Clinical manifestation of Kaposi’s sarcoma in HIV-infected boy

The description of a case of Kaposi’s sarcoma in HIV-infected child showing some features of the clinical course of disease and about the positive results of therapy with the inclusion into complex treatment the drug “Viferon”.

Khalida Khalidova,
Farkhad Nabiev

Republican Specialized Research Practical Medical Center of Dermatology and Venereology, Uzbekistan

Keywords: Kaposi’s sarcoma, HIV-infection, HHV-8, Viferon, boy, clinical picture.

UDC: 616-006.311.04:616.98:578.828.6-053.2

Introduction

Kaposi’s sarcoma is a multifocal tumorous disease affecting reticuloendothelial system of the body. As clinical entity it was described in 1972 by Hungarian dermatologist M.Kaposi and named as “idiopathic multiple pigmented sarcoma of the skin”. In the literature this disease meets under various names: Kaposi’s sarcoma, idiopathic multiple pigmented hemorrhagic sarcoma, Kaposi’s angiomatosis, Kaposi’s angiosarcoma, Kaposi’s hemangiosarcoma, Kaposi’s telangiectatic pseudosarcoma. At present time some forms of this disease have been described: classic, endemic, iatrogenic and epidemic (Fitspatrick et al., 1999).

Before HIV/AIDS pandemia Kaposi’s sarcoma (KS) was relatively rare, mainly in men of elderly age and characterized by slow long-term clinical course. Kaposi’s sarcoma associated with HIV-infection has been found 20 times more often predominantly among young norm- and bisexual men (50-60%), and disease is characterized by aggressive malignant clinical picture. In the progressing of immune balance disorder in HIV-infected patients there is observed development of various opportunistic diseases including Kaposi’s sarcoma (KS). Identification of Kaposi’s sarcoma cases among women with AIDS has been found relatively rarely (2-4%), so as among HIV-negative females, however, progressing of disease has more aggressive character than in males (Beral et al., 1990; Pokrovskiy et al., 2000).

Clinical course of Kaposi’s sarcoma

Since the moment of KS description the multiple theories of etiology and pathogenesis of disease have been proposed. Now etiological agent of Kaposi’s sarcoma is considered human herpes virus 8 (firstly isolated from biopsies of focus of AIDA-associated KS in 1994). A number of the most important factors such as sex, age, HLA antigens have been confirmed, the characteristic features of immune and cytokine systems, which have significant role in the development of disease, have been determined (Chang et al., 1994; Molochkov et al., 2002; Poljacki et al., 2003; Servin et al., 2003).

The presence of active virus in the body predicts the variability of the ways of HHV-8 transmission. The possibility of sexual, hematogenous and other ways of this virus transmission has been shown in some reports. In some studies HHV-8 was identified in the endothelial, spindle cells, prostate epithelium, macrophages and saliva in the patients with KS, virus showed its infectious properties in the tissue culture, that confirms its biological activity (Molochkov et al., 2002; Molochkov, 2003; Chigvineva et al., 2003; Servin et al., 2003).
The common ways of HHV-8 and HIV-infection transmission (hematogenous and sexual way) allow suggestion of wide distribution of HHV-8 among HIV-infected patients that resulted in increase of risk of KS development in association with HIV-induced immune deficit.

KS clinical picture is rather variable that results in diagnostic difficulties. Classical form of disease occurs among men above 50-60 years of age in the most of cases and is characterized by appearance of angiomatous pale-pink, red-purple, red-brown spots of irregular form which localized in the sites of bone prominence of lower extremities (malleoluses, toes and back of the foot). During growing they transform into dense purple-red livid or slate-grey nodules, plaques and nodes. The edema of extremities with signs of lymphostasis is frequently found, it results in subsequent development of elephantiasis. At first the focuses locate asymmetrically, then during disease progressing they acquire tendency to symmetric location. On the surface of focal lesions there may be observed hemorrhages, telangiectasias, hyperkeratich layers, verrucous growth, scary atrophy or ulcerations. Disease manifestations can appear even in the internal organs. Subjective sensations are usually not significant, however, in ulcerative nodes there is noted burning and tenderness in the focuses of disease.

