RARE LARYNGEAL KAPOSÍ'S SARCOMA: CASE REPORT AND INNOVATIVE SURGICAL APPROACH

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ABSTRACT

Kaposi's sarcoma is an angioproliferative neoplasm that usually appears on the skin, but can also involve all organs and anatomic locations. The atypical manifestations of Kaposi's sarcoma can mislead the diagnosis, which can result in a poor case management. The authors present a HIV-negative patient with Kaposi's sarcoma with both usual and unusual locations such as the larynx, eyelids and bones. In the pre-therapeutic balance, we used NBI, which showed an intensely vascularized tumor in the larynx. The chosen method for treatment consisted in subtotal epiglottectomy performed under TransOral UltraSonic Surgery (TOUSS) approach. The use of TOUSS endoscopic surgery helped reduce the time of hospitalization, the patient did not need a nasogastric tube and was orally fed from the first postoperative day, with a better and faster functional recovery.

Keywords: Kaposi's sarcoma, TOUSS, NBI, larynx, endoscopic

Introduction

Kaposi's sarcoma (KS), was first described by the Hungarian dermatologist Moritz Kaposi in the late 1800s. It was first believed to be AIDS related, but in 1994, the newly discovered human herpesvirus-8 (HHV-8) was linked to every single case of KS and gained the alternate name Kaposi's sarcoma-associated herpesvirus (KSHV). Although a good functioning immune system of HHV-8 infected people can keep the virus at bay, in a weakened immune system, the HHV-8 can trigger the debut of KS (1). HHV-8 can be transmitted through saliva, organ transplantation and blood transfusion (2).

The epidemiological classification of Kaposi's sarcoma has four displays: the classic KS, the endemic or African KS, the iatrogenic KS and the AIDS-associated KS (epidemic).

The classic variant of KS has a typical appearance in elderly men, with a 15:1 male to female ratio. The main site of appearance is the skin of the lower extremities and the evolution can be described as indolent because the patients can live up to 10 years or more. The endemic form of KS, also named African KS, gain its reputation after a massive occurrence spike in central Africa in 1950s (3). This variant of the disease has a more aggressive evolution than the classic form and the skin is extensively infiltrated.

There are two divisions of this form. The African lymphadenopathic KS that occurs in children under 10 years and involves the lymph nodes and the African cutaneous KS that appear in men between 20 and 50 years with the characteristic appearance of infiltrative, nodular and vascular masses on the extremities (4). The iatrogenic form of KS was observed in immunosuppressed patients and organ transplant recipients. In the case of immunosuppression, the occurrence of KS disappears when the immunosuppressant is stopped (5). As in the case of organ transplant recipients, KS can appear due to the fact that the donor was infected in advance with HHV-8 or due to the reactivation of a latent HHV-8 in a post-transplant immunosuppressed state (6). In contrast to the classic form of KS, the locations of the lesions can be more variable (4). The AIDS-associated form (epidemic) was the one of the first diseases to be associated with HIV infected patients. The evolution has a rapid progression if the treatment is not administrated promptly. Highly active antiretroviral therapy (HAART) prevents and treats KS (7). This variant of KS can be present in mucocutaneous, lymph nodes and visceral organs (4).

Signs and symptoms

There are three clinical stages the Kaposi's sarcoma can be classified in: the patch stage represented by macular lesions, the next step in evolution is the plaque stage where macules develop into plaques and the final step is described as a nodular stage where the plaques evolve into a tumoral form (8,9). The KS lesions may appear as red, brown, purple or black papules. The typical site for these lesions is the skin with usual spread to the oral mucosa, gastrointestinal tract and lungs (10).

At skin level, the most common areas to be affected by KS are the lower limbs, frequently the soles of the feet, followed by the back, face and genitalia. The lesions can extend to the local lymphatic vessels and obstruct them, which will ultimately lead to lymphedema. In the oral cavity, the hard palate and the gums are the most frequent affected structures. Lesions at this level decrease the quality of life because they are prone to bleeding and infection, thus affecting alimentation (11). If the gastrointestinal tract is involved, the symptoms may vary from weight-

loss to hematemesis or hematochezia and even intestinal obstruction (12). The implication of the respiratory tract can show as dyspnea, hemoptysis or can be incidentally found on a chest x-ray. Biopsies can be taken by bronchoscopy. This lesion site has an unfavorable prognosis (13).

Kaposi's sarcoma lesions are known to appear in usual locations such as the skin, oral mucosa, lymph nodes (superficial and deep), lungs, endobronchial tract and pleura, gastrointestinal tract, external genitalia, oropharynx, tonsils, nasal cavity, liver, spleen, bone marrow. The unusual locations that can be the site of KS are represented by the bones and skeletal muscles, peripheral nerves, brain and spinal cord, larynx, eye and ear, major salivary glands, adrenal and thyroid gland, heart, thoracic duct, kidney, ureter and urinary bladder, breast, gonads, pancreas, wounds and blood clots.

There are less than 30 cases documented of KS of the larynx and the majority of the patients had had AIDS-related KS (9). The lesions may appear as purple vascular masses and are often accompanied by laryngeal edema. Dry secretion deposits may give a verrucous appearance to the lesions. Positive diagnosis is given by laryngoscopy with biopsy. A CT scan can help visualize the tumoral spread. The inferior eye lid, followed by the ocular annexes (nasolacrimal duct, conjunctiva), represents the predominant lesion site in ocular KS. Periorbital edema accompanies the tumoral growth. Mass lesions, according to the affected structures, can give symptoms such as epiphora, blood-flow sludging in the conjunctival sac. Only approximately 70 cases are reported with osseous KS. Ulcerated KS lesions of the skin or mucosa that erode to the adjacent bone represent the usual mechanism. The endemic (African) and the classical KS forms usually involve the peripheral skeleton whereas the AIDS-related KS involve the axial skeleton and the maxillofacial massif with a poorer prognosis. Some characteristics of osseous KS are the asymmetric bone implication and the osteolysis with cortical destruction. As for symptoms, bone pain, mobility limitations and spinal cord compression can be observed, but the lesions can be asymptomatic and only incidentally discovered. KS of the bone does not appear alone, but as a lesion accompanying other

localizations. Imaging investigations such as CT scan or MRI are superior, to the detriment of a classic x-ray. Biopsy is helpful for the differential diagnosis (9).

Pathology

The histopathological appearance of KS is characterized by the presence of spindle cells that are tumoral cells with an elongated shape. An abnormal display of the blood vessels that spread through the dermis and down to the subcutaneous tissue is also found. KS lesions display a slit-like intracytoplasmic aspect with numerous intratumoral vascular spaces that contain red blood cells. The mitotic activity is moderate as is the cytonuclear pleomorphism. A moderate chronic inflammatory infiltrate and macrophages are present (8).

Immunohistochemistry

KS tumoral cells show positive for the endothelial markers factor VIII-related antigen, CD34, CD31, VEGFR-3, LYVE-1 D2-40, Prox-1, and Bcl-2. In an advanced stage of KS, CD34 appear stronger than CD31. The most helpful method to differentiate KS from other similar lesions is the identification of a major latent nuclear antigen (LNA-1) in the HHV-8 genome (8,14).

Treatment

The treatment for the classic form of KS consists of radiation therapy with low doses of radiation on the affected areas of the skin. Low-voltage photon radiation (100kv) can be used with 8Gy to 10Gy administered as a single dose or 15Gy to 20Gy administered in one week. With electron-beam radiation therapy (EBRT), 4Gy are administered once per week for 6-8 weeks with a 4-MeV to 6-MeV electron beam. Minor excision surgery can also be used, but the rates of reoccurrence are increased (15). Chemotherapy is used when more than 30 lesions are present. Vinblastine administered once a week gave an excellent response. Local injections with vincristine can be used and often, the treated lesions disappear completely (16). Skin electroporation in combination with bleomycin administered intravenous with a great response. In most cases, lesions have shown a response after the first dose (17). In the African (endemic) variant of KS, besides radiotherapy with 20Gy doses and chemotherapy, HAART is

used, along with prophylactic treatment of the opportunistic infections (18). Surgical excisions, cryotherapy, electrodesiccation and curettage can also be used in treating the lesions (15). In iatrogenic KS, reducing the dose or changing the immunosuppressants can lead to KS regression. If not, radiotherapy and chemotherapy can be used (19). For the AIDS-related form, HAART is the principal method of treatment by preventing the multiplication of HIV and allowing the immune system to fight against HHV-8. In some cases, chemotherapy and interferon therapy may be needed (20). Treating the KS lesions with any of these methods does not ensure a full recovery because they can reappear, especially in the untreated areas. In these cases, is indicated to repeat the treatment (1).

