KAPOSI'S SARCOMA – CLASSICAL OR IATROGENIC? – CASE PRESENTATION

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Summary

The Kaposi's sarcoma is a vascular neoplasia mainly related to the HIV infection, with an increased incidence among these patients. In the general population, it has an incidence of 0.02% in Europe and 3-9% in Africa and it can reach up to 34% among the HIV-positive patients.

We present the case of a 74-year HIV-negative heterosexual male patient diagnosed with Kaposi's sarcoma on the thigh while being monitored for chronic kidney failure.

The challenges were represented by the diagnosis difficulties, the differential diagnosis during the progress and, last but not least, the establishment of a therapeutic strategy appropriate to the case.

Key words: *nephrotic syndrome,imunosupression, Kaposi sarcoma.*

Received: 5.05.2020 *Accepted: 3.06.2020*

Introduction

The first KS case was described by Moritz Kaposi in 1872 under the name of „pigmented multifocal hemangiosarcoma". The first KS case related to the kidney transplant was diagnosed in 1969. Until 1980, it was considered as a rare disease, becoming important in the following period with the increased spread of AIDS.

The Kaposi's sarcoma is a vascular neoplasia mainly manifested at the cutaneous-mucous level, with typical localization at the extremities - typical lower limbs, upper limbs, face. The specific lesions are represented by red-violet or to dark brown infiltrated plates tending to increase and invade. It can also extend to other organs - lymph nodes, gastrointestinal tract, lung, liver.

KS can be divided into 4 types:

- epidemic, related to HIV infection;
- classical sporadic form;
- endemic form (especially in Africa);
- iatrogenic (in immunocompromised patients).

Classical KS is frequently met in elders, predominantly in males. It is generally located in the lower limbs, and its progress is slow, lasting 10–15 years.

Epidemic KS – is related to the HIV infection and especially in patients diagnosed with AIDS. The lesions may appear in the entire body and may affect the lymph nodes, liver, gastro-intestinal tract, lung

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The endemic KS is met especially at the population living in Equatorial Africa. It clinically resembles the classical form, but the age when the disease appears is lower. A particular form which appears in prepubertal children is also described. In general, there are cutaneous lesions but they do not affect the internal organs. They are related to the herpes virus 8 infection or the conditions destabilising the immune status (chronic infections, malaria, malnutrition)

Iatrogenic KS (acquired) – is related to the immunosuppression, being met in the transplant persons. In this case, the risk of occurrence is 150-200 times higher than in the general population.

From a clinical point of view, skin lesions appear in the form of plates, infiltrative lesions of red-violet to brown colour. The lesions are painless but lymphedema may appear as a result of the lymphatic compression.

The onset is also possible with nonspecific manifestation – cough, chronic abdominal pain, diarrhoea, the lesions being accidentally discovered, during the investigations of the symptoms (endoscopy, bronchoscopy, colonoscopy). The imaging is useful to assess the disease extension (CT, MRI, PET).

The certainty diagnosis is based on the anatomopathological examination as a result of the lesion biopsy. The appearance is of vascular proliferation, spindle-shaped cells and lymphoplasmacytic infiltrate, in variable proportions depending on the stage. The microscopic characteristics of KS may be affected by comorbidities, immunosuppression, HAART therapy. There are also more than 10 described variants due to the vast spectrum of vasoproliferative disorders that mimic KS. The IHC tests have become the gold standard in establishing the diagnosis. The CD31, CD 34 antigens and FVIII factor are essential for the positive diagnosis.

Since HHV8 was discovered there was a good understanding of KS pathogenesis so that HHV8 positivity is a mandatory requirement, but it is not enough for KS occurrence.

The etiopathogenesis of the disease is multifactorial, being incompletely explained. It seems that the HHV8 infection, the angiogenesis disorder and the presence of proinflammatory cytokines have an important role.

The risk factors are represented by

- the male gender (men are twice more affected than women);
- Mediterranean population in the Middle East, Africa, Jews - it is explained by the inheritance vulnerability of HHV8 infection (which may be sexually transmitted by saliva but also vertically from mother to foetus);
- HIV infection - KS incidence up to 34% and in case of AIDS, the presence of KS lesions becomes a diagnosis element;
- immunosuppression – increased incidence to patients suffering a kidney transplant, diabetics, undergoing cortisone treatment, etc.

Treatment - till now there is no unanimous consensus accepted as regards the therapeutic indication of each case. The treatment depends on the stage of disease and the associated circumstances, as HIV, in which the antiretroviral therapy (HAART) is applied.

The therapeutic modalities may include surgical methods (the resection of the lesions using the classical method or by electrocautery, cryoablation) which is done in case of small lesions. Radiotherapy - external or brachytherapy - is usually the treatment basis in KS. It may be the alternative to surgery or may be applied to complete the surgery. The chemotherapy is reserved to the advanced relapsed cases, with inconsistent results. Biological therapies or immunotherapy (with IFN alfa) and antiviral treatments were also tried but the results were disappointing.

Material and method

We present the case of a 74 year male patient, known with diabetes, gout and high blood pressure admitted to the Nephrology Clinic for monitoring the kidney disease.

