CASE REPORT

Kaposi's sarcoma associated with AIDS

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Abstract

In 1872, Moritz Kaposi, first described "Idiopathisches multiples Pigmentsarkom der Haut", which has become known as Kaposi sarcoma (KS). In the present KS is considerate an opportunistic neoplasm rather than a genuine cancer. It is a disease with clinical aspects extremely different, associate with some immunological deficits. The discovering in 1994 of a new type of human herpes virus called human herpes virus type 8 (HHV8) in the KS lesions sustains also a viral etiology. Four forms of Kaposi's sarcoma are recognized: classical, endemic (associated with AIDS), epidemic and iatrogenic (usually after transplant). All these forms have the same histopatologic aspects and are associated with HHV. However, these differ in prognosis and treatment. The authors present a KS case associated with AIDS occurring at a patient in the childhood. The particularities of the case are the presence of only two cutaneous lesions, from which one giant tumor, and the other nodular in aspect and the appearance of an infection HIV in the childhood with involvement of others risk factors except homosexuality. It is important, on one side the importance of the histopathologic exam of an angiomatous tumor for the establishing the diagnosis of KS even when is solitaire and appear in the child, and the other side the absolute necessity to search an eventual concomitant infection with HIV in the presence of a KS.

***Keywords*:** epidemic Kaposi's sarcoma.

Introduction

Classic Kaposi's sarcoma (KS) has been described in 1872 by Marie Kaposi like a idiopathic multipigmented skin sarcoma [1]. However, the clinical aspects extremely vary and its association with some of the immune deficits, Kaposi's sarcoma concerns the internists, infectionists dermatologist, immunologists and oncologists.

In the present, the Kaposi disease is considerate like an opportunist neoplasm rather than a genuine cancer. Precocious exeresis of a lesion not stop the apparition of another with other location [2].

Four forms of Kaposi's sarcoma are recognized: classical, endemic, epidemic and iatrogenic (usually after transplant).

All these forms have the same histopatological aspects and are associated with a new herpes virus, human herpes virus 8. However, these differ in prognosis and treatment.

Patient and methods

We present the case of a young male, now of 18 years age, which in the childhood had frequently episodes of pulmonary infection for which he hospitalized in a rural hospital. Around five years he presented pruriginous erythematous squamos cutaneous eruption, psoriasis-like or papulous, rebellious at the treatment and extremely recidivated.

At age of 11 years, in a moment with a progressive weight loss, in the medial maleolas region of the foot appeared a prominent violaceous patch.

Four months later, the state of the child aggravated, it solicited pediatric exam, at which it discovered the presence of a cutaneous lesions.

Results

The dermatological exam constants on the medial face of left shank, in the 3rd inferior, maleolas dorso-lateral a round tumor, angiomatous, prominent more than 1 cm with the base and the surface smooth glossy, irregular, violaceous with half firm consistence, with 10 cm diameter (Figures 1 and 2).

It can be observed in the superior part another cutaneous lesion with nodular form, violaceous, of about 2 cm diameter. Around both lesions, the skin was an erythematous and violaceous infiltrate, with reticular aspect (Figure 3). The clinical aspect was suggestive for a nodular KS. It has been discussed a pyogenic granuloma tumor, a bacillary angiomatosis, an arteriovenous malformation.

The cutaneous biopsy realized after the total exeresis confirms the diagnosis of KS, the imagines showed a mixture of vascular structure and fusiform cells making areas, which spare vascular clefts without a well-defined endothelium. It is important the absence of a inflammatory infiltrate (Figures 3–10).

Biologically, the laboratory tests showed: increased

ESR, anemia, HBs antigen positive but negative after one year, normal immunogram. In addition, the ELISA test was positive.

The diagnosis established on the base of clinical, histological and immunobiological data is the Kaposi disease associated with AIDS.

The patient followed an antiviral therapy (associating at least three antiviral) which proved efficient. It has appeared no new lesions of KS.

