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IATROGENICALLY INDUCED SARKOMA KAPOSI IN A PATIENT WITH PEMPHIGUS VULGARIS

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RESUME:

This is a case of iatrogenically induced Sarkoma Kaposi in a 68-year-old patient suffering from Pemphigus vulgaris. The Pemphigus in question is mucous, localized in the mouth cavity, and two years old.

In the course of treatment with parenterally applied corticosteroid products was observed the appearance and dynamic spread of numerous tumor-like formations of Kaposi Sarcoma type on the limbs, torso and face.

The appearance of Kaposi sarcoma as a result of the continuous immunosuppressive therapy with corticosteroids and cytostatics is discussed.

Key words: iatrogenic, Kaposi's sarcoma

Sarcoma Kaposi is a vascular neoplasm, described for the first time in 1972 by Kaposi as multiple benign pigment idiopathic hemorrhagic sarcoma. Later Piette distinguished five types of the malady: classical Kaposi Sarcoma (KS), African skin type KS, African adenopathic type KS, KS in immunosuppressed individuals in combination with AIDS, KS in immunosuppressed individuals in combination with lymphomas or chemotherapy.

Since 1981 more frequent have become the reports of KS, developed on the basis of acquired immune deficiency with AIDS and HIV positive individuals (5, 6, 18, 33). The cases of iatrogenically induced KS described in literature are mainly of patients with organ transplantation (9, 15, 28) and long-term immunosuppressive therapy (15, 16, 20, 28) applied to autoimmune diseases, lymphoproliferative and other non-immune diseases. Cases of KS are described, developed after immunosuppressive therapy of bronchial asthma (7), of multiple myeloma (22), of dermatomyositis (37), temporal angiitis (21, 32), of erythematosus (16), of hemolytic anemia (38), of rheumatoid arthritis (2, 3, 4, 31), of pericarditis(29).

Comparatively few are the reported cases of KS after a lengthy therapy with corticosteroids and immunosuppresants for treatment of Pemphigus vulgaris (1, 12, 14, 27) and Pemphigoid (23, 30).

Most authors in these cases suggest genetic predisposition of the individual to the development of KS, provoked by lengthy corticosteroid therapy (3, 29, 34, 35, 36) etc. More recent research points out a theory of virus genesis of KS (13, 15, 25). The assumption that Herpes-virus 8 has a pathogenic role for the development of KS is confirmed. Some authors refer this claim mainly to the classical type of the disease (15, 25), and others – to all its forms(13).

DESCRIPTION OF THE CASE:

The patient is a 68-year-old man who was subjected to corticosteroid therapy for two years because of diagnosed autoimmune disease – Pemphigus vulgaris (mucous form) – clinically expressed with bullous – erosive changes of the hard and soft palate, the buccal mucosa, sublingually and histologically proven. The initial dose of corticosteroid (Methylprednisolon) was 120 mg, injected because of stomach ulcer. A week later the daily dose was gradually reduced with 10 mg at an interval of 10 -12 days until a sustaining daily dose of 16 mg corticosteroid was reached.

A year after the initiation of the corticosteroid treatment during the sustaining therapy of 16 mg Methylprednisolon - im, was observed the appearance of single nodulous lesions of bluish – brownish color and the size of a pea on the distal surfaces of the upper limbs, which underwent regressive development to hyperpigmented maculas after the daily supporting dose of corticosteroid was reduced to 8 mg (im) within 8 months. Consequently a recurrence of the bullous – erosive pemphigus rash in the mouth cavity required the increase of the daily corticosteroids to 80 mg with subsequent gradual reduction to 16 mg within three months. During this period the appearance and dynamic progressive development and spread of numerous tumorlike formations of the Kaposi Sarcoma type on the upper and consequently on the lower limbs, the torso and the face was observed. Some of them were the size of a child's fist and required surgery. No regressive development of the tumorlike formations was observed after reaching the supporting dose corticosteroid, applied im. During the initial treatment and the relapse of pemphigus lesions simultaneously with the corticosteroid Imuran was also applied with initial daily dosage of 3X1 tablet and gradual decrease, for 2 months (Fig. 1, Fig. 2 Fig. 3).

