CASE REPORT

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Unilateral presentation of pseudo-Kaposi's acroangiodermatitis – a diagnostic and therapeutic challenge

Jednostrana prezentacija pseudo-Kaposijevog akroangiodermatitisa – dijagnostički i terapijski izazov

Georgi Tchernev*, James W. Patterson†, Julian Ananiev‡, Michael Tronnier§

***Polyclinic of Dermatology and Venerology, University Hospital Lozenetz, Medical Faculty, Saint Kliment Ohridski University, Sofia, Bulgaria; †Division of Surgical Pathology and Cytopathology, University of Virginia Hospital, Charlottesville, VA, USA; ‡Department of General and Clinical Pathology, Medical Faculty, Trakian University, Stara Zagora, Bulgaria, §Department of Dermatology and Venerology, Klinikum Hildesheim GmbH, Hildesheim, Germany**

Abstract

Introduction. Acroangiodermatitis is a rare skin disease characterised by hyperplasia of pre-existing vasculature due to venous hypertension from severe chronic venous stasis. Clinical appearance of this condition is often similar to Kaposi sarcoma and is creating serious differential diagnostic difficulties. **Case report.** A patient with acroangiodermatitis was presented and the differential diagnosis discussed. Examination of the patella of the affected area showed grayish-blue to brown infiltrates and reduced elasticity, located in the supra- and infrapatellar regions. Clinically, Kaposi's sarcoma was suspected. Histopathologically there were acanthosis and compact hyperkeratosis. The underlying papillary dermis showed fibrosis and edema. A subepidermal lobular vascular proliferation with hemosiderin deposition was also noted. This consisted of multiple newly formed capillaries, featuring small blood vessels with dilated, rounded lumina. Serologies for HIV and *Borrelia burgdorferi* were negative, as was a HHV-8 PCR in lesional tissue. Doppler analysis of the vessels of the extremities showed chronic venous insufficiency, insufficiency of *v. perforantes*, insufficiency of the Cockett II-III. No deep thromboses in the area of the shank and thigh were found. Initially, treatment consisted of clindamycin 600 mg 3 times per day, intravenously, during a 2-week period. After that the treatment was continued with prednisolone, 30 mg daily in combination with furosemide 40 mg/day, as well as lymph drainage and adequate compression therapy. The consequent clinical improvement allowed the patient to be discharged from the clinic. **Conclusion.** The most important differential diagnostic marker in distinguishing between acroangiodermatitis and Kaposi sarcoma seems to be the confirmation of the presence of genetic material of HHV-8 in the affected skin areas in patients with Kaposi sarcoma.

Key words:
acrodermatitis; skin diseases, vascular; venous insufficiency; diagnosis; diagnosis differential; drug therapy; treatment outcome.

Apstrakt

Uvod. Akroangiodermatitis spada u retko oboljenje kože koje karakteriše hiperplazija već postojeće vaskulature zbog venske hipertenzije usled ozbiljne venske staze. Klinička slika ove bolesti često ima sličnosti sa Kaposijevim sarkomom čime ozbiljno otežava diferencijalno dijagnostikovanje. **Prikaz bolesnika.** Prikazan je bolesnik sa akroangiodermatitisom uz komentar diferencijalne dijagnoze. Pregled kolena u zahvaćenom delu pokazao je sivoplave do braon infiltrate i smanjenu elastičnost u supra- i infrapatelarnim delovima. Klinički, sumnjalo se u Kaposijev sarkom. Patohistološki, nađena je akantoza i kompaktna hiperkeratoza. Papilarni dermis imao je znake fibroze i edema. Takođe, primećena je potkožna lobularna vaskularna proliferacija sa depozitom hemosiderina. Ona se sastojala iz brojnih novoformiranih kapilara, sitnih krvnih sudova proširenog, kružnog lumena. Serologija na HIV i *Borrelia burgdorferi* bila je negativna, kao i HHV-8 PCR za obolelo tkivo. Dopler krvnih sudova ekstremiteta pokazao je hroničnu insuficijenciju vena, insuficijenciju perforantnih vena i insufijenciju Cocket II-III. Nije nađena duboka tromboza u zoni potkolenice i butine. Početno lečenje baziralo se na primeni klindamicina 600 mg, tri puta dnevno, intravenozno, tokom perioda od dve nedelje. Lečenje je, zatim, nastavljeno prednisolonom 30 mg dnevno, u kombinaciji sa furosemidom 40 mg dnevno, kao i drenažom limfe i odgovarajućom kompresijom. Nastalo kliničko poboljšanje omogućilo je otpuštanje bolesnika iz bolnice. **Zaključak.** Najvažniji marker diferencijalne dijagnoze za razlikovanje akroangiodermatitisa od Kaposijevog sarkoma jeste potvrda postojanja genetskog materijala HHV-8 u zahvaćenim zonama sa Kaposijevim sarkomom.

