CASE REPORT

Secondary involvement of lymph nodes in Kaposi sarcoma

M. TURCU1), O. S. COTOI2), LILIANA CHIRA1), EMŐKE HORVÁTH1), S. H. MORARIU3)

1) Department of Pathology
2) Department of Cell and Molecular Biology and Pathology
University of Medicine and Pharmacy of Targu Mures
3) Department of Dermatology and Venereology, County Hospital, Targu Mures

Abstract

Kaposi sarcoma is a low-grade neoplasm first described by Moricz Kaposi in 1872. Although many attempts have been made to explain its pathogenesis, its etiology still remains obscure. In this regard, many aspects of the disease’s genetic, epidemiological and histopathological backgrounds are even today unclear. We present the case of a 57-year-old male patient, constant HIV negative, with a history of plaque-like lesions on his right foot approximately two years ago. Following surgical removal, a diagnosis of Kaposi sarcoma, plaque stage was settled. One year after, the patient was admitted to the hospital for pain in the right ankle and foot, associated to paresthesia and trophic lesions at this level. Similar lesions developed in the popliteal fossa. Biopsy and subsequent histological and immunohistochemical examination revealed a KS at that level. The most recent hospital admission revealed the appearance of an indolent lymphadenopathy in the groin. Our case represents a rare occurrence of Kaposi sarcoma at a HIV-negative patient, which, after several local recurrences and progressive behavior, produced a lymph node involvement at the groin level. The immunohistochemical assessments have confirmed the diagnosis.

Keywords: Kaposi sarcoma, lymph node.

Introduction

Kaposi sarcoma (KS) is a low-grade neoplasm first described by Moricz Kaposi in 1872. Although many attempts have been made to explain its pathogenesis, its etiology still remains obscure. In this regard, many aspects of the disease’s genetic, epidemiological and histopathological backgrounds are even today unclear [1]. The 2002 the WHO classification of soft tissues included KS in the group of vascular tumors, code 9140/3 [2, 3]. According to this classification, KS is a locally aggressive endothelial tumor, with typical skin lesions, in the form of multiple patches, plaques or nodules, which may eventually extend through the subcutaneous tissue towards lymph nodes and deeper tissues and organs. Synonyms used along the times, accepted by WHO, include: idiopathic multiple pigmented sarcoma of the skin, angiosarcoma multiplex, granuloma multiplex haemorrhagicum, Kaposi disease [4].

Materials and Methods

Our case represents a rare occurrence of Kaposi sarcoma at a HIV-negative patient, which, after several local recurrences and progressive behavior, produced a lymph node involvement at the groin level.

Tissue fragments were processed using standard histopathological methods: 10% formalin-fixation, paraffin embedding, 4–5 µm sections, Hematoxylin–Eosin staining. Additional procedures were used – immunohistochemistry: the ABC-complexes method. This included the use of Avidin–Biotin complex, heat induced antigen retrieval, overnight incubation with primary antibody on 4°C, incubation with biotin-linked secondary antibody, DAB staining, counterstaining with Hematoxylin. For each antibody, specific internal and external controls were used. We evaluated the expression of the following cellular components: vimentin, CD34, CD3 and CD20.

Table 1 shows detailed information about the antibodies used.

Table 1 – Antibodies used in this study

<table>
<thead>
<tr>
<th>Name and features of the primary antibody</th>
<th>Antigen retrieval</th>
<th>Antigen localization</th>
<th>Results in this case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimentin (Clone V9), dilution 1:100, Lab Vision</td>
<td>Humid heat (boiling) 10–20 minutes in citrate buffer, pH 6</td>
<td>Cytoplasm</td>
<td>Positive cytoplasm in tumor cells</td>
</tr>
<tr>
<td>CD20 Ab-1 (Clone L26), dilution 1:250, Lab Vision</td>
<td>No special pretreatment</td>
<td>Cytoplasm and membrane</td>
<td>Positive B-lymphocytes</td>
</tr>
<tr>
<td>CD3 Early T-Cell Marker (Clone SP7, rabbit monoclonal antibody), dilution 1:150, Lab Vision</td>
<td>Humid heat (boiling) 10–20 minutes in citrate buffer, pH 6</td>
<td>Membrane</td>
<td>Positive T-lymphocytes</td>
</tr>
<tr>
<td>Name and features of the primary antibody</td>
<td>Antigen retrieval</td>
<td>Antigen localization</td>
<td>Results in this case</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>------------------</td>
<td>----------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>CD34 Ab-1 (Endothelial cell marker), dilution 1:200, Lab Vision</td>
<td>No special pretreatment</td>
<td>Cytoplasm and membrane</td>
<td>Positive cytoplasm and membrane in tumor cells and normal endothelium</td>
</tr>
</tbody>
</table>