During histological investigation at early stages (stage of a stain) there are indentified perivascular proliferates of various sizes around the large vessels in the mesh layer of derma, consisting from spherical-oval cells with big nucleus among which there are available lymphoid elements, histiocytes, and plasmocytes. The focuses of hemorrhages and hemosiderin accumulations are noted in some places. At the stage of mature elements (nodules, plaques, nodular-tumorous masses) the histological picture depends on prevalence of composing components - proliferative vessels and neoplasms of spindle cells. In the focus of lesion there is large amount of vessels (angiomatous variant) at the different stages of differentiation from focuses of oval cells to formed vessels. The vessels are sharply dilated and overflowed by blood, forming lacunas such as “blood lakes”. The proliferation of lymphatic vessels with their cystic dilatation is observed. In the focuses of proliferation the stretched cells (fibroblastic variant) are distributed like fibrous cord bound in various directions. The cells have longitudinal nuclei of structure similar with fibroblasts. There are mitosis, diffusive proliferation of spindle cells occupying the whole thickness of the derma, or limited like nodes surrounded by connective tissue capsule. Between spindle cells there are visible freely laying lymphocytes, areas of new formed vessels at the different stages of formation. There are observed focal hemorrhages with hemosiderin deposition. The sharply dilated venous and lymphatic vessels are visible in the peripheral margins of proliferation focuses in the surrounding tissue. In the cases of mixed variant in the histological picture there are found angiomatous changes and proliferation of spindle cells, considerable deposition of hemosiderin.

KS should be differentiated from hemangioma, dermatitis, dermo-hypodermal vasculitis, hemangiopericytoma and dermatofibrosarcoma (Tsvetkova et al., 1986).

Clinical picture of AIDS-associated KS differs from idiopathic variant of disease that is characterized by development of the pathological process at younger age with primary lesion of the facial skin, oral mucosal membranes and upper extremities. The favorite localization is the tip of nose and hard palate. On the trunk the elements have oval or lengthened form and settle down in parallel to Langerhans lines. Further, there are observed rather fast disseminated eruptions over the skin surface, affecting any sites of the body where the spotty elements are quickly transformed in plaques, nodes of purple-brown color which at ulceration are accompanied with pain syndrome. There are found lesions of the internal organs (gastrointestinal tract, pharynx, larynx, lungs, lymphatic nodes) in 75% of cases in HIV-infected patients that is accompanied by different symptom complex in relation to the damaged organ aggravating the disease development, that is the reason of lethal outcomes in 10-20 % of the patients with AIDS. In 5% of cases there can be isolated lesions of the internal organs (Molochkov et al., 2002).
The important role in the development of KS and other tumors in HIV-infected patients belongs to irreversible balance disorder in the system of immunity, that promotes disturbance of immune control of them and results in aggressive development of the pathological process with unfavorable outcome of disease.

Till now both in the scientific literature, and in clinical practice we have not met cases of KS in children. However, recently in clinical practice we have met the second case of KS among HIV-infected children at 2-5 years of age.

**Case study report**

The patient С., born in 2005, inhabitant of the Fergana area, Kokand-city, was admitted to the Clinic of RSRPMC of dermatology and venereology (Uzbekistan) (Medical History No.645) on 18.03.2010 with the complaints on eruptions in the oral cavity, on the skin of floor of the auricle, trunk, and extremities without subjective sensations.

From words of the mother of child, for the first time the occurrence of pink-violet spotty eruptions was noticed 3 months ago, which were appeared on the mucosa of the oral cavity and on the skin of upper and lower extremities. During the last month she noted fast increase in the sizes and colors of the elements of lesion (the spotty elements with pink-violet coloring got more intensive brown - violet coloring, towering above a level of a healthy skin, and in the mouth cavity there was intensive growth of an element of lesion (up to the sizes of a small chicken egg). Additionally there was revealed appearance of new spotty elements on the skin of the both floor of auricles, thorax, trunk, and upper and lower extremities for last month too.

Then the mother addressed to Republican center of AIDS, then she was directed for diagnostics and treatment to the 2 department of the Clinic of RSRPMC of dermatology and venereology.

From epidemiological anamnesis: From words of the mother on 7 day after delivery the child had sudden increase of body temperature, and she had to address to the Children’s Hospital in Kokand, where the diagnosis of sepsis was made. The child received antibacterial therapy; however, he was periodically ill due to dyspeptic events during 3 months after that. The child received hemotransfusion during the next deterioration of the state at the age of 3 months, and he was discharge home with improvement of health. For the period since 2006 to 2008 the child had periodically increase in body temperature without visible reasons, because of this the child blood was examined with use of IEA (immune-enzymatic assay) for antibodies to HIV and the results were positive. Since August 2008 after confirmation of the results of IEA examination by immunoblotting analysis the child was under dispensary observation in the RC AIDS (Uzbekistan). The blood examinations to antibodies for HIV from the both parents showed negative result.

**Objectively:** Skin-pathological process has the widespread character, distributed on the skin of floor auricles, thorax, trunk and both extremities. It is expressed by multiple spotty-papular and nodosal-plaque elements from pink-purple to purple-brown color, of various sizes with tendency to peripheral growth. On the skin of upper posterior surface of the both floor articles there is found one spot looking like hematoma with sizes 0.5 x 1.0 cm of pink-purple color. The small popular single elements with sizes of small grain, of pink-purple color with smooth surface, dense-elastis consistency, of round-oval, lengthened form located along the skin Langerhans lines are visible on the skin of nose right wing, distal phalange of the right second finger and in the projection of subclavicular area.

