Kaposi’s Sarcoma after Repeated Surgical Procedures in an Immunocompetent Patient: The Lymphatic Hypothesis


Departments of Dermatology and Radiology, Geneva University Hospital, and Department of Cellular Physiology and Metabolism, Anatomy Sector, University of Geneva, Geneva, Switzerland

Abstract

A 63-year-old Swiss patient developed acquired nodules on his right palm after 3 localized surgeries, called ‘needle fasciotomy’, for Dupuytren’s disease. Kaposi’s sarcoma (KS) was diagnosed in a biopsy of a nodule. A positive immunolabeling and serology for human herpesvirus 8 has been found, but human immunodeficiency virus and hepatitis C identification remained negative. The nodules were limited to the surgically traumatized area. This first report of a nonimmunocompromised patient developing a KS after repeated surgeries in a unique peculiar localized area with a dense lymphatic network sustains the hypothesis that tissue alterations involving the lymphatic system could play a central role in the occurrence of KS.

Case Report

A 63-year-old Swiss male patient is known for Dupuytren’s disease, a fixed flexion contracture of the middle palmar aponeurosis due to a fibroblastic proliferation that leads to a progressive flexion of the fingers and a disability to extend them [7]. He underwent a surgical procedure, the so-called needle fasciotomy, a minimally invasive surgical procedure that is performed under locoregional anesthesia [8]. With a sharp subcision needle, the fibrotic tissue was cut in a plane just above the fascia of the tendons (fig. 1). Afterwards, the treated finger was put in extension for a period of 48 h. This treatment was repeated 2 more times at a 6-month interval. After the third session, the patient developed a red, painless lesion on his right palm. Later on, some new similar lesions appeared close to the first one. Physical examination revealed fixed red pap-
Fig. 1. a Anatomy of the palm. b Palmar lymphatic drainage.

Fig. 2. Red papules on the right hypothenar eminence. Evolution from 2006 to 2010.

Fig. 3. a Dermal cellular infiltrate surrounding vascular spaces of irregular shape. b Proliferation of spindle cells, admixed inflammatory cells and extravasated erythrocytes. c Spindle cells positive for HHV-8.
ules of 3–8 mm diameter localized on the patient’s right hypothenar process (fig. 2). The patient had no debilitating disease, did not take any drugs and had no allergies. After 2 years, the nodules had slowly increased in size and the clinical diagnosis of KS was confirmed by a histological examination. The specimen was characterized by the presence of slit-like vascular channels and the proliferation of atypical spindle cells (fig. 3a). The immunohistochemical study demonstrated the presence of spindle-shaped cells positive for CD34. A strong D2-40 immunolabeling, involving a monoclonal antibody used for the identification of lymphatic endothelium [9], was observed, putting in evidence the existence of lymphatic vessels in the lesion (fig. 3b). There was an HHV-8-positive serology and the virus was also detected on histological sections by a positive immunolabeling (fig. 3c). HIV and hepatitis C serologies were negative several times. The patient did not present any clinical or biological sign of immunodepression.

Five years later, the lesions remained localized to the right palm with a moderate increase in volume. No KS lesions occurred at other anatomical locations. A local treatment with imiquimod (3 times per week) was effectuated for 1 month, without any modification. Until now, no other treatment has been performed.

Discussion

As far as we know, this is the first reported case of an immunocompetent patient who develops a KS after a localized surgical trauma. Our patient underwent an interventional procedure on his right palm, in which a subcutaneous section of fibrotic tissues on a plane above the fascia of the tendons had been performed. We suppose that this traumatic procedure, repeated 3 times at a very limited and defined location, and furthermore in a very peculiar area, led to modifications of the local lymphatic circulation in his right palm. The 18-month delay between the first surgery and the occurrence of KS suggests that the probable link between these 2 events is a progressive change in lymphatic circulation and probably not the posttraumatic inflammation and the repair process with the diffusion of factors that stimulate angiogenesis. However, posttraumatic inflammation seems to contribute to the development of this tumor as well. In particular, macrophages participating in wound healing produce growth and angiogenic factors that may recruit HHV-8 to the tissues. Furthermore, the nodules were located in the mid-dermis, far from the plane affected by the fasciotomy, again suggesting that the tissue modification – and not direct molecular changes or various soluble factors – was responsible for the occurrence of KS.

Lymphatic differentiation has a central role in KS development [2]. Perturbation of lymphatic drainage could be involved in the pathogenesis of this tumor as lymphatic stasis causes local cellular immune dysfunction and lymphocytic traffic and stimulates lymphangiogenesis and angiogenesis [10]. As it is known, the skin lymphatic network can be classified into superficial and deep. The superficial skin plexus is avascular and hypodermal. The deep lymphatic network is situated on the suprafascial layer of the skin. However, numerous anastomoses between these 2 systems have been described [11]. The traumatic procedure our patient went through might have affected the lymphatic vessels of this area as the subcision needle passed over the fascia of the tendons. However, MRI did not show any anomaly on the plane of the bone or tendons, except for a fibrosis of the palmar fascia probably due to previous interventions for Dupuytren’s disease (fig. 4).

Trauma-induced KS has already been described in HIV-positive patients [3, 4]. The mechanism proposed is related to the possible inflammatory, trauma-induced changes that may recruit HHV-8 to the site. This rhadinovirus infects both lymphatic and blood vascular endothelial cells in vitro [2]. It encodes proteins similar to human oncoproteins which modify cell proliferation and apoptosis [12]. Latent HHV-8 products induce tumor hyperplasia and spindle cell proliferation. The lytic cycle is induced when latently HHV-8 infected cells are exposed to inflammatory cytokines such as interferon-γ, interleukin-1β and tumor necrosis factor-α. The lytic gene products promote tumor development and induce angiogenesis even via paracrine mechanisms [13].

As HHV-8 was detected in our patient’s serum and on histological sections, we made the hypothesis that the trauma-induced changes of the local lymphatic circulation and the secretion of angiogenic molecules have both contributed to the development of KS under the influence of virus activation. A direct viral inoculation during the needle fasciotomy seems very unlikely as the procedure was performed by a specialist in a French medical center.

This case supports the hypothesis that lymphostasis and/or lymphangiogenesis could play a central role in the occurrence of KS, at least in immunocompetent patients. Indeed, in this form, skin lesions usually appear on the lower extremities and lymphedema is almost always present at the time of diagnosis. Whether the lymphedema precedes or progresses from KS remains unsolved [14, 15].
References