Ključne reči:
akrodermatitis; koža, vaskularne bolesti; venska insuficijencija; dijagnoza, dijanoza diferencijalna; lečenje lekovima; lečenje, ishod.

Correspondence to: Georgi Tchernev, Polyclinic of Dermatology and Venerology, University Hospital Lezenetz Saint Kliment Ohridski University, Medical Faculty, Sofia, Bulgaria. Phone.: 00359 885 588 424. E-mail: gtchernev@yahoo.de

Introduction

Acroangiodermatitis, also called pseudo-Kaposi's sarcoma or Morbus Mali (M. Mali), is a disease that can simulate true Kaposi's sarcoma, both clinico-morphologically and histologically. Histological findings include vascular proliferations that are most frequently localized in the upper dermis with no infiltrative features [1]. Bilateral lesions are usually associated with chronic venous insufficiency, whereas unilateral lesions suggest an underlying vascular malformation. Acroangiodermatitis is a hyperplasia of pre-existing vasculature, as opposed to Kaposi's sarcoma, in which vascular proliferation is independent of the existing vessels [2] .

The concept of "acroangiodermatitis" is described in the literature in two forms: M. Mali, clinically manifested by skin alterations on the lower extremities in middle-aged to elderly patients with chronic venous insufficiency [3], and unilaterally manifested pseudo-Kaposi's sarcoma in young patients with congenital arteriovenous anastomoses of the inferior extremities, such as occurs in the Klippel-Trenaunay syndrome [4].

In addition, single reports in the literature describe the appearance of M. Mali in patients with amputated or paralyzed extremities, as well as in iatrogenically caused arteriovenous shunts (for example, in patients on hemodialysis) [5–7]. It was also thought to be secondary to a chronic trauma to some areas due to a prolonged stance in bed in the emergency room, for example [8].

Case report

A 56-year-old patient, German sailor, complained of recurring erysipelas and phlegmon in the area of the knee joint of the left leg since childhood. After adequate antibiotic therapy, the skin alterations always used to heal without any complications. Before coming to the hospital he ran a high temperature and felt heat and pain in the area of the knee joint. His general condition grew worse, so he was hospitalized.

Examination of the patella showed grayish-blue to brown infiltrates and reduced elasticity, located in the supra- and infrapatellar regions (Fig. 1a). Clinically, Kaposi's sarcoma was suspected.

Histopathologically, there were acanthosis and compact hyperkeratosis. The underlying papillary dermis showed fibrosis and edema. A subepidermal lobular vascular proliferation with hemosiderin deposition was noted. This consisted of multiple newly formed capillaries, featuring small blood vessels with dilated, rounded lumina (Fig 1b). The surrounding connective tissue featured erythrocyte extravasation and a perivascular lymphocytic infiltrate. Abnormal laboratory values included: ESR 10/16 mm, haemoglobin 13.8 g/L, antistreptolysin titre 706 E, blood sugar 6.4 mmol/L, CRP 7.8. Serologies for HIV and *Borrelia burgdorferi* were negative, as was herpes virus 8 (HHV-8) PCR in lesional tissue.