The elements of lesion on the skin of anterior abdominal wall are presented by multiple, clustering round-oval spots of light brown color and sizes 0.2 x 0.3 cm, located parallel to skin abdomen folds. On the skin of lumbar area and both upper and lower extremities there is noted symmetric lesion by elements of popular-plaque character distributed more frequently on the extension skin surface of the arm and posterior-lateral surface of the both cruses of diameter to 1.5 cm, of round-oval form with relatively clear borders, brown-purple color, surrounded in the peripheral area with green-yellow ring. At
palpation: there is found dense-elastic consistence, their true sizes fall outside the limits of visible elements of lesion, which reach 2.0-2.5 cm.

Examination of the mucous membrane of the oral cavity in the projection of the lower right jaw on the gingiva with transition to the mucous right cheek there is noted focus of lesion, the node of sizes 4.0 x 6.0 cm of purple-brown color with rather clear borders and rough knobby surface without deformation of the bone tissue. In a projection of element of lesion there is noted the loss of teeth. Subjectively: without pathological sensations.

Examinations: the common analysis of blood - Hb 90g/l, erythr. 2,8x10^{12}/l, CI 0.8; leucocytes 3.9x10^{9}/l, segm./neutroph. 60%, eosinophiles 8 %, lymph. 30 %, mon. 2 %, ESR 5 mm / hour. Total protein 70.4 g/l, urea 1.9 mmol/l; ALT- 0.46, AST- 0.39, bilirubin total - 13.8 mmol/l, glucose - 4.8 mmol/l. HBsAg - neg., serological reaction complex - neg. The common urine analysis is without pathological changes. In feces there are found out lamblia cysts.

Immunogram: CD4 + (abs.) - 1731 kl/mkl.

IERA for HHV-8 such as Ig G)OP) 1.320.

PCR for HHV-8: in the saliva there is found out HHV-8.

Histological investigation biopsies № 149-150 of knotty - plaque element in the area of right arm: non-uniform acanthosis, hyperkeratosis, parakeratosis. In derma on the background of sharp disorganization of fibers there is found proliferation of new formed vessels, a lot of accumulated spindle cells, fibrocytes, fibroblasts.

Ultrasonography of the abdominal cavity: the data of focal lesions of parenchymatous organs are not revealed.

R-graphy of the chest: roentgenological findings of the lesion of the thoracic organs are not revealed.

On the basis of anamnesis data, clinical picture and results of laboratory examinations the patient was made the basic diagnosis: HIV-infection IV clinical stage (by WHO classification), epidemic form of disseminated Kaposi’s sarcoma.

Accompanied diagnosis: Anemia stage 1, intestinal lambliosis.

The patient received treatment in the 2 department of the Clinic of RSRPMCDaV including: prospidin injections 75 mg i/m every day (3.0 g for the course), suppositories “Viferon-2” rectally x 2 times a day (course 30 mln.Un), tablets Acyclostad 200 mg 1 tablet x 3 times/day, No.10, tablets Apecosyl 1 tablet x 2 times/day No.10, tablets Ascorutin 1 tab. X 3 times/day No.10, tablet Zentel 200 mg every day No.5. Externally: Application of 0.05% of Prospidin solution, ointment “Dermoveit” under occlusive dressing on the large elements of lesions. Diet is rich of proteins, vitamins.

Oral cavity: irrigation with solutions of Furacilline (1:10000) after each meal, treatment of the focus of lesion with 2% of water solution of methylene blue 2-3 times/day and application of 0.05% solution of prospidin.

After the treatment performed the general health state of the patient was satisfactory, clinically there was observed persistent stabilization of the appearance of new elements of KS, there is noted resorption of old knotty-plaque elements. There is found residual spots of dark-grayish-brown color at the place of regressive elements, and laminar desquamation on the surface of some elements. After the complex therapy of KS the patient was directed to the clinic of Research Institute of Virology for prescription of APV therapy. The patient is under the further supervision.

**Conclusion**

Thus, in this report there is presented the case of clinical manifestation of Kaposi’s sarcoma in HIV-infected boy of 5 years, there are shown clinical signs and character of the development of epidemic Kaposi’s sarcoma in a child, that is characterized by
aggressive development, fast dissemination of the elements of lesion over all skin surface during short period of time. The early therapy of KS with use in a complex of preparation “Viferon” and cytostatic preparation “Prospidin” provides fast stabilization and resorption of the elements of lesion and early preparation of the patients to Anti-retro-viral therapy (ARV), reducing risk of development of KS lesions in the internal organs.

References


Tsvetkova, M., Mordovcev, N., 1986. Pathomorphological diagnosis of skin diseases [Patomorfologicheskaya harakteristika diagnostiki zabolevaniy koji], in Russian, Moscow: Medicine, pp.276-78