**Results**

We present the case of a 57-year-old male patient, constant HIV negative, with a history of plaque-like lesions on his right foot approximately two years ago. Following surgical removal, a diagnosis of Kaposi sarcoma, plaque stage was settled. One year after, the patient was admitted to the hospital for pain in the right ankle and foot, associated to paresthesia and trophic lesions at this level. Similar lesions developed in the popliteal fossa. Biopsy and subsequent histological examination revealed a KS at that level.

The most recent hospital admission revealed the appearance of an indolent lymphadenopathy in the groin. The patient’s history suggested secondary involvement of the lymph nodes by KS. Surgical removal is recommended and the bioptic material is analyzed in the Pathology Laboratory of the Emergency County Hospital, Târgu Mureș.

The gross appearance of the excised material consisted of three nodular tissue fragments with the following dimensions: 20×30 mm, 30×30 mm and 30×40 mm, white appearance, clear-cut borders, solid on section (inguinal lymph nodes).

On microscopic examination, two of the three lymph node had a normal histological aspect with sinus histiocytosis.

The third lymph node however presented normal appearing tissue only at the periphery of the specimen, the rest being replaced by a proliferation of spindle cells, arranged in short fascicles within compartments, limited by collagen fibers. Among the spindle cells, a proliferation of blood vessels was described, suggesting a pseudovascular aspect (Figures 1 and 2).

Given the patient’s history, we used specific immunohistochemical markers, such as vimentin and CD34. The tumor cells were positive for both of these markers (Figures 3 and 4).

The diagnosis of secondary involvement of lymph node by Kaposi sarcoma is made.

![Figure 1 – Lymph node with central sarcomatoid proliferation (HE staining, ob. 2×).](image1)

![Figure 2 – Proliferation of spindle cells arranged in short fascicles, separated by fine collagen bands (HE staining, ob. 4×).](image2)

![Figure 3 – Vimentin positive in cytoplasm of tumor cells (immunohistochemistry, ob. 10×).](image3)

![Figure 4 – CD34 positive cytoplasm and membrane in tumor cells and normal endothelium (immunohistochemistry, ob. 10×).](image4)
Discussion

The particularities of our case are the fact that KS appeared in a HIV negative patient, with initial involvement of the lower extremity, having a progressive and recurrent nature that eventually lead to secondary involvement of lymph nodes. Such cases are seldom reported since lymphonodular involvement is rare in KS and only affects patients in advanced stages of the disease.

Currently there are four types of KS, according to the WHO classification, based on clinical, epidemiological, anatomical and geographic distribution. These types are as follows:

- Type 1: Classic indolent form, the one that Kaposi described, occurring predominantly in elderly men of Mediterranean/East European descent, lesions are predominantly localized in the lower extremities [5].
- Type 2: Endemic African KS that occurs in middle-aged adults and children in Equatorial Africa who are not HIV infected [6, 7]. Affects extremities of the body and frequently is associated with secondary involvement of lymph nodes in children.
- Type 3: Iatrogenic KS appearing in solid organ transplant recipients treated with immunosuppressive therapy and also in patients treated by immunosuppressive agents, notably corticosteroids. In these cases lower extremities are mostly affected [8, 9].
- Type 4: Acquired immunodeficiency syndrome-associated KS (AIDS KS), the most aggressive form of the disease, found in HIV-1 infected individuals, that is particularly frequent in homo- and bisexual men [10, 11]. In this case, lesions are present on the extremities and also on the face and genitals. Visceral involvement is also frequent in this type [12–14].

The agent responsible for the disease is known and, according to Chang’s studies in the 90’s, is a human herpes virus (HHV-8), termed Kaposi Sarcoma Associated Virus [15–17].

Infection with this virus has showed to exist in all four types of the disease and possibly other factor, such as immunological and genetic, play a role as well.

The prognosis and evolution of KS depend on the clinical status and immunologic competence of the patient. Generally, the progression of the disease is slow and therefore the patient may be treated with complex surgical therapy associated with radio- and chemotherapy. The AIDS-related Type 4 of the disease is a more aggressive form.

Cases with advanced stage disease have poor response to therapy and usually present with widespread organ and lymph node involvement, consequently these cases have poor prognosis.

Microscopic findings are similar between different types and correlate well with disease stage [18]. Thus, initial skin lesions are non-specific.

In the patch-stage of the disease, microscopic examination reveals the increase in number of vessels and vascular spaces of various shapes and sizes with the consequent dissection of the collagen fibers of the dermis. The newly formed vessels are predominantly localized perivascular and perinodal (hair follicles, sebaceous glands). Pre-existing blood vessels occasionally protrude into the lumen of new vessels. Endothelial cells lining the newly formed vascular spaces are flattened or oval, with only little atypia.

In plaque stage, similar lesions exist as in the previous one, however these characteristics are exaggerated. A more extensive angio-proliferation is observed with dense chronic inflammatory infiltrate (lymphocytes and plasmocytes). Also, extravascular red cells and siderophages are numerous. Hyaline globules are frequently found.

Nodular stage is characterized by well-defined nodules of intersecting fascicles of spindle cells with only mild atypia and vascular spaces containing red blood cells. Some of the spindle cells show mitoses. Numerous hyaline globules may be observed inside and outside the spindle cells. At the periphery of the lesion dilated vessels may be observed, which resemble lymphangioma [19].

If the lymph nodes are affected, the tumour infiltrate may be uni- or multi-focal and the lymph node may be entirely affected. Early lesions may show only increased number of vascular channels associated with perivascular plasma cell infiltration.

In visceral organ involvement, the lesions are described mostly along vascular structures, bronchi, portal areas in the liver, generally respecting the architecture of the organs involved, the surrounding parenchyma being generally normal [12].

Immunohistochemical studies prove the endothelial origin of the tumor cells, which are usually positive for vascular markers, such as CD34 or CD31, but are factor VIII negative [20].

It appears that VEGF/VPF and FGF growth factors are involved in the neoplastic transformation of cells. Tumor cells also express mesenchymal markers such as vimentin. All four types are HHV-8 positive, and currently a new marker is being tested called FLI1, a nuclear transcription factor, which appears to be expressed in almost all different vascular tumors, including KS [16, 17].

Cytogenetic studies involve the study of ras and p53 genes [21]. A positive diagnosis is made based on the microscopic appearance correlated with the clinico-epidemiologic type of the disease.

In differential diagnosis problems, immunohistochemistry is of great use, especially the CD31 or CD34 markers (membranous staining) and lately the HHV8, which has nuclear staining [16, 20, 22]. Molecular biology and genetic studies are of limited use and currently are limited to research purposes only.

Conclusions

Our case represents a rare occurrence of Kaposi sarcoma at a HIV-negative patient, which, after several local recurrences and progressive behavior, produced a lymph node involvement at the groin level. The immunohistochemical assessments have confirmed the diagnosis.
References


Corresponding author
Mihai Turcu, Associate Professor, MD, PhD, Department of Pathology, University of Medicine and Pharmacy of Târgu Mureș, 38 Gheorghe Marinescu Street, 540000 Târgu Mureș, Romania; Phone +40265–269 904, +40740–026 393, e-mail: mturcu@yahoo.com

Received: July 20th, 2010
Accepted: June 25th, 2011