In the present, the patient has a good health. The clinical, radiological and ultrasound exams not discovered KS lesions. In addition, it cannot be identified any cutaneous lesion.

Discussions

Kaposi's sarcoma (KS) is an unusual neoplasm that has proved to be an enigma in many ways since its original description in 1872 [3].

Both epidemiological and molecular studies support the role of an infectious agent in the causation of KS in 1994 a new human virus, HHV8, also termed KS herpes virus (KSHV) has been discovered in AIDS-associated KS biopsies [4], and is a strong candidate for the KS agent [5]. The sequence of this KSHV is found in virtually all KS lesions [6] and experimental infection will produce KS-like lesions in animals [7].

HHV-8 is a T2 herpes virus (rhadinovirus) whose natural appears to be humans (there is no published evidence for natural infection of other animal species [5]), has been detected in endothelial and spindle cells, primary effusion lymphoma cells, B cells, macrophages, dendritic cells and prostatic glandular epithelium [8–13].

Spindle cells present the characteristic cell type surrounding the slit-like spaces present in advanced KS lesions. Endothelial cells (either vascular or lymphatic endothelium), cells from lymphatic junctions, fibroblasts, smooth muscle cells, dermal dendrocytes and macrophages have all been proposed as possible progenitors of KS spindle cells [14–16].

Studies of HHV8 genes have reveled that they encode homologies of several human genes that participate in cell proliferation. These include cytokine IL-6, chemokine MIP-1α, a G-protein coupled chemokine receptor, cyclin D and the antiapoptotic Bcl-2. In addition, KS cells can produce a variety of other cytokines including TNF-α, IL-1, colony-stimulating factor, basic fibroblast growth factor of spindle cells in an autocrine and paracrine way [17, 18].

Clinical and epidemiological, have been identified four major forms.

Chronic, called classic KS, occurs primarily in older men of Eastern Europe or Mediterranean descent (male to female ratio of 10–15:1). It generally involves lower extremities, especially the ankles and soles.

Cutaneous lesions of KS usually begin as discrete red or purple patches that become elevated, involving into modules and plaques. The modules tend to enlarged into dome-shaped tumors.

The disease may be limited to a single or a few discrete macular or popular lesions that can range in size from a few millimeters to several centimeters in diameter. This form of Kaposi's sarcoma was also recognized in association with other malignancies, particularly lymphoma, but is not associated with HIV infection.

Endemic or African KS was recognized in areas of Central Africa, prevalent among young Bantu children in whom the disease is extremely aggressive, but was not related to infection with HIV. Skin lesions are infrequent.

Iatrogenic KS appears months of years after receiving high doses of immunosuppressive therapy, particularly for renal and hepatic transplant. Other disorders of the immune system, including systemic lupus erythematosus and *pemphigus vulgaris* have also been associated with Kaposi's sarcoma. In this (form) clinical setting, skin lesions are infrequent.

Epidemic or AIDS-associated KS is found in over one forth of AIDS patients [3].

Incidence of KS has been estimated to be 20 000 times greater among HIV-infected individuals than in the general population. AIDS-associated KS is more frequently seen among homosexual or bisexual men with HIV than other risk group wit the virus.

Clinically the AIDS-related KS is quite different from the sporadic, classic form. They are characterized by multifocal, widespread lesions at the onset of illness and, in contrast to the cutaneous lesions pf classic KS, tend to be smaller, pink and located on the upper trunk and the head/neck areas [19].

These lesions may involve skin, oral mucosa, lymph nodes and visceral organs, such as the gastrointestinal tract, lung, liver and spleen [20].

The earliest faint, flat, macular lesions (patch stage) may be unobstructive to be totally overlooked [5].

The mucocutaneous KS lesions are usually asymptomatic, may be single or multiple, and sometimes appear simultaneously or sequentially. New lesions usually continue to appear throughout the course of the disease. They may be found in localized clusters, and can be widely disseminated.

