to the HIV infection or drug consumption. We present the case of a 3 ½ month old infant coughing for 2 ½ month until he was diagnosed with TB. Initially, the mother of the child strongly denied the presence of cough to any family member, making the diagnosis even more difficult and arriving too late.

Keywords: tuberculosis, infant, diagnosis

Tuberculosis (TB), one of the most dreaded diseases in the last century, knows nowadays a new recrudescence in Romania, after the initial decrease of the prevalence by the introduction of the antituberculous treatment and by the improving of the nutritional and life conditions (1). This recrudescence of the TB infection was coincident with the higher prevalence of the human immunodeficiency virus infection, with the increasing immigration from endemic regions, with the augmentation of the unemployment and with the increase of drug consumption. An extremely important factor to contribut to the higher prevalence of the TB is the TB decreasing control in high-risk population by the primary medicine care system (1). The BCG (Bacille Calmette Guerin) vaccination should normally contribute a lot to the decrease of the TB prevalence. However,

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metaanalyses on this subject proved that only a half from the vaccinated people is protected against TB infection (2,3,4). The percent could be even lower in some geographic regions with a very high incidence of TB infection (Sub-Saharan Africa, West Pacific region) (5). Nevertheless, it seems that a better effect of the BCG vaccination is present in infants, especially in girls from developing countries (6). In patients with TB major immunity defects were not proved (for instance in the cytokines pathway) (7). For a better TB control, the prophylactic administration of the isoniazid is indicated, even when the exposure to the TB infection of the newborns and infants is sporadic (8).

Tuberculosis in children represents 15-20% from the general TB infection (9). However, it is probably the most neglected disease in children, even in the endemic regions (10). The transmission from an adult to a child is present into the majority of the cases. The situation of a child responsible for an adult TB infection is also possible, and in this case the prophylaxis against TB is necessary (11). There are cases of congenital TB, transmitted from a mother to the fetus (12), which is hard to be diagnosed (13). There are authors who consider that the TB forms in children are mild ones (14). The disease gravity depends very much of the age of the child, with severe TB forms especially under the age of 3 (15). In infant and small child the most severe form – the disseminated disease form is present in the highest percentage (81.8%) (16), as well as the tuberculous meningitis (76.9%) (15). The signs which suggest the TB diagnosis in children are frequently present (17) and have a persistent character. However the association of the persistent cough, over two weeks, to the failure to thrive and asthenia was proved to be less sensitive under the age of 3 (sensitivity 51.8 %, specificity 92.5%) comparing with the group over 3 years (sensitivity 62.6%, specificity 82.3%) (18). Confirmation of the diagnosis is difficult due to the nonspecificity of the disease signs, to the coexisting malnutrition, to the polymorphic radiology imaging – nonspecific or to small to be seen on a chest radiography [ex. miliary in initial stage and into the strictly endobronchial forms (19)], as well as to the poor bacteriologic confirmation in the paucibacillary forms (9). An extremely important element to sustain the diagnosis is to exclude other diseases, especially bronchopneumonia, using clinical, radiological, and bacteriological grounds. The radiological aspect of the bronchopneumonia can lead to confusions (as in our case). The typical radiological aspects of bronchopneumonia consist in increased peribronchial markings and diffuse, bilateral, small fluffy infiltrates (20). The non-confluent character of the small opacities is the sign which differentiates the miliary TB from bronchopneumonia. There are authors sustaining the introduction of new diagnosis protocols in TB, which would be extremely beneficial to the children (21). ❑

CASE PRESENTATION

A male, BML, aged of 3 months and 3 weeks (birth date – 07.08.2007), from a local Municipal Hospital, was brought into our Institute, on November 28, 2007. He was transferred with the diagnosis of a persistent febrile syndrome, persistent bronchopneumonia, hepatomegaly, splenomegaly, chronic diarrhea, mild malnutrition, and hypotonia.

The mother, 21years, had an elementary degree of education and was raising her first child. The father, 29 years, denied any chronic disease. The mother was asked specifically about TB or chronic cough. At the beginning, she denied, but, after insistence, she recognized that both the maternal grandfather and the maternal uncle (never investigated) cough for a very long time.

BML was the first child, born at 36 weeks gestation age, with birth weight 2000 g and height 47 cm, Apgar 7. He was breastfed for 3 ½ months.

HISTORY

The onset was at the age of 1-month, with repeated vomiting and *spastic cough*, but the physician considered these signs as due to a gastroesophageal reflux.

- After 2 weeks, the signs were considered as due to an acute pneumonitis and the child was treated at home with ampicillin and gentamicin.
- His first hospitalization was at the age of two months, at the local Emergency Hospital, for fever, cough, dyspnea, meteorism, and diarrhea. Clinical examination at that date noticed 4000 grams weight (ponderal index = 0.77), hepatomegaly, splenomegaly, meteorism.

Laboratory findings noticed anemia (no type specification, hemoglobin = 8.6 g/dl) and radiological findings with *confluent micronodular opacity overall right pulmonary area and on the inferior ½ of the left pulmonary area*. He proceeded with antibiotic treatment – ampicillin and gentamicin, for five days. The course was unfavorable, with persistent fever, intensified diarrheic syndrome and another antibiotic attempt followed, with ceftriaxone, ciprofloxacin, in addition to the nutritional treatment. The parents asked for going home after 10 days in hospital with unsuccessfull therapy, against the doctor's advice.

- The family kept the baby at home for several days. His situation was worsening, having fever, cough, dyspnea, anorexia, vomiting, diarrhea and abdominal meteorism.
- After four days, he returned to the local Emergency Hospital with high fever 39.7°C, pallor, dehydration, dyspnea, tachypnea, intercostal retractions, bronchial breath sounds, meteorism, hepatomegaly, splenomegaly. Laboratory findings at this time noticed anemia (Hgb: 8.8 g/dl), leucocytosis (WBC 19,000/mm3, with 8607 granulocytes/mm^3, and 9,405 lymphocytes/mm^3). Biochemistry showed important inflammatory syndrome (erythrocyte sedimentation rate = 76 mm/h, C-reactive protein = 9.6 g/dl), and TGO = 29 IU/l, TGP = 30 IU/l, urea = 24.6 mg/dl, hypoproteinemia (5.5 g/dl). The seric proteins electrophoresis showed hypoalbuminemia, hyper α2 globulinemia, hypo γ globulinemia of 7.9 g/l (albumin 49.9%, α1globulin 5.3%, α2 globulin 16.6%, β globulin 13.7%, γ globulin 14.5%). The cultures from blood, feces, and urine were negative. Pulmonary radiography identified *an image almost identical with that of the first examination* and suggested the diagnosis of bronchopneumonia. The abdominal echography showed hepatomegaly (left lobe 30 mm, right lobe 68 mm), with normal echographic structure, spleen 62 mm, with normal echographic features as the whole exam (gall bladder 28 mm, transonic, right kidney 57 mm, left kidney 61 mm). Transfontanelar echography was normal. The antibiotics were changed with cefuroxime associated to meropenem. In addition, he was hydrated and than he received nutritional therapy with Humana SL and probiotics (the product and the quantities were not specified on the discharged letter) for 6 days and hydrocortisone (no mention about the dose, administration mode and period on the discharged letter). After 48-72 hours, the symptoms reappeared with fever, dyspnea, tachypnea, intercostal retractions, meteorism, and diarrhea. After a week, he was evaluated biologically, and because there was no amelioration, he was sent to our Institute.

We received him apyretic, 36.6°C, weighting 4,100 grams, with bad general condition. He was hypotonic, with a look of "sun at sunset". The tegument and mucosa were pale, with a very visible thoracic and abdominal circulation. *He had no BCG vaccination scar.* He presented severe cough, prolonged expiration, wheezing, tachypnea, 80 respirations/min, intercostal retractions, thoracic and abdominal balance and disseminated bronchial rales. O_2 saturation was 96%, cardiac rate was 170/min, sinus rhythm, no cardiac murmurs. The patient presented flatulence, hepatomegaly, with inferior border at 4 cm under the costal margin, high consistent, round shape, splenomegaly, with the inferior border at 3 cm under the costal margin.