Case report

A 67-year-old male patient, diagnosed in 2017 with Kaposi's sarcoma, known with hypertension, hypertensive retinopathy and hepatic steatosis, presented in the ENT Clinic of Colțea Clinical Hospital with an approximately 1-month history of dysphagia and odynophagia. The patient was admitted in the hospital for specialized investigations and treatment.

From the personal pathological background it is to mention that in April 2017 the patient was admitted in the hospital for a tumoral mass on the left inferior eyelid. It was removed via surgical excision and sent to histopathological and immunohistochemistry examination. The microscopic aspect was compatible with Kaposi's sarcoma in the nodular stage. The immunohistochemical tests were positive for HHV-8, CD34 and SMA. Two months later, in June 2017, the patient presented to the emergency department with a 4-day history of paresthesias in the left limbs. The neurological examination revealed left palpebral ptosis and left central facial paresis, superficial tactile sensitivity disorder on the left side of the body, left hemiparesis 3+/5 BMRC brachial and 4-/5 BMRC crural, Romberg maneuver with minimal unsystematic oscillations. The cerebral CT scan only revealed minimal cerebral atrophy. The Doppler cerebrovascular examination revealed minor right carotid atheromatosis. All results

were compatible with an acute ischemic lacunar stroke. In January 2018, the patient was admitted in a dermatovenerology clinic for an ulcerated tumoral mass with hematic crusts on top, located on the dorsal side of the left hand for which surgical excision was performed. The piece was sent for histopathological examination that concluded the same KS diagnosis. The patient also had multiple angiomatous masses in the scrotal area for which electrodesiccation was performed. Later that year, in July, the patient was admitted again in the same hospital for the apparition of new angiomatous masses in the scrotal area, hands, eyelids and anterior thorax. Some lesions were covered with hematic crusts. Electrodesiccation under local anesthesia was performed. In August 2018, the patient was tested for HIV infection, but the result turned back negative. In the same month, one day later, the patient was once again admitted to the dermatovenerology department for new angiomatous lesions in the scrotal area, hands and eyelids for which electrodesiccation under local anesthesia was performed. From 20th of August to 21st of September 2018, the patient was admitted in the radiotherapy department in order to start the radiation therapy sessions. It was administered a total dose of 40Gy/target volume (1.6Gy/fraction, 25 fractions, 5 fractions per week). The treatment was discontinued following the discovery of similar lesions in the larynx.

At presentation, ENT physical examination revealed, at the endoscopic larynx examination an oval vegetative tumoral mass situated on the right half of the epiglottis, which measured approximately 1cm in diameter, with a violaceous coloration and irregular margins. At the Narrow Band Imaging (NBI) examination was observed a rich vascularization at the level of the tumoral mass and at its implantation base (Figure 1).

Figure 1. A: Oval vegetative tumoral mass situated on the right half of the epiglottis. B: NBI visualization that shows the rich vascularized tumoral mass

At the general clinical examination, multiple angiomatous lesions were observed on the anterior thorax, on the conjunctiva of the left eye (Figure 2), on the inferior limbs and on the soles of the feet. Congenital palpebral ptosis and facial asymmetry were also observed.

Figure 2. A: multiple angiomatous lesions on the anterior thorax. B: singular angiomatous lesion on the conjunctiva and hyperemia

At the routine blood tests, a mild inflammatory syndrome was present. The patient was once again tested for HIV infection and, in addition, for hepatitis B and C, all which came back negative. At the chest x-ray examination, it was observed, a sclerotic bone lesion located on the third anterior right costal arch, of about 1.5/0.7cm and well limited. Bilateral basal interstitial fibrosis of the lungs and right anterior mediastinal pahipleuritis were also present.

