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Acrokeratosis paraneoplastica Bazex syndrome associated with esophageal squamocellular carcinoma

Acrokeratosis paraneoplastica Bazex sindrom udružen sa skvamocelularnim karcinomom jednjaka

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Abstract

Background. *Acrokeratosis paraneoplastica* Bazex (APB) is a very rare disease in the group of obligate paraneoplastic dermatoses, associated mostly with squamous cell carcinoma of the upper aerodigestive tract and metastatic cervical lymphadenopathy. The disease is characterized by violaceous erythemosquamous changes on the acral regions. This entity was first reported by Bazex in 1965. About 160 cases have been presented so far. **Case report.** We presented a patient with a three-month history of violaceous erythema, edema, erosions and scaling on the acral regions, elbows and knees and severe nail dystrophy. When the diagnosis was established, he did not have any symptom of internal malignancy. Esophagogastroscopy revealed ulcerovegetant lesion of the esophagus, while histology showed squamocellular invasive carcinoma. Surgical tumor removal resulted in significant improvement of skin changes in 15 days. Unfortunately, four months later, extensive skin lesions pointed to metastasis of squamous cell carcinoma. **Conclusion.** Skin changes can precede a few years the first manifestations of neoplasia. The course of the disease in our patient proved that APB is a specific marker of underlying malignancy.

Key words:
paraneoplastic syndromes; carcinoma, squamous cell, skin diseases; diagnosis, differential.

Apstrakt

Uvod. *Acrokeratosis paraneoplastica* Bazex (APB) retko je oboljenje iz grupe obligatnih paraneoplazijskih dermatoza. Najčešće, udružen je sa skvamocelularnim karcinomom gornjeg aerodigestivnog trakta ili metastatskom supradijafragmnom adenopatijom. Karakteriše se pojavom lividnih eritemoskvamoznih lezija na akralnim regijama. Ovaj entitet prvi je opisao Bazex 1965. godine, a do sada je prikazano oko 160 slučajeva. **Prikaz bolesnika.** Prikazali smo bolesnika sa tromesečnom pojavom lividnog eritema, edema, erozija i skvame na akralnim regijama, laktovima i kolenima i teške distrofije nokatnih ploča. U trenutku postavljanja dijagnoze bolesnik nije imao simptome maligniteta. Ezofagogastroskopijom uočena je ulcerovegetantna lezija jednjaka. Histološki je potvrđen skvamocelularni invazivni karcinom. Hirurško uklanjanje tumora dovelo je do značajnog poboljšanja kutanih promena za 15 dana. Nažalost, četiri meseca kasnije ekstenzivne kutane promene ukazale su na metastaze skvamocelularnog karcinoma. **Zaključak.** Promene na koži mogu i nekoliko godina prethoditi manifestacijama maligniteta. Slučaj našeg bolesnika potvđuje da APB predstavlja specifičan marker postojećeg maligniteta.

Ključne reči:
paraneoplastički sindromi; karcinom, skvamocelularni; koža, bolesti; dijagnoza, diferencijalna.

Introduction

Acrokeratosis paraneoplastica Bazex (APB) is a very rare disease in the group of obligate paraneoplastic dermatoses, associated mostly with squamous cell carcinoma of the upper respiratory and upper digestive tract and metastatic cervical lymphadenopathy [1, 2]. The disease is characterized by symmetrical psoriasiform lesions on the acral regions, especially on the nose, ears, hands and feet [1, 3, 4]. The disease is characterized by the presence of symmetric violaceous erythematous and scaly acral lesions and it has three stages of evolution. In the first stage cutaneous lesions are not precisely defined and usually are located on helices of ear lobes, nose, fingers and nails; associated tumor is usually asymptomatic. In the second stage lesions involve hands and feet, and local symptoms of existing malignancy are showing. In the third stage, if the tumor is not treated, areas of erythema and scale affect elbows, knees and trunk. Skin changes may precede

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several months to a few years the first manifestations of underlying malignancy. After the removal of cancer, skin lesions disappear very quickly [2]. Since the malignancy is revealed in a late stage in the majority of cases, the prognosis is mostly poor.

Case report

A 50-year-old white man was admitted to our Institute with a 3-month history of erythema, edema and scale on the nose, chin, auricles, hands and feet. The changes were followed by intensive itch and pain. When APB was established his general condition was satisfying, he did not have any symptom of internal malignancy.

Physical examination revealed an intensive violaceous erythema, edema, erosions and yellowish crusts on the nose, chin and auricles (Figures 1 and 2). Erythematous plaques covered by nonadherent psoriasiform scale and dark crusts were found in the elbows and knees. Erythematous papules and plaques measuring up to 7 × 6 cm were present in the shoulders, presternal region, and upper arms. Palmar and plantar regions were affected with diffuse dense yellowish hyperkeratosis and fissures and dorsa of the hands had erythema with scale. Perionychium was erythematous, edematous and thickened (Figure 3). The fingernails were yellowish, dystrophic, with subungual hyperkeratosis. Supraclavicular lymph nodes were enlarged.

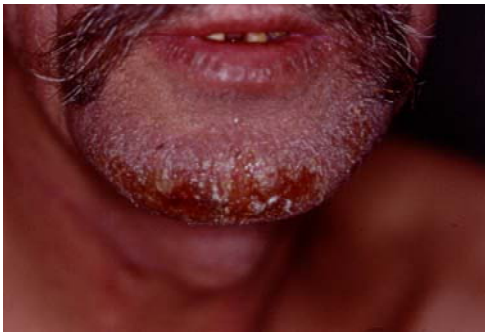

Fig. 1 – Erythema, edema, erosions and crusts on the chin

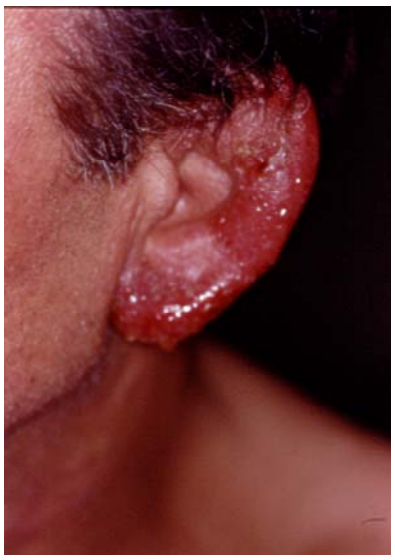

Fig. 2 – Edema and erosions on the auricle

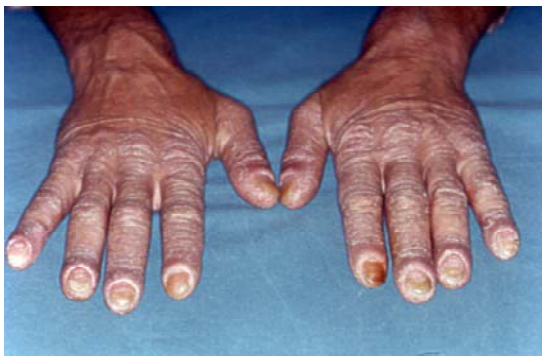

Fig. