PECULIARITY OF MYCOBACTERIAL INFECTION IN PRIMARY IMMUNODEFICIENCY PATIENTS

(SINGLE CENTER STUDY)

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The overspread of Mycobacterial Infection in PID patients

- 9% Mbt infected
- 91% PID patients

The overspread of Mycobacterial Infection in Russian population

- 0.13% Mbt infected
- 100% Russian population

32 Mbt infected patients among 319 of Russian Children’s Clinical Hospital database

134 infected persons in 100 000 according to WHO data
Distribution of Mbt infection among PID patients

- CGD 19: 2 Not infected by Mbt, 12 Infected by Mbt, 5 Multifocal Mbt infection
- SCID 12: 7 Not infected by Mbt, 5 Infected by Mbt, 0 Multifocal Mbt infection
- HIGM 14: 11 Not infected by Mbt, 3 Infected by Mbt, 0 Multifocal Mbt infection
- NBS 15: 13 Not infected by Mbt, 2 Infected by Mbt, 0 Multifocal Mbt infection
- CVID 26: 25 Not infected by Mbt, 1 Infected by Mbt, 0 Multifocal Mbt infection
- XLA 44: 43 Not infected by Mbt, 1 Infected by Mbt, 0 Multifocal Mbt infection
- ALPS 27: 26 Not infected by Mbt, 1 Infected by Mbt, 0 Multifocal Mbt infection

Legend:
- Not infected by Mbt
- Infected by Mbt
- Multifocal Mbt infection
MYCOBACTERIA’S INTERACTION WITH IMMUNE SYSTEM

Macrophage

- R1
- R2
- IFNγR
- MHC I
- IL-12
- IL-18
- Mbt

Th1-lymphocyte
- CD3
- TCR
- IFNγ
- TNFα
- γδT-lymphocyte

CD4
- IL-2

CD8
- αβCD8+ T-lymphocyte
- TCR
- Granulysin
- Perforin
M.K. 2 y.o. - Chronic Granulomatous Disease
Disseminated mycobacterial infection, soft tissues mycobacteriosis

- 2 months – V BCG;
- 5 months left axillary lymphadenitis;
- 1 year – pneumonia, recurrent purulent skin infection;
- 2 years – left foot abscess with fast spread over the whole leg

Admission to Russian Children’s Clinical Hospital – evaluation of CGD and Multifocal mycobacterial infection of lungs and soft tissues;

- Cytological confirmation (Ziehl-Neelsen positive staining, Acid-fast bacteria revealed twice in the inflammatory discharge);
- Histological findings of soft tissues mycobacteriosis “spread necrosis with multiple Langhanse giant cells”
- Admission of long term specific tritherapy with good clinical effect.
M.K. 4 y.o. – Chronic Granulomatous Disease
Disseminated mycobacterial infection, mycobacterial osteomyelitis

- 4 days of life – V BCG;
- 1 month – omphalitis, skin infection, stomatitis;
- 1y 8mo – suspicious for intestinal obstruction - laparotomy revealed multiple nodules over peritoneum with histological confirmation of granulomatous inflammation;
- 1y10mo – soft tissues abscess, lymphadenitis with histological signs of tuberculosis;
- 2y – Multifocal tuberculosis of lymph nodes, lungs, pleura, peritoneum, liver, spleen. CGD diagnosis suspected;
- 4y - Admission to Russian Children’s Clinical Hospital, evaluation of the above diagnoses;
- Deterioration of mycobacteriosis – osteomyelitis, spondilitis;
- PCR Mbt tuberculosis positive;
- Admission of the specific pentatherapy + granulocytes transfusion with partial clinical effect.
Y.S. 4 y.o. - Chronic Granulomatous Disease
Disseminated mycobacterial infection, spleen mycobacteriosis

- 4th day of life – V BCG;
- 1 month – debut of skin and gastrointestinal infections;
- 1 year – goat milk consumption;
- 2 year – left axillary lymph node ulceration with caseous discharge, hepatosplenomegaly;
- 4 years admission to Russian Children’s Clinical Hospital – evaluation of CGD and Multifocal mycobacterial infection of lymph nodes, liver and spleen;
- PCR Mbt bovis wild strain positive;
- January 2004 - Spleenectomy, mesenteric lymph node and liver biopsy revealed histologic findings of mycobacteriosis.
- Specific quadri therapy + granulocyte transfusion with good clinical effect.
V.R. 1 y.o. – Severe Combined Immunodeficiency T- B-Disseminated mycobacterial infection, Skin mycobacteriosisis

- 4th day of life – V BCG;
- 3 months – debut of recurrent infections and failure to thrive, permanent lymphopenia;
- 6 months – appearance of nodular elements over the skin surface;
- 9 months – ulceration of BCG site and fistulas formation above skin nodules with acid-fast positive staining with further scarification

- Admission to Russian Children’s Clinical Hospital – evaluation of SCID and BCG-osis:
  - 11 months – HLA matched sibling bone marrow transplantation;
  - Histological findings of skin mycobacteriosisis, admission of specific quadri-penta therapy with good clinical effect.
THE REASONS OF HIGH SUSCEPTIBILITY TO MYCOBACTERIAL INFECTION:

• Specific defects of antimycobacterial immunity presented in patients with Mendelian susceptibility – deficiency of IFNγ, IFNγR, IL-12, IL-12R and signaling molecules STAT, JAK;
• Defects of T-cell function in SCID, HIGM, Nijmigen syndrome patients;
• Phagocytes defects (CGD, Hyper IgE syndrome).

PECULIARITY OF MYCOBACTERIAL INFECTION IN PID PATIENTS:

• Caused by atypical mycobacteria;
• Atypical and multiple sites of infection;
• Severity and long term of infection;
• Low efficacy for standard specific therapy.