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Common variable immunodeficiency in adults

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Definition

- Common variable immunodeficiency - most prevalent of the primary immunodeficiency disorders.
- Reduction in serum levels of both IgG and IgA, with or without low IgM.
- Recurrent bacterial sinopulmonary infections, which led to complications, especially pulmonary damage.

Prevalence

- 1-2 / 100 000
- Lithuanian population 3.5 mln.
- Expected number of patients 35-70.
- Number of diagnosed CVID is 5 cases in our clinic.

Experience

- From 1998 to 2006.
- Five cases (3 males, 2 females).
- Diagnosis made between 23 - 48 years of life.
- An average diagnostic delay ~ 7 y.

Which specialist suspected hypogammaglobulinemia?

- 1 – haematologist
- 1 – rheumatologist
- 3 – pulmonologist

Where is primary physician ???

Onset

- In 4 cases disease manifested with recurrent infections of upper and lower respiratory tract.
- In 1 case recurrent infections of respiratory tract were associated with benign lymphadenopathy.
- In 1 case - enterogenic reactive arthritis and urinary tract infection .

Laboratory tests

- Low level of IgG, IgA and IgM was found.
- Number and function of T lymphocytes – N.
- Number of B lymphocytes – 7-9 %.

Complications

- Bronchiectasis was detected in 3 cases (by CT).
- Amyloidosis of AA type in 3 cases (renal or gum biopsy).
- 1 death in 5th y after CVID was revealed.

Associated diseases

- Benign lymphadenopathy – 1
- Reactive arthritis – 2
- COPD – 1
- Rhinosinusitis – 1

Treatment

- Substitutional therapy with intravenous immunoglobulin (Endobulin) was initiated in 2 cases.
- Concomitant pathology treated in ordinary way.
- Exacerbation of infections were treated with antibiotics.

Cases

Case 1

- Patient P.S., male, 38 years old.
- Rhinosinusitis - since 9 years old.
- Subfebrile fever - 12 y.
- Loss of weight - 16 y.
- Recurrent infections of the respiratory tract - since 22 years (bronchitis 3 times a year).
- Bronchiectasis was diagnosed - 29 y.
- Dyspnea, weakness, often exacerbations of bronchiectasis were presenting.

Laboratory test

1998 y

- γ-globulins - 2.7 %
- IgG – 0,96 g/l, IgM <0,2 g/l, IgA <0,29 g/l
- CIC - 0,006 (N 0,06-0,08)
- B lymphocytes 9 %, 243/mm (N 11-16 %, 200-400)
- CD4+ - 24 %, 648 /mm (N 38-46 %, 700-1100)
- CD4/CD8 - 0,5

Effect of treatment with intravenous immunoglobulin

- Since 1998 level of IgG ranges from 0,96 to 4,5 g/l
- Pneumonia and acute sinusitis (2001).
- Bronchiectasis exacerbated 2-3 times a year.
- Atrophic gastritis and H.zoster (2005).
- No hospitalisation since 1998.

Case 2

- I. T., 50-year-old women
- Recurrent purulent infections of upper and lower respiratory tract from childhood.
- Bronchial asthma diagnosed in 20 y.
- Hypogammaglobulinemia revealed in 24 y.
- 8 y treated with intramuscular Ig.
- Hypertension and proteinuria was observed about 10 years.
- Admited to hospital with dyspnea, cough, crural oedema, eczema

Laboratory tests

- Blood count: leucocytosis.
- IgA - 0,69 g/L (N 0,88-4,1), IgG – 0,07 g/l (N 6,9-14), IgM - 0,17 g/L (N 0,34-2,1),
- CIC – 0,018 (N 0,06-0,08).
- Lymphocytes – 1400/m3; CD19+ (B lymphocytes) – 7 %, 98/mm3;
- CD4/CD8 – 1,26.
- Serum creatinine – 149 μmol/l, urea – 24,69 mmol/l,
- Proteinuria – 2 g/l and 2,56 g/24 h, cholesterol - 7,54 mmol/l.

Imaging studies and biopsy

- CT revealed pneumofibrosis, atelectasis of S10/9, mediastinal lymphadenopathy and pleural effusion.
- Pleural fluid was transudate, specific or atypical cells were absent (flow cytometry).
- Renal ultrasound showed parenchymas changes typical to chronic renal disease.
- Renal biopsy elicited amyloidosis (AA).

Comment

- No bronchiectasis in the presents of amyloidosis.
- Long outlive without treatment.

Case 3

- J.M., female, 27 years old.
- Gastrointestinal infection 26 y (salmoneliosis?).
- Urinary tract infections.
- Admited to hospital with pain and swelling in the left knee, diarrhea.

Laboratory test

- Blood count - iron deficiency anemia.
- CRP - 136 mg/l.
- RF - N.
- Faeces culture - Campylobacter.
- γ-globulin – 5,1 %.
- IgG < 1,7 g/l, IgA <0,24 g/l, IgM – 1,7 g/l.
- B lymphocytes - N.

Imaging tests

- Chest x-ray - N
- Chest CT - N.
- Sonography and x-ray of the knee: arthritis.

Comment

- Enterogenic reactive arthritis or arthritis associated with primary agammaglobulinemia?

Case 4

- G.J., male, 27 y.
- Recurrent infections of the respiratory tract since childhood.
- Severe pneumonias occured since 21y.
- Pleuritis three times since 22 y.
- Hypogammaglobulinemia in 23 y
- Reactive arthritis was suspected in 25 y.

Case 4 (cont.)

- At the age of 27 y admited to hospital because of fever, cough, diarrhoea, pain of shoulders and knees, crural oedema.
- Chest CT elicited bilateral bronchiectasis.
- Amyloidosis was confirmed by gum and gut biopsy

Laboratory tests

- IgG<1,35 g/l, IgM-0,17 g/l, IgA<0,23 g/l.
- CD19+ - 8 %, CD4+ - 15 %, CD4/CD8 - 0,19.
- Blood count - leucocytosis.
- CRP – 72 mg/l.
- Hypoproteinemia (30,9 g/l), hypoalbuminaemia (14,8 g/l).
- Proteinuria (8,4 g/l, 21,42 g/24 h), granular casts in urine.
- Urea and creatinin values were normal.

Comment

- 4 years without treatment were crucial for the development of complications.
- Patient died 2 y after initiation of replacement therapy.

Problem?

- Long delay in diagnosis and treatment of CVID.