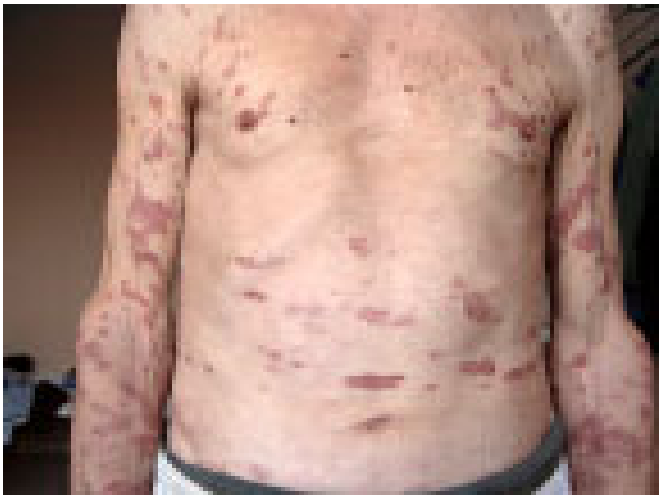

Figure 1.

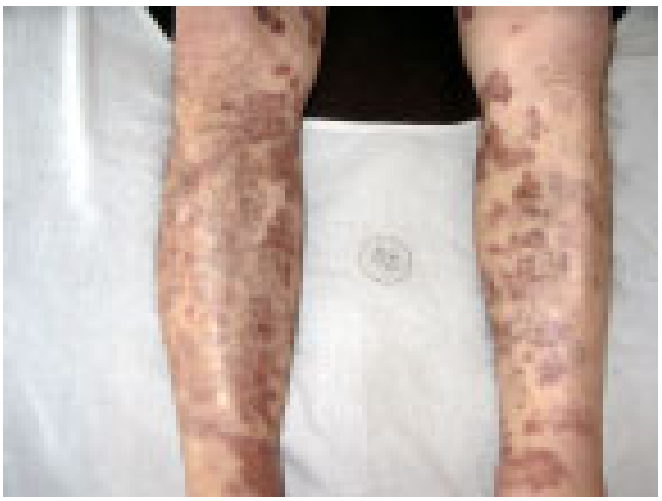

Figure 2.

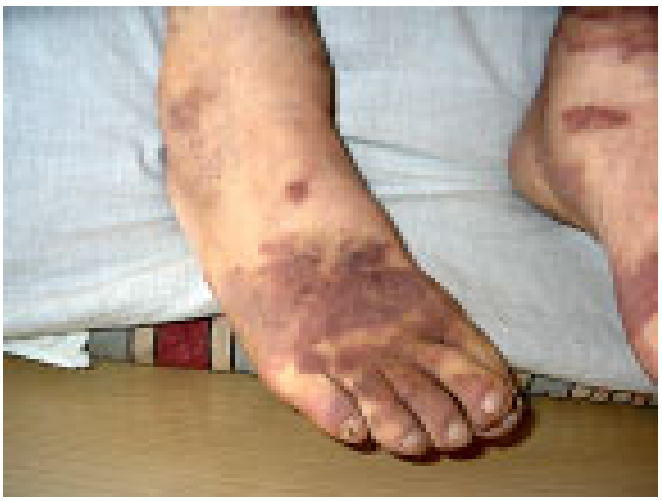

Figure 3.

The patient had no history of homosexual contacts or venous application of medicaments. No lymphadenopathy was found or lung symptoms. The serologic tests for lues, hepatitis A and B were negative, as was the blood analysis for HIV.