Laboratory findings confirmed the anemia (hemoglobin = 7.3 g/dl, RBC = 3,180,000/mm^3, Hct 23.7%, MCV = 74.5 fL, MCH = 23 pg/cell), leucocytosis (WBC 15,900/mm^3 with 4,929 lymphocytes/mm^3, 652 monocytes/mm^3, 10,255 granulocytes/mm^3, 32 basophils/mm^3). Platelets were normal (166,000/mm^3). Blood gases were normal. The electrolytes blood levels showed hyponatraemia, hyperkaliemia (Na = 123→132mmol/l, K = 5.1→5.2 mmol/l, Ca = 1.31→1.25 mmol/l, Cl 98 mmol/l). The blood glucose level was normal.

The hepatic enzymes were normal: TGO = 31 IU/l, TGP = 34 IU/l, and the hepatitis B antigen (HbsAg) was negative. The metabolic investigations showed: hypocholesterolemia (seric cholesterol = 103 mg/dl), hypoproteinemia (5.28 g/dl) with hypoalbuminemia (49.4%) hiper-α1globulinemia (6.2%) and hiper-α2globulinemia (15.4%). The C-reactive protein was 27 mg/dl, three times higher than one week before. The cultures from feces and urine were negative.

The child's radiography (**Photo 1**) showed numerous micronodular opacities. There were two types of such micronodular opacities: one type was non-confluent, diffuse, bilateral (miliary type) and the other confluent, especially on the right pulmonary area (bronchopneumonia type).

We decided to perform radiography to the mother. The mother's radiography showed cavity type lesions, at the right lung (**Photo 2**).

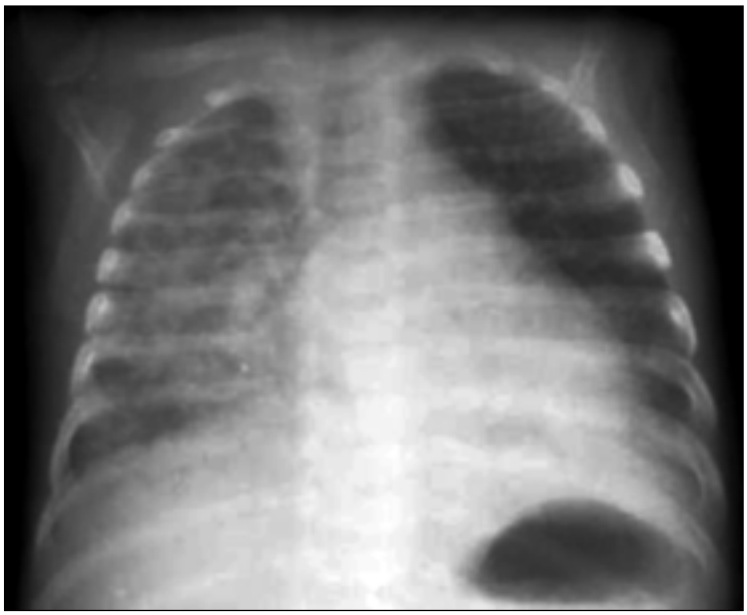

PHOTO 1. Numerous bilateral non-confluent micronodular opacities. Right pulmonary confluent opacities.