He was registered by the Clinic in September 2017 when he was assessed from a nephrologic point of view for increasing azotemia and nephrotic proteinuria in the outpatient care. It was initially interpreted as a nephrotic syndrome in the context of rapidly progressive glomerulonephritis, which is why they decided to make a puls-therapy with methylprednisolone iv. 1 g, 3 days, followed by the administration of prednisone 0.5 mg/kgc/day. Subsequently, the

patient was repeatedly admitted to hospital on a monthly basis to be given the iv. treatment (methylprednisolone 1g iv. 3 days, alternatively with cyclophosphamide 600 mg) for 7 months. The response to treatment was instable in terms of proteinuria remission, with repeated relapses. In August 2018, a renal biopsy with establishing the diagnosis of membranous glomerular nephropathy was performed. They decided to stop the cytotoxic therapy and to give the patient cyclosporine 200 mg/day. The response to treatment is satisfactory, with the decrease of proteinuria from 14 g/24 h to 3.6 g/24 h.

The patient currently takes prednisone 40mg/day, cyclosporine 200mg/day, perindopril 5 mg/evening, furosemide 40 mg 2 cp at 2 days, sintrom $^{1}/_{2}$cp daily, atorvastatin 20 mg 1 cp/evening, milurit 300 mg 1 cp/day, glurenorm 2 cp day.

In January 2019, about 18 months after the first admission to hospital, the patient came for his kidney function to be monitored. The increased creatinine is recognised (with progressively increased values, up to 5.6 mg/dl), proteinuria 8g/24h. In the clinical examination, the presence of a painless lilac placard having the sizes of 15/20 cm, affirmatively noticed for a few weeks and the sizes of which increased progressively was noticed on the right thigh.

Ultrasound of soft parts - showed the derma thickening, intense oedema, without localized formations and 5/4 cm inguinal adenopathic blocks.

The skin biopsy and lymph node biopsy are decided to be performed.

The anatomopathological result reveals - lymph node pack with the presence of a vascular neoplasia infiltration, made of spindle-shaped cell bundles with moderate cyto-nuclear pleomorphism that delimits the small vascular spaces. The vascular spaces with cavernous appearance, mitotic index 8 mitoses/10 fields 40x/0.65 can be focally noticed. Skin fragment showing diffuse vascular proliferation with imprecisely delimited vascular structures, with numerous extravasated red blood cells, extending from the papillary dermis to the hypodermis. The vascular structures are delineated by thin walls, focally with spindle-shaped cells and seem to dissect the stroma of the reticular dermis and hypodermis. The pathological appearances plead for a neoplastic process of angiosarcoma type.

The recommended IHC tests showed CD34 and CD 31 positive.

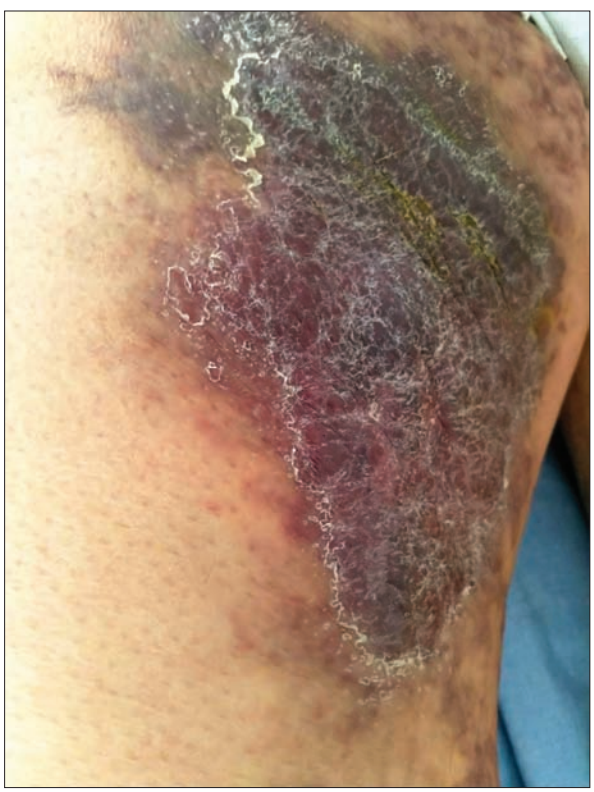

Figure 1. Kaposi Sarcoma clinical aspect

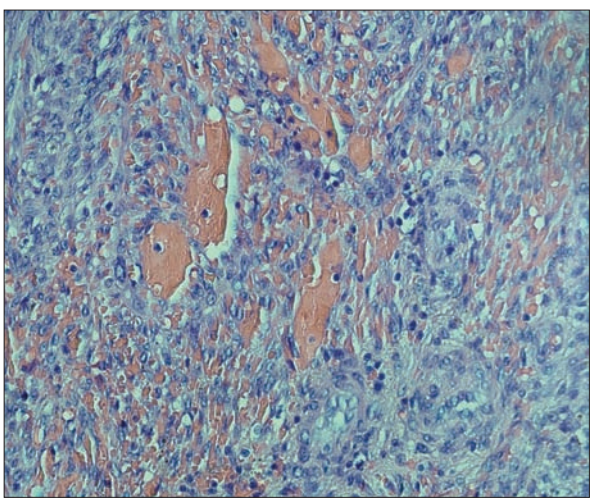

Figure 2. Kaposi's angiosarcoma. Coloration HE ob. 10x. Fusiform cell bundles with moderate anaplasia, with frequent mitosis, with vascular slits