The skin lesions are often elongated with a fusiform or oval shape. As these tumors evolve, the flat lesions rapidly become elevated, developing into papules or plaques (plaque stage).

Eventually, the plaque stage lesions may enlarge, coalesce and become elevated nodules (nodules stage). Therefore, three distinctive stages of skin lesions may be occurred according to the evolution: patch, plaque and nodular stage.

Systemic symptoms may be present simultaneously or even precede the appearance of the tumor lesions and include persistent or intermittent fever, weight loss, diarrhea, malaise and fatigue. Impetigo, prurietic skin eruptions, superficial fungal infections of the skin and nails, oral or esophageal candidiasis, herpes simplex infections or severe herpes zoster infections are commonly observed in patients which AIDS and KS lesions [21].

The histopathology of the process begins in the mid dermis and extends upwards to raise the epidermis, which may be thinned, or acanthotic and verrucose.

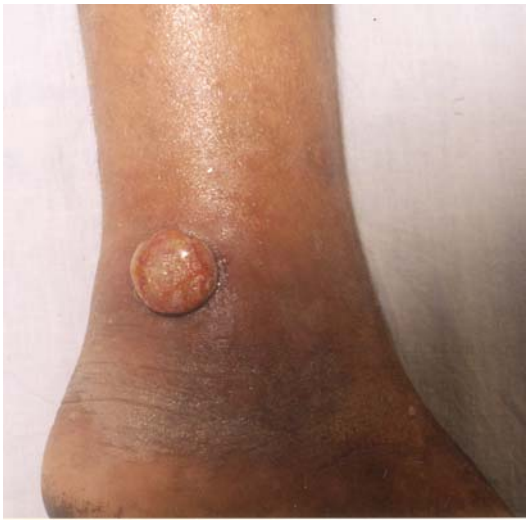

Figure 1 – ***Kaposi's sarcoma, clinical aspect***

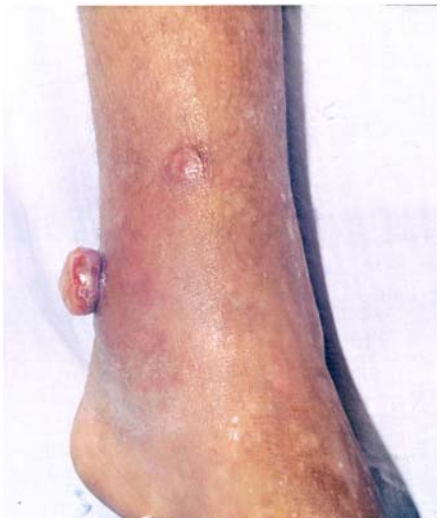

Figure 2 – ***Kaposi's sarcoma, clinical aspect***

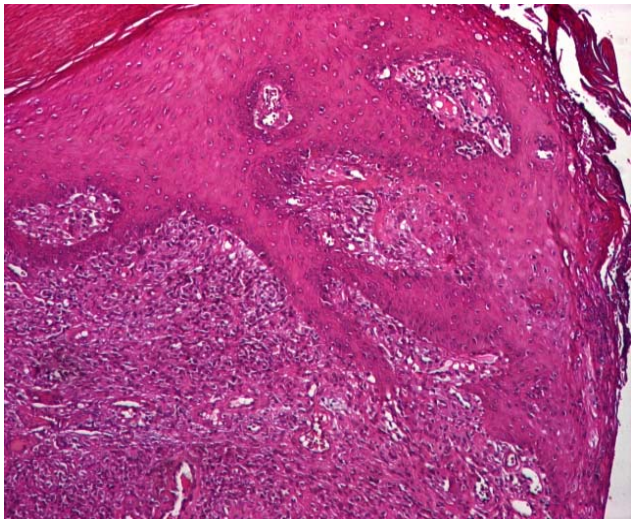

Figure 3 – ***Skin, subjacent thick cellular zone represented by fusiform cells and narrow vascular spaces (HE stain, ×4)***