The oncology committee opted for the surgical treatment. The patient was informed about the therapy options and surgical benefits and risks were explained. The informed consent was signed by the patient. An endoscopic method was used. The chosen method for subtotal epiglottectomy was under TransOral UltraSonic Surgery (TOUSS) approach. Under general anesthesia and orotracheal intubation, with the patient in supine position, the anatomical mouth retractor (FK-WO TORS Laryngo-Pharyngoscope Retractor) was mounted and to create space, the anterior retractor was placed at the base of the tongue. The pharyngolaryngeal transoral approach was performed. Under endoscopic control, with the aid of the Thunderbeat instrument, subtotal epiglottectomy was performed (Figure 3) with integrated hemostasis control. The excised tumoral mass was sent for histopathological examination (Figure 4). The result of the histopathological examination concluded an epiglottic fragment showing tumoral proliferation consisting in numerous spindle cells arranged in fascicles, with

moderate nuclear pleomorphism, relatively rare mitosis and numerous vascular spaces containing red blood cells, suggestive for KS that invades the epiglottal cartilage.

Figure 3. Intraoperative findings (A) and use of the Thunderbeat instrument (B and C)

Figure 4. The tumoral mass after excision

The post-operative evolution under antibiotic, analgesic and anti-inflammatory treatment was favorable (Figure 5) and the patient was discharged as cured.

Figure 5. Endoscopic larynx examination post subtotal epiglottectomy status under TOUSS approach

At the controls that followed, the local evolution proved to be favorable and without over-added morphopathological changes.

Discussions

KS is not considered to be a true sarcoma, despite its name, which is a tumor arising from the mesenchymal tissue. Its histogenesis remains controversial. KS arises as a cancer of the lymphatic endothelium and forms vascular channels that are filled with blood cells, giving the tumor its characteristic bruise-like appearance. HHV-8 proteins are uniformly detected in the KS cells (21).

The rarity of KS reports in uncommon regions may be due to underreporting, asymptomatic lesions and underrecognition of signs by health care providers. Laryngeal involvement is somewhat of an infrequent manifestation.

For the patient presented by us, the laryngeal localization was not necessarily a surprise because the patient already had many other lesions in other locations for which he had received treatment (the patient was already diagnosed) so the suspicion of KS was quite high. In the pre-therapeutic balance, we also used NBI, which showed an intensely vascularized tumor that reinforced the suspicion of diagnosis. NBI is an optical imaging technology that enhances the visibility of vessels and other tissue on the mucosal surface. NBI works by filtering the white light into specific light wavelengths that are absorbed by hemoglobin and penetrate only the surface of human tissue. As a result, with NBI, capillaries on the mucosal surface are displayed in brown and veins in the submucosa are displayed in cyan on the monitor. NBI represents a conceptual revolution in the “biologic endoscopy” field because its main focus is not on evaluation of the neoplasm itself, but on its vascularization and allows visualization of the lesions that are not otherwise visible to obtain a so-called “optical biopsy”. It is addressing the neo-angiogenic patterns inside and surrounding a target lesion, with a significant reduction in the number of false positives. NBI is not used to replace histopathological sampling as a means of diagnosis (22).

The treatment options for KS include local therapy (surgical excision, cryotherapy, and electrocoagulation), radiation therapy,

chemotherapy and immunotherapy. People with suppressed immune system due to medication can manage KS by switching or decreasing their drug regimen. Antiretroviral therapy is a combination of anti-HIV drugs that make treatment for KS more effective. It can be used in combination with chemotherapy and it increases its effectiveness.

In the case of the presented patient, following the decision of the oncology committee, we used surgery as a treatment. Biopsy of such vascular laryngeal lesion has been associated with brisk and potentially fatal bleeding. We used TOUSS, which is a minimally invasive, endoscopic approach for benign and malignant lesions in the upper aerodigestive tract. Thunderbeat is an instrument that incorporates both ultrasound and bipolar energy in one device, thus allowing the fast and effective dissection plus safe and reliable hemostasis at the same time. Using this device, we had an optimal view of the lesion through magnification and high definition. So, the lesion was resected via transoral and minimally invasive approach. KS is a bleeding tumor, but, using ultrasound, the resection was non-bleeding. The operation was strictly at the level of the lesion and its surgical safety margins.

Conclusions

KS is not curable, but it can often be treatable for many years. In establishing the therapeutic plan of a patient with KS, we must consider the complexity of the disease and we must take into account the efficacy of treatment, the side effects of therapy, life expectancy and the quality of life. The use of TOUSS endoscopic surgery helped reduce the time of hospitalization, the patient did not need a nasogastric tube and was orally fed from the first postoperative day, with a better and faster functional recovery. The tumor was ablated with its surgical safety margins.

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Conflict of interest

The authors declare that there is no conflict of interest.

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