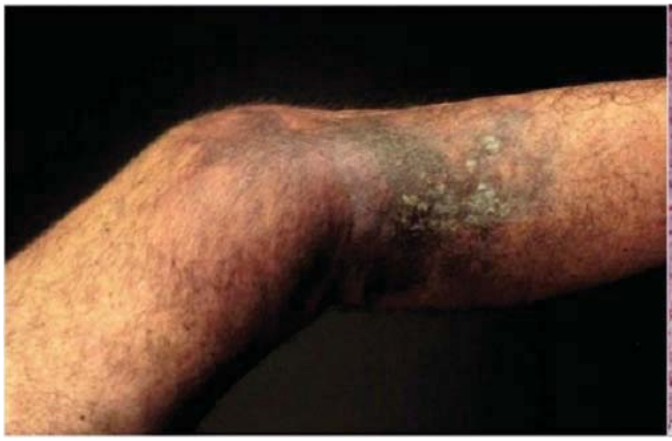

Fig. 1a – Clinical presentation of a patient with pseudo-Kaposi's acroangidermatitis

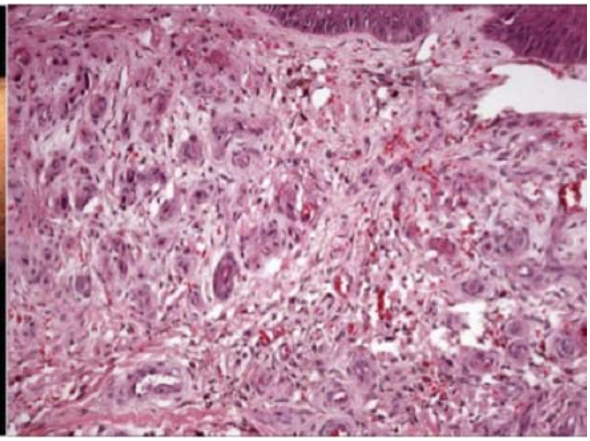

Fig. 1b – Histopathology of pseudo-Kaposi form of acroangiodermatitis with proliferative small vessels, fibrosis with some spindled cells, and hemosiderin deposition

Doppler analysis of the vessels of the extremities showed chronic venous insufficiency, insufficiency of v. perforantes, insufficiency of the Cockett II-III. No deep thromboses in the area of the shank and thigh.

Initially, the treatment consisted of clindamycin 600 mg, 3 times per day, intravenously, during a 2-week period. Due to the consequent slight improvement and to the suspicion of an inflammatory process, Kaposi's sarcoma was excluded and the diagnosis of pseudo Kaposi's acroangiodermatitis or M. Mali, complicated by erysipelas, was made. Due to severe aching and a sense of stress in the knee joint area, the treatment was initiated with prednisolone, 30 mg daily in combination with furosemide 40 mg/day, as well as lymph drainage. The consequent clinical improvement allowed the patient to be discharged from the clinic. Adequate compressions therapy was performed several weeks after the hospitalization.

Discussion

The differential diagnosis between Kaposi's sarcoma and the so-called pseudo-Kaposi's sarcoma or acroangiodermatitis of the feet is often fraught with difficulty, not only

on clinical but also on histological grounds [1]. However, considering clinical picture, histological and immunohistological findings, and also data from biomolecular analyses and electron microscopy, a clear and certain differentiation between these two diseases can be made [1, 3, 4].

In the early stages of Kaposi's sarcoma, the histological differential diagnosis may be difficult, if not impossible, since cellular atypism is not observed [1]. The histological picture includes proliferation of the vessels in the superior part of the corium and a nonspecific lymphomononuclear perivascular infiltrate. Histological picture in acroangiodermatitis may be similar. In more advanced, tumorous stages of Kaposi's sarcoma, cellular atypia becomes apparent and allows differentiation between Mali's acroangiodermatitis and true Kaposi's sarcoma. At this stage, main alterations affect the structures of the vascular wall and the endothelium [1].