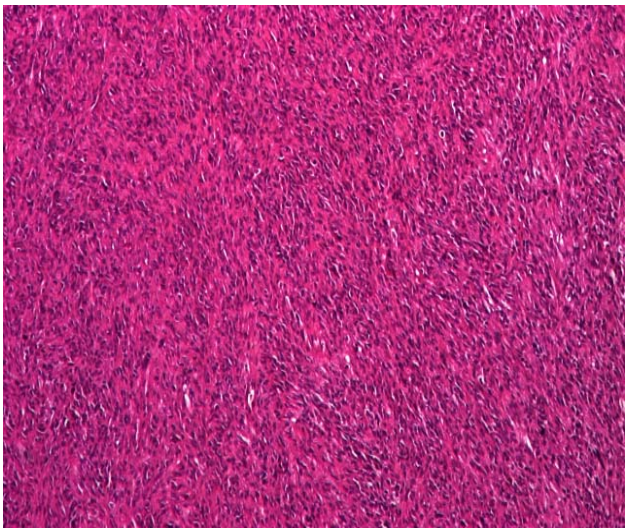

Figure 4 – ***Fusiform cell disposed in island form and narrow vascular spaces (HE stain, ×4)***

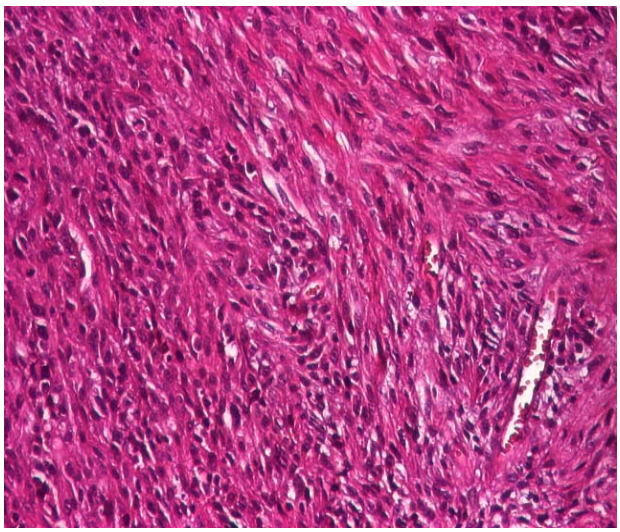

Figure 5 – ***Narrow vascular spaces, delimited by fibroblast-like cells (HE stain, ×10)***

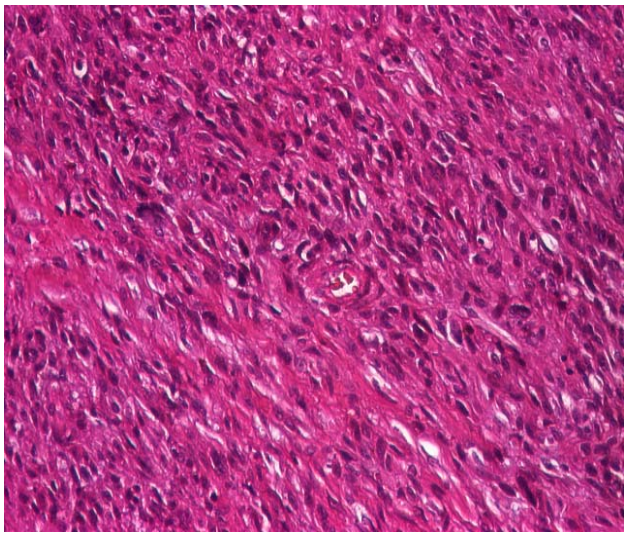

Figure 6 – ***Aspect of endothelium (central), surrounded by fibroblast-like cells (HE stain, ×10)***

