DYSLIPIDAEMIA ASSOCIATED WITH ACUTE INFECTION WITH EPSTEIN BARR VIRUS

[1]VICTORIA BÎRLUŢIU, [2]CRISTINA REZI, [3]LUIZA TIUREAN

[1]"Lucian Blaga" University of Sibiu, [2,3]Infectious Diseases Hospital, Sibiu

Abstract: *The Epstein Barr virus (EBV), included in the herpes family, determines minor clinical manifestations or asymptomatic forms in young children, susceptible after the disappearance of the maternal antibodies transmitted through the placenta. Adolescents and young adults develop different symptoms in 30-50% of the cases and sometimes, these may take severe aspects. EBV persistence in the body is correlated with the development of a multitude of malignancy: lymphoproliferative disorders, Hodgkin lymphoma, Burkitt lymphoma, nasopharyngeal carcinoma, cerebral lymphoma in patients with AIDS, highlighting the viral genome in the tumour cells. We report the case of a young female patient who was diagnosed with acute infection with Epstein-Barr virus, who was hospitalized with persistent fever, intense physical asthenia, abdominal pain, lymphadenopathy, jaundice, hepatosplenomegaly. Para-clinic investigation revealed the presence of a minimum fluid retention in pelvis, right basal pleural effusion, leukocytosis with lymphocytosis, low fibrinogen levels, liver cytolysis and cholestasis, positive Waller Rose reaction, mixed dyslipidemia, with an ameliorated lipid profile one month after the follow up, situation less common in specialized literature.*

Keywords: *The Epstein Barr virus (EBV), acute infection, dyslipidemia*

Rezumat: *Virusul Epstein Barr (EBV), inclus în familia herpesvirusurilor, determină tablouri clinice minore sau forme subclinice de boală la copiii mici, susceptibili după dispariţia anticorpilor materni transmişi transplacentar. La adolescenţi şi adultul tânăr, formele clinice manifeste în 30-50% din cazuri, îmbracă uneori tablouri clinice severe. Persistenţa EBV în organism, se corelează cu dezvoltarea unei multitudini de afecţiuni maligne: boli limfoproliferative, limfoame Hodgkin, limfom Burkitt, carcinom nasofaringian, limfom cerebral la pacientul HIV în stadiul SIDA, cu evidenţierea genomului viral în celulele tumorale. Raportăm cazul unei fete de 18 ani, diagnosticată cu infecţie acută cu Epstein-Barr, internată pentr febră persistentă, astenie fizică marcată, dureri abdominale, adenopatii, icter, hepatosplenomegalie, investigaţiile paraclinice evidenţiind prezenţa unei minime cantităţi de lichid în pelvis, pleurezie bazal drept, leucocitoză cu limfomonocitoză, hipofibrinemie, citoliză şi colestază hepatică, R Waler Rose pozitivă, dislipidemie mixtă, situaţie mai puţin întâlnită sau studiată în literature de specialitate.*

Cuvinte cheie: *Virusul Epstein Barr (EBV), infecţie acută, dislipidemie*

INTRODUCTION

EBV infection is ubiquarian; the specific antibodies are present in approximately 95% of the adults between 30-40 years serologically investigated. Primary EBV infection occurs after exposure to contaminated oropharyngeal secretions (the so-called "kiss disease"), by freshly contaminated objects, transfusions, after transplant, or sexually. The virus has tropism regarding the epithelial cells and lymphocyte B.

After **an incubation** period of 4-6 weeks, the onset is gradual with moderate fever 38°C, headache, anorexia and the emergence of hemorrhagic spots on the soft palate. During the status of severe, the forms of disease persist: fever 39-40°C, typical tonsillopharyngitis with exudate (with pseudo-membrane), accompanied by an important submandibular and laterocervical lymphadenopathies, respiratory distress due to edema of the cervical region, oral breathing, difficulty in deglutition, feeding difficulties, hepatomegaly with liver cytolysis, rarely jaundice, splenomegaly. Transient rash may occur: rubelliform, petechiae, erythema polymorphous; administration of ampicillin or amoxicillin is associated with a maculopapular eruption in 90-100%, which is not predicting for a future aminopenicilins allergic reaction.

Complications may occur:

- The nervous system: meningitis, encephalitis, cerebellar syndrome, optical neuritis, paralysis of cranial nerves, neuropathy of cervical plexus, polyradiculopathy, Guillain Barre syndrome, demyelinating, hemiplegia;
- Hematological: hemolytic anemia, thrombocytopenic purpura, hemophagocytic syndrome, agranulocytosis, cryoglobulinaemia;
- Cardiac: infarction, pericarditis, ST-T elongation
- Spleen rupture
- Lung: pleurisy, exceptionally interstitial pneumonia.

Approximately 7% of patients with immunodeficiency may develop lymphoproliferative

disorders in association with transplant of bone marrow, kidney, liver, heart-lung; high malignancy lymphomas, leiomyosarcoma in child with HIV infection, hairy leukoplakia in HIV patient. The implications of EBV in gastric cancer, breast and liver are under evaluation.

The evolution is slowly favourable, with regression of fever in 10-14 days, death being unusual in immunocompetent patients, but it may occur due to neurological complications, spleen rupture, upper airway obstruction or hemophagocytic syndrome.