In the case of acroangiodermatitis, a new formation of small, oval vessels arises and the vascular wall is thickened. In the case of Kaposi's sarcoma, lumina of the vessels are irregularly configured, and their walls are reinforced by thin endothelial cells with oval nuclei [1, 3]. The vascular formations in M. Mali are located, as a rule, at the superior part of the dermis. The Stewart-Bluefarb syndrome is an exception, because then the proliferating vessels cover the whole dermis. Kaposi's sarcoma is characterized by the generation of new vascular formations around the normal vessels. This provokes a wrong impression of newly formed or secondarily inserted normal structures in the area of the pathologic vessels [1, 3].

In both Kaposis sarcoma and M. Mali there are spindle-shaped cells, histogenetically related to fibroblasts. They predominate in the advanced stages of Kaposi's sarcoma. Augmentation of the aforesaid cells in M. Mali arises in connection with the fibrosis induced by stasis, and quantitatively they are much fewer in the number than the spindle-shaped cells in Kaposi's sarcoma. In Kaposi's sarcoma, they tend to form oblong cavernous formations, partially filled by erythrocytes. The phagocytosis of erythrocytes by the spindle-shaped cells is not characteristic for M. Mali, in contrast to Kaposi's sarcoma. Cellular atypism is observed at the late Kaposi's sarcoma stages. In spite of these morphological differences, it can be difficult to differentiate these diseases on histologic grounds alone, especially when Kaposi's sarcoma is in its early stages [9].

Immunohistological and biomolecular analyses are extraordinarily important in making the correct diagnosis. In the classic HIV-associated Kaposi's sarcoma, an expression of CD-34 antigen is observed, not only in the endothelial cells, but also in the surrounding spindle-shaped cells. The spindle-shaped cells in acroangiodermatitis are negative with respect to the CD-34 antigen [1, 10].

MS-1 high molecular weight protein (MS1-HMWP) and RM 3/1 are superficial antigens of activated macrophages. They are found not only in cases of acroangiodermatitis, but also in classic and HIV-induced Kaposi's sarcoma. It has been proved that these macrophages possess a strongly expressed angiogenic activity. But as they are observed in both diseases, they cannot be used as a differential diagnostic marker [1].

Confirmation of the presence of genetic material of HHV-8 in skin lesions of patients with Kaposi sarcoma provides the most definitive confirmation of the diagnosis [1]. HHV-8 has been found in all the forms of Kaposi's sarcoma. The lack of HHV-8 in pseudo-Kaposi's acroangiodermatitis, as was the case in our patient, demonstrates that the determination of HHV-8 by PCR is the most important and certain marker in elucidating the etiology of skin lesions when the differential diagnosis is focused on these two entities. Ideally, however, the diagnosis should be supported by histological and immunohistological analyses, if possible at all [1, 10].

Conclusion

The pathogenesis of Mali's acroangiodermatitis is not yet clear, nor are the roles of the activated macrophages in M. Mali and in Kaposi's sarcoma or the reasons for their activation. It is supposed that the increased vascular pressure in chronic venous insufficiency is capable of inducing vascular proliferation.

Important differential diagnostic markers in distinguishing between acroangiodermatitis and Kaposi's sarcoma are:

1. Confirmation of the presence of genetic material of HHV-8 (PCR – HHV or Immunhistological methods) in the affected skin areas in patients with Kaposi's sarcoma.

2. Confirmation of the presence of CD-34 antigen in the interstitial spindle-shaped cells in any form of Kaposi's sarcoma and its absence in patients with M. Mali. Immunolabelling for the CD34 antigen appears to be a valuable tool in the differential diagnosis between Kaposi's sarcoma and pseudo-Kaposi's sarcoma (interstitial cells).

3. In differentiating the two diseases, classic histological analysis and the clinic image also play some role, but are less definitive than the aforementioned methods.

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