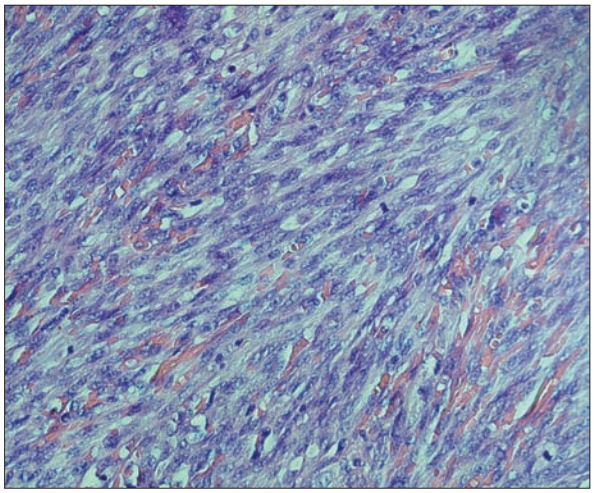

Figure 3. Kaposi's angiosarcoma. Coloration HE ob. 20x. Fusiform cell bundles with moderate anaplasia, with frequent mitosis, with vascular slits

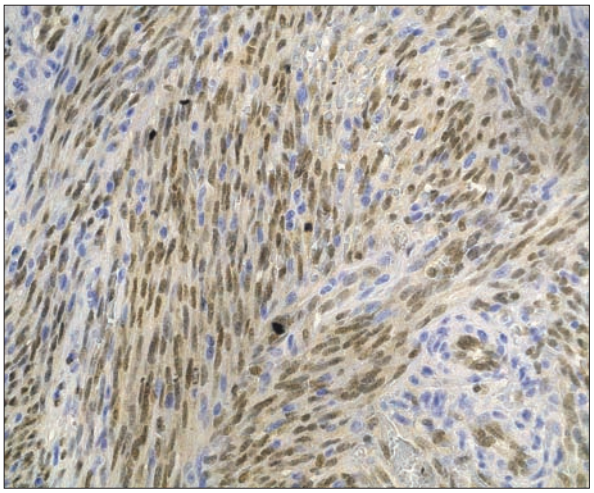

Figure 4. Kaposi's angiosarcoma. Col. IHC for ERG1, with diffuse nuclear labelling, highlighting the endothelial origin of tumor cells. Ob. 40x

The certainty diagnosis was established as a result of the anatomopathological examination completed with immunohistochemistry tests, namely Kaposi's sarcoma.

The patient was subsequently sent to the oncology network and was prescribed local radiotherapy.

The last known appearance was 8 months after establishing the diagnosis, the patient declaring that the local symptoms aggravated by the extension of the placard to the thigh level, the occurrence of a new lesion on the calf, intense painful oedema in the right lower limb. The renal impairment parameters were also increased, proteinuria 20 g/24 h.

Discussions

Generally, the diagnosis of Kaposi's sarcoma is easily established based on clinical criteria and by anatomopathological examination completed by IHC. The specific skin lesions are highly suggestive and the progress is slow.

As regards the treatment, there is no accepted unanimous consensus but the control of disease may be obtained for longer periods of time by radiotherapy.

In this case, it is about an elder HIV-negative diabetic patient who was initially diagnosed and treated for the nephrotic syndrome with repeated relapses. The patient received large doses of immunosuppressive medication - prednisone, cyclophosphamide, cyclosporine.

The occurrence of the rapidly progressive lesion was initially interpreted by the patient as a local hematoma (the patient was given anti-coagulants by mouth - sintrom) which is why the medical examination had not been immediately requested.

The routine scheduled admission lead to noticing the lesion and subsequently to establishing the diagnosis.

Given the local extension and the patient's deficiencies, the surgery and chemotherapy are out of the question (contraindicated in case of renal imapairment function).

The only available treatment - radiotherapy did not help unfortunately to control the disease, the patient subsequently presenting with locally aggravated signs (pain, tumefaction and local extension of the lesion).

Conclusions

The particularity of the presented case consists of the long progress of a nephrotic syndrome that did not respond to the treatment, the patient being subsequently diagnosed, after 18 months, with Kaposi's sarcoma.

In this case, we can talk about an atypical presentation – nephrotic syndrome being interpreted as paraneoplastic and long before the diagnosis of neoplastic disease. At the same time, the patient received the immunosuppressive medication in large doses and for a long period of time in order to improve the deterioration of renal function.

In this case, we discuss about the differential diagnosis between the two possible forms of KS - classical or iatrogenic, having arguments for each of them. The prognosis or treatment are not influenced of the specific form, is more a scientific discussion trying to elucidate the possible etiology.

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Conflict of interest
NONE DECLARED

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