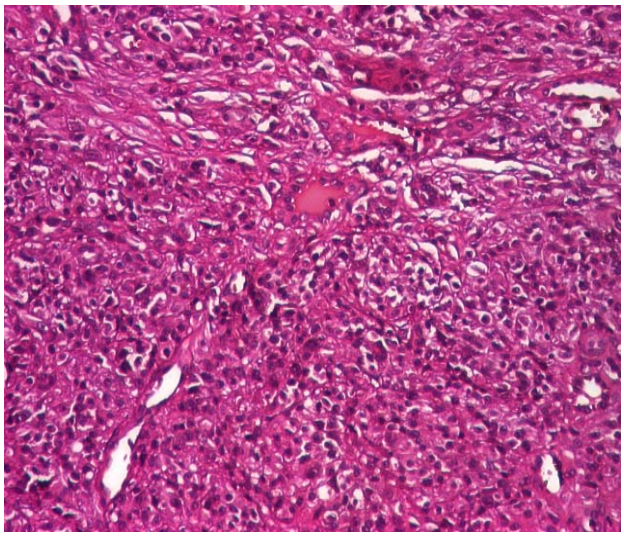

Figure 7 – ***Vascular spaces bordered by tall endothelial cells, surrounded by fusiform cells (HE, ×10)***

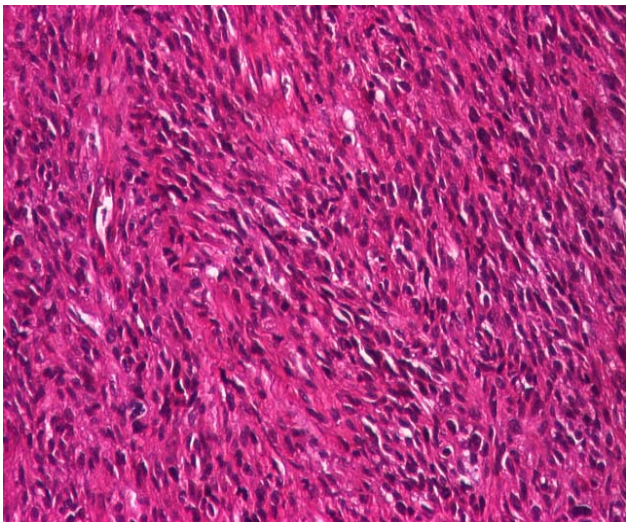

Figure 8 – ***Fusiform cells which delimited rare vascular spaces (HE stain, ×10)***

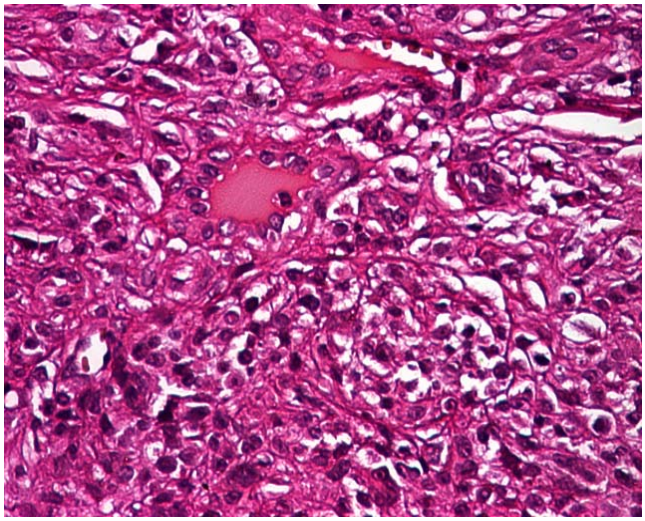

Figure 9 – ***Vascular spaces bordered by tall endothelial cells, surrounded by fusiform cells (HE, ×20)***