The biopsy sample from the knotty lesion on the hand showed the histological picture of KS: vessel proliferation in the papillar and upper reticular derma, with many endothelial cells and isthmuses spindle cells with vascular leaks. Extravasal erythrocytes and hemosiderin were found; chronic lymphocyte inflammatory infiltrate. (Fig. 4).

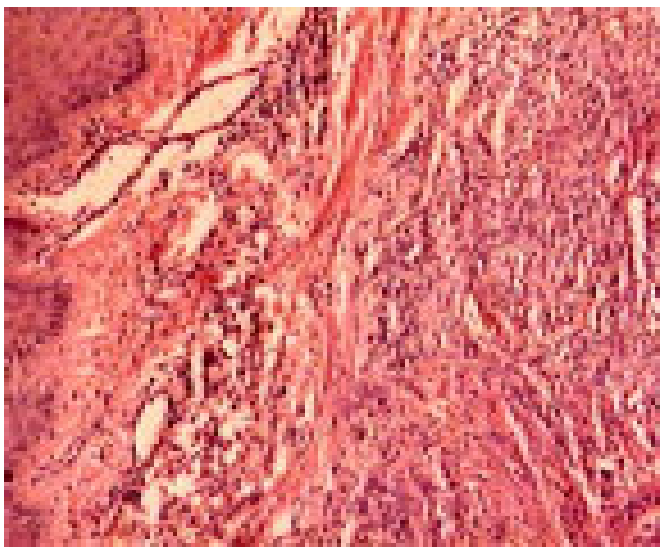

Figure 4.

During the first months of the development of the Kaposi type lesions, because of their asymptomatic development, they were not treated. Consequently the rapid increase of the number of tumorlike formations, the considerable size of some of them, as well as the impossibility of stopping the corticosteroid for a long time, chemiotherapeutic immunosuppressive therapy had to be applied and partial surgical treatment of the big tumor formations.

The tests for visceral localization of KS were negative.

DISCUSSION:

Taking into account the sequence of the pathological processes - first, pemphigus lesions, then, a year after the corticosteroid therapy, the appearance of tumorlike lesions of KS type with fast dynamic progression upon corticosteroid dosage increase - the causative link between KS and immunosuppressive therapy can be discussed. In this case the lengthy corticosteroid treatment led to the development of KS which clinically is not different from the classical type of the disease.

The initial lesions were noticed (as is reported in lit-

erature data) originally on the upper and lower limbs. A few authors report initial tumor changes on the torso (35), and even fewer authors – their visceral localization (19, 36).

The way of application and probably also the duration of the high dosage of the corticosteroid seem to have had certain influence on the period during which the initial lesions appeared. In the described case the patient developed KS a year after the beginning of the corticosteroid treatment, which was im. Similar cases are reported, in which KS is developed after a lenthy peroral corticosteroid therapy (2, 19), and others - in which KS is developed after a short one, but the corticosteroids are applied either ia (36) or intradurally (35).

The interval between the beginning of the corticosteroid therapy and the appearance of KS is different, from 22 days to several years, as the mean one is about 27 months (36).

The way the steroid – induced KS develops is unpredictable. There are cases of regressive development of the tumor lesions soon after the interruption of the corticosteroid therapy (8, 21, 34, 35), or even before its end (10, 11, 17).

But there is literature data of regressive development of KS 14 months after the end of the corticosteroid therapy, and consequent spontaneous recurrences (29). There are reports of progress of KS long after the end of the corticosteroid (7, 17).

In literature there is an increase of the cases of KS induced by corticosteroid treatment of an autoimmune or other disease. Predominant is the opinion of genetic predisposition of patients to malignization, i.e. the corticosteroids suppress the effector ramus of the immune response in susceptible individuals (35). This hypothesis is supported by many authors. More contemporary is the theory of the virus genesis of KS.

CONCLUSIONS:

The iatrogenically induced KS is not a rare disease anymore and should not be ignored in our differential and diagnostic search in patients with disseminated knotty lesions, which have appeared on the back ground of a lengthy immunosuppressive therapy.

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