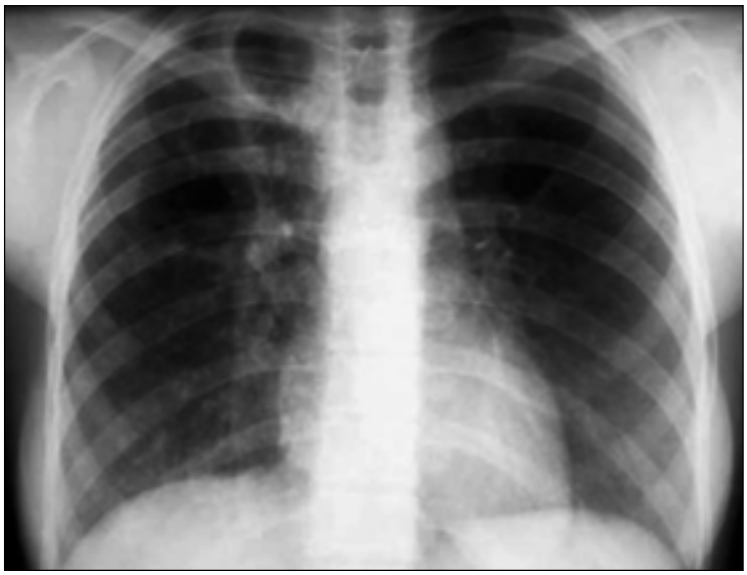

PHOTO 2. Well delimited pulmonary cavities

Although the lumbar puncture was necessary, we did not perform it due to his extremely severe condition, the infant presenting respiratory arrest when we put the peripheral venous line.

We initiated hydration and nutritional treatment. Initially we administered dexamethasone 1 mg/kg/dose, aerosols with adrenaline, antibiotic therapy with ceftriaxone 100 mg/kg/day, gentamicin 5 mg/kg/day, and Biseptol, 20 mg trimetoprim/kg/day (suspicion of Pneumocystis carinii infection) and IV immunoglobulin, 600 mg/kg/day, unique dose.

After clarifying the diagnosis, we sent the mother and the child to the "Marius Nasta" Institute for Lung Diseases and Tuberculosis, where the tuberculosis – disseminated form – was confirmed by directly bacteriologic exam from gastric aspirate secretions. He started the antituberculous treatment. The isoniazid (IM) and streptomycin (IM) were associated with rifampin, and pyrazinamide (oral administration). Prednisone, 1 mg/kg/day, orally, was associated to the therapy for its anti-inflammatory action. In the next days, the evolution was extremely severe. He died four days after starting the antituberculous treatment. His parents refused the necropsy.

The mother, diagnosed with pulmonary tuberculosis – 2 cavities, started also the antituberculous treatment, and the other members of the family had to go to antituberculosis local center to start investigations. ❑

DISCUSSIONS

This case illustrates the diagnosis difficulties of the TB in infants in a country where the TB is an endemic disease. The screening methods applied to his family would avoid this situation but, nowadays, the periodic control in the general population is not performed in a rigorous manner.

Although in this infant's case the tuberculin skin test with two tuberculin units would not be helpful (immunodeficiency associated), this case moot the problems of BCG vaccination in a children born prematurely, who escapes from the vaccination protocol.

Another issue to discuss is the problem of breastfeeding in infants from a TB infected mother. In this case, the vicinity of his mother, who was massively infected and without antituberculous treatment, was the decisive factor. There are authors who consider that the TB infection of the mother is a contraindication for breastfeeding (22). Other authors consider a contraindication for breastfeeding the TB mastitis only and give the permission to perform

it if the infected mother followed the anti-tuberculous treatment for at least two weeks (12).

The corticosteroid treatment in massive invasive forms can limit the bronchial and pulmonary sequelae (pulmonary fibrosis, bronchiectasis, atelectasis, etc.) and the neurologic sequelae in some patients with tuberculosis meningitis (3). We recommended the corticosteroid therapy in our patient in order to limit the intense inflammatory process.

The moment of infection in this case is hard to be precised because there are some compatible elements for congenital infection: prematurity, small birth weight, other signs associated (splenomegaly, hepatomegaly) but the vicinity of the infected mother and other infected relatives at least catalyzed the evolution in this case.

Conclusion

1. Although there are 125 years from the description of the Koch bacillus, 86 years from the BCG vaccine introduction to the humans and 61 years from the first antibiotic treatment (streptomycin), children's tuberculosis remains a dangerous disease, difficult to diagnose and, in situations in which the family do not collaborate with the medical staff, may become fatal.

2. An extremely important issue of the pulmonary micronodular opacities is the differential diagnosis of the bronchopneumonia with the miliary tuberculosis. If the diseases are intricate, in cases with chronic cough, in order to eliminate the TB suspicion, the first step is to perform radiography to the mother.

3. Other factors like small age, poor nutritional status, anemia, immunodeficiencies, and the continuous and massive infectiousness of the undiagnosed mother have a bad influence over the TB prognosis in children.

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