EUROPEAN HEMATOLOGY ASSOCIATION

EHA-TSH Hematology Tutorial

Self-assessment Case – Immune Neutropenia

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Introduction

- 8-year-old boy
- Referred to us due to neutropenia detected when he had lymphadenitis
- Physical examination:
  - Weight: 22 kg (10– 25th percentile) Height: 123 cm (25th percentile)
  - Other systems were normal

Medical and family history

Repeated oral aphthous ulcers and otitis media

Consanguinity: first degree cousin marriage

Laboratory results

Full blood count: haemoglobin 131 g/l, leucocytes 5.9 x 10^9/l, platelets 160 x 10^9/l, neutrophils 0.6 x 10^9/l, lymphocytes 4.1 x 10^9/l

- Peripheral blood film: neutrophils 10% (0.6 x 10^9/l), lymphocytes 70%, eosinophils 4%, monocytes 16% (0.95 x 10^9/l)

More test results

Blood biochemical analysis: normal

Vitamin B12, folate, and ferritin: normal

Q1) Which laboratory test should be performed?

1. Chromosomal analysis
2. Bone marrow aspiration
3. Quantitative immunoglobulin levels and lymphocyte subset analysis
4. Direct and indirect Coombs tests
5. Antinuclear antibody test

Other laboratory tests

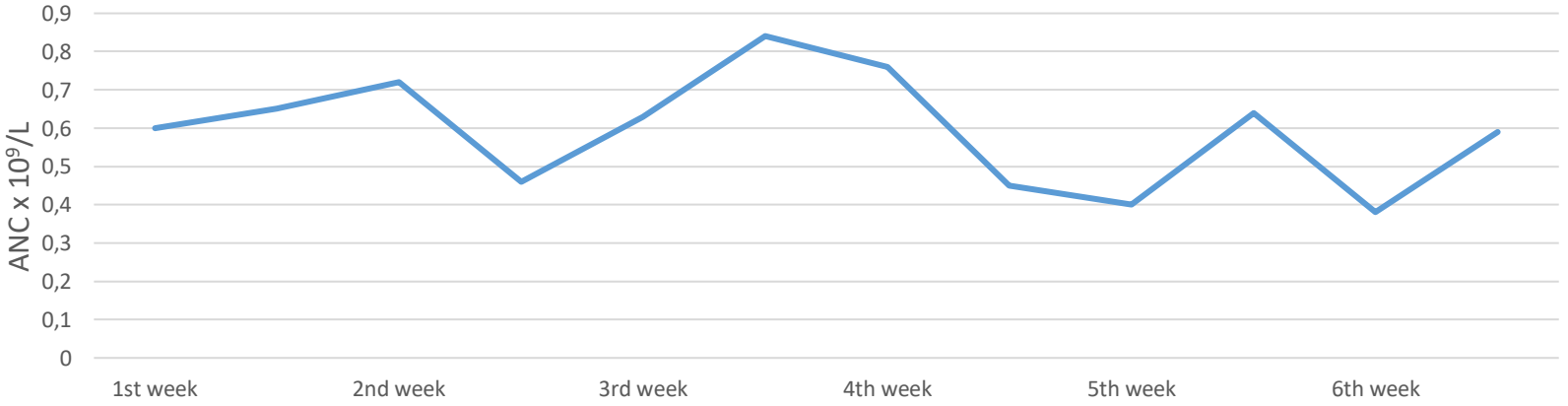
- Quantitative immunoglobulin results

IgA: 1.1 g/l (0.5-2.4)
IgG: 10 g/l (5.4-16.1)
IgM: 0.91 g/l (0.5-1.8)

- Lymphocyte subset: CD19+ 12%, CD3+ 64%, CD3+CD4+ 56%, CD3+CD8+ 36%

Follow-up

- Full blood count analysis was performed twice a week for 6 weeks



Q2) How do you plan the patient's treatment?

1. Monthly follow-up without treatment
2. Granulocyte colony-stimulating factor 3 times a week
3. Trimethoprim sulfamethoxazole prophylaxis
4. Methylprednisolone 1 mg/kg/day
5. Aciclovir prophylaxis

Follow-up

- Six months later he was admitted with extensive petechiae
- Full blood count: haemoglobin 121 g/l, leucocytes 4 x 10^9/l, platelets 10 x 10^9/l, neutrophils 0.5 x 10^9/l, lymphocytes 2.6 x 10^9/l

Bone marrow aspiration film

- Cellular bone marrow
- Increased number of megakaryocytes, myeloid hyperactivity

Q3) How do you define the patients' condition?

1. Chronic idiopathic thrombocytopenic purpura
2. Evans syndrome
3. Autoimmune neutropenia of childhood
4. Chronic benign neutropenia
5. Congenital neutropenia

Feedback

- The term ‘Evans syndrome’ is often applied to autoimmune haemolytic anaemia plus autoimmune thrombocytopenia
- However Chou and Schreiber in the 8th edition of Nathan and Oski’s *Hematology and Oncology of Infancy and Childhood* suggest that it can also be applied to other combinations of autoimmune cytopenias

Clinical follow-up

- Pulse methylprednisolone was administered for 7 days
- Full blood count result after treatment:

Haemoglobin 120 g/l, leucocytes 6 x 10^9/l, platelets 100 x 10^9/l, neutrophils 2 x 10^9/l, lymphocytes 3.5 10^9/l

Clinical follow-up

- During follow-up, thrombocytopenia and neutropenia recurred, thus intravenous immunoglobulin and methylprednisolone treatments were used
- Anti-granulocyte antibody: positive (immunoflourescence assay)

Q4) What is the most likely diagnosis?

1. Severe combined immune deficiency
2. Chronic benign neutropenia
3. Congenital severe neutropenia
4. Myelodysplastic syndrome
5. Common variable immune deficiency

Clinical follow-up

- Patient was evaluated by Immunology Department and accepted as having common variable immune deficiency
- Mycophenolate mofetil treatment was initiated, at the third month of treatment: platelets 96 x 10^9/l, neutrophils 1.2 x 10^9/l

Q5) If this patient had accompanying splenomegaly and lymphadenopathy, what would be your diagnosis?

1. Autoimmune lymphoproliferative syndrome
2. Cartilage hair hypoplasia
3. Schimke immuno-osseous dysplasia
4. Poikiloderma with neutropenia
5. X-linked agamaglobulinaemia

Clinical follow-up

- Four months later the patient had chronic diarrhoea and abdominal pain
- Intestinal endoscopy and pathology were compatible with Crohn disease

Q6) Which gene do you want to analyse for further diagnosis of this patient?

1. *FAS*
2. *FOXP3*
3. *LRBA*
4. *STAT3*
5. *Perforin*

Clinical follow-up

- Homozygous mutation in *LRBA* gene (c5047C>T) was detected
- Abatacept treatment was initiated
- After 1 year of therapy he is well without cytopenia

Discussion

- Autoimmune neutropenia and other autoimmune cytopenias can be consequent on commmon variable immune deficiency and isolated IgA deficiency
- Primary immune deficiencies with decreased immunoglobulin production may be associated with neutropenic syndromes
- Immunosuppresive therapy may be effective in patients with autoimmune neutropenia and immune deficiency
- Further genetic and molecular analysis can reveal different kinds of immune deficiencies and specific treatments can be used

References

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