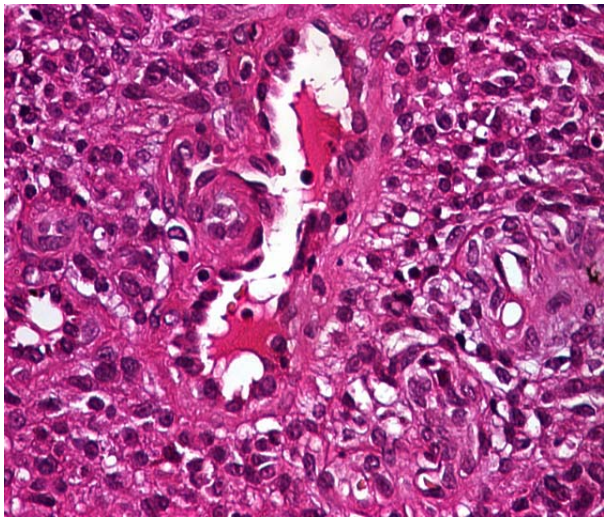

Figure 10 – ***Other aspect of endothelial cells, which obliterates vascular lumen, surrounded by fusiform cell with type of fibroblast-like (HE stain, ×20)***

The characteristic histopathology of all KS types is similar regardless of the different clinical forms. In the early phase of the disease presenting as a macular lesion (patch stage), there is an unapparent proliferation of thin-walled, angulated vessels throughout the dermis.

Scant inflammatory infiltrate rich in plasma cells, lymphocytes and haemosiderin deposits accompany the lesion. In this stage, the lesion becomes more evident with formation of areas showing angiomatoid vascular spaces filled with red blood cells and surrounded by spindle cells arranged in short fascicles (plaque stage).

The spindle cells may show a wide range of nuclear pleomorphism. The vascular component may appear as cleft-like spaces between the spindle cells or as delicate capillaries. Mononuclear cell infiltration may be present, particularly in earlier lesions. At this stage, the process involves the completely reticular dermis and extends to the subcutis.

In the later nodular stage, the tumor nodules become more solid with an extensive component of uniform spindle cells arranged in sheets. Intra or extracellular eosinophilic hyaline globules 0.5–10 μm in diameter are commonly seen [21, 22]. In general, there is little mitotic activity or cellular atypia of the spindle cells.

In classic KS, based on variations in quantity of the vascular component, the presence of spindle cells, fibrosis and nuclear pleomorphism in the tumor, two different histopathological patterns may be identified [5].

The angiomatous pattern usually consists of marked proliferation in a random fashion. Most often, the endothelial cells are not atypical and the lumina either are empty or contain erythrocytes. Capillaries as characteristic vascular slits or clefts embedded in a network of reticular and collagen fibers are the predominant features of this form of KS. Rarely the lesions extend to the subcutaneous fat.

The sarcomatous pattern is characterized by fibroblastic proliferation and spindle cell formation in the dermis, which contains small vascular spaces and extravasated erythrocytes.

The degree of atypia of the spindle cells and the numbers of mitoses are variables, and often, haemosiderin granules are present. Intermediate stage and/or combinations of the two above-mentioned patterns are also seen. Multiple lesions with different histological patterns can be present in the same patient.

In epidemic KS the histopathology of the earliest patch-stage skin lesions can be difficult to identify due to the subtlety of changes, which include a slight increase in the number of bizarre-shaped, dilated, vascular spaces lined with thin endothelial cells located in the upper portion of dermis. Furthermore, in the dermis there is a sparse superficial a deep perivascular mononuclear cell infiltrate composed of lymphocytes and plasma cells [24].

An increased number of jagged, irregularly shaped, endothelium-lined vascular spaces histopathologically characterize KS plaque lesions. Throughout the dermis, a dense, mononuclear, inflammatory cell infiltrate composed of plasma cells and lymphocytes is present and these is an increased number of grouped spindle-shaped cells located between collagen bundles. Characteristically, a few extravasated erythrocytes are often found interspersed in the intercellular spaces between the spindle cells [5].