EBV is associated with chronic fatigue syndrome and also with an active chronic infection, with significant viremia, with the clonal multiplication of EBV infected lymphocytes: CD4+, CD8+ or NK lymphocytes, with disease progression, occurrence of pancytopenia, hypogammaglobulinemia, lymphoproliferative disorders and death approximately 10 years after the primary infection.

The **diagnosis** is suggested by the clinical presence of leucocytosis with 60-80% limphomonocytosis and the presence of more than 10% atypical lymphocytes, positive heterophile antibodies (Paul Bunell reaction), serological response to specific antibodies against capsidic antigen, early antigen, nuclear antigen (EBV nuclear antigen EBNA-).

The **treatment** of acute EBV infection is made with symptomatic drugs, antipyretics, nonsteroidal anti-inflammatory drugs; short therapy with corticosteroids is advisable in severe forms, with suffocation phenomena, or in hematological, cardiac and neurological complications.

There is no effective antiviral treatment, the administration of acyclovir or gancyclovir was not associated with a real clinical benefit. There are under evaluation two types of vaccines targeted against glycoprotein gp350, respectively a vaccine containing multiple epitopes EBV.

We intend to present an unusual combination of a sever form of acute EBV infection with multiple organs damage, hepatitis with jaundice and important disorders of lipid metabolism, in a young 18 years old female.

CASE REPORT

The 18 years old female patient was hospitalised after a week of febrile syndrome (fever 38, 7°C), fugitive skin rash, lymphadenopathy, epigastric pain, meteoric abdomen, nausea and vomiting, intense physical asthenia, somnolence, coloured urines. Upon examination, the patient presented: somnolence, malaise, jaundice of sclera and skin (medium intensity), BMI 17.14 kg/ m², occipital, laterocervical, subangulomandibular, lymphadenopathies, with an approximate diameter of 1 cm, dullness in the inferior 1/3 of the right thorax, with no vesicular murmur at this level, rhythmic cardiac sounds, HR 106/min, BP 110/70 mmHg, pharynx and tonsils hyperemia with pseudo membrane at the level of right tonsil, firm grade II hepatosplenomegaly.

The paraclinical investigations revealed: Le14541/ mm³, Er4.03 mil/ mm³, Hb12.6g/dl, Ht37.5%, Tr 213000/mm³, leucocytes formula: S11%, N 2%,E1%, B0%, Ly76%, M10%, plasmocytes 1/100, erythrocytes morphology: normal coloured erythrocytes, 1.5% reticulocytes. Lymphocytic population: moderate heterogeneous, formed by reactive lymphomonocytes, with a rich and basophile cytoplasm; in conclusion an aspect which suggests infectious mononucleosis; fibrinogen level 175 mg/dl, C reactive protein 31,2 mg/dl, GOT 173 U/l, GPT 371U/l, alkaline phosphatasis 224U/l, GGT 570U/l, direct bilirubin 3,50 mg/dl, total bilirubin 4,67 mg/dl, cholesterol level 328 mg/dl, triglycerides level 272mg/dl, total lipids 1803 mg/dl, HDL-cholesterol 12 mg/dl, total proteins 6,1 g/dl, albumin 40%, α1 4,6%, α2 12,3% , β1 9,5%, β 24,5 %, γ 20,1%, A/G ratio 0,96 , rheumatoid factor <8 UI/ml, Waller Rose reaction 32 UI/ml, anti-nuclear antibody-absent, MNI heterophile antibodies – present, VCA present, C3 102, CIC20 DO, IgM HAV-absent, Ag HBS-negative, Ac anti HBc-absent, HCV-nonreactive, Ac anti HIV-negative, IgM CMV negative, IgM Toxoplasma gondii negative.

The pulmonary radiography showed: opaque right costal diaphragmatic sinus; the abdominal ultrasound revealed: liver with right lobe of 19 cm, left lobe of 9 cm, with normoechogenicity homogenous, spleen with 15.7/7.5 cm, minimum fluid retention in pelvis.

The patient evolution was favourable; she developed no fever under therapy with corticoids, cholestasis syndrome and dyslipidemia regressed slowly, within a month. One month after, the biochemical tests were: GOT 37 U/l, GPT 54 U/l, cholesterol level 271 mg/dl, triglycerides level 115 mg/dl, total lipids 816 mg/dl, HDL-cholesterol 39 mg/dl.

This case report suggests the necessity of a current evaluation of the lipid profile in the patients with mononucleosis hepatitis at any age, and the necessity of monitoring these patients 6 months after the acute episode for the detection of the chronic cases of EBV infection**.**

BIBLIOGRAPHY

1. Borza CM, Hutt-Fletcher. Alternate replication in B cells and epithelial cells switches tropism of Epstein Barr. Nat Med 2002;594-599.
2. CDC- Disease Information.
3. Mandell, Douglas and Bennett's. Principles and Practice of Infectious Diseases, sixth edition, 2004.
4. Macsween KF, Crawford DH. Epstein Barr virus-Recent advances. Lancet Infect Dis 2003;(3):131-140.
5. Victoria Bîrluţiu. Boli Infecţioase, Editura ULB Sibiu, 2008;173-179.