KS nodular lesions are characterized by very few, thin endothelium-lined, vascular slits that are surrounded and compressed by dense, interweaving bundles or fascicles of spindle-shaped cells. Some erythrocytes and plasma cells can be seen within the exceedingly fine vascular clefts. In the nodular stage of KS lesions, the inflammatory cells are absent, but a few extravasated erythrocytes and haemosiderin-laden macrophages are seen throughout the interstices between the spindle cells. The mononuclear cell infiltrate consisting of lymphocytes and plasma cell seen in the patch and plaque stage lesions is absent in the nodular lesions.

KS may be mistaken in the skin for an inflammatory dermatosis, pyogenic granuloma, angiodermatitis or pseudo-Kaposi's, bacillary angiomatosis, angiosarcoma, bullous lesion in the rare cases of lymphangioma-like or bullous KS, or arteriovenous malformations [25–27].

Bacillary angiomatosis and pyogenic granuloma can simulate clinically KS, but histological distinction is usually not problematic. The early KS macular lesion may resemble a benign dermal infiltrate rich in plasma cells around an unapparent proliferation of thin-walled angulated vessels through the dermis. Although subtle, characteristic spindle-shaped cells loosely arranged in fascicles are diagnostic.

Angiosarcoma shows more cytological cell multilayering is present. Epitheloid haemangio-endothelioma has typically polygonal to spindle-shaped endothelial cells arranged in cords surrounded by myxoid or chondroid stroma. Lymphangioma-like pattern resembling lymphangioendothelioma has to be recognized [28].

Electron microscopy and immunohistochemical features of KS may be important. Immunohistochemical detection of CD31, CD34 antigens, FVIII-Rag and sialic acid expression may be useful to support or confirm the diagnosis of RS [29, 30]. While the blood vessels in KS are positive for various endothelial cell markers, the spindle cell population is consistently positive for CD34 and often CD31 [3].

Evolution of epidemic KS is much more aggressive than the classical form with a more disseminated cutaneous involvement. The survival is correlated with the number of circulating lymphocytes CD4 and the CD4/CD8 ratio, the presence of the general signs and the opportunistic infections [31].

Immunological, the modification of the number of CD4 lymphocytes and the ratio CD4/CD8, during epidemic KS, has been presented diminution the lymphocyte proliferation tests in presence of the mitogens and alloantigens, diminution the activity of circulating NK (natural killer) [32].

During the classic and endemic KS are usually modified neither the number of CD4 lymphocytes nor the ratio CD4/CD8. It notified a diminution of the NK activity miscorrelated with the disease [33, 34].

Therapeutically, the control of infection with the

AIDS virus with antiviral association permits a response partial or complete KS in 50–80% of cases [35, 36].

A rapid evolutive KS can justify the introduction, parallel with the antiviral threetherapy of interferon α (in minim tolerate dose) on systemic way of the patients which CD4 number is over 200/mm^3 or bleomycine (15 mg at two weeks).

In our case, appears to be a genuine example of form KS associated with AIDS, occurring at a child and supposes the intervention of other risk factors concerning obtaining the infection with HIV that presented at homosexuals.

Clinically, it distinguished with the developing from the beginning of nodules, tumor lesions without crossing the classic stages of patch, plaque and nodule.

Histopathologically, the aspect is identical with that of classic form of KS, but is absent the infiltrate. These absence is correlated with the form of presentation, KS nodular, it be present only in the path and plaque stage. Therapeutically, the antiviral tripletherapy has proved efficient.

Conclusions

Kaposi's sarcoma may be suggestive for an infection with HIV, it is necessary because of the reason the research of this infection of all patients including the cases appeared at child.

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Received: June 15th, 2007

Accepted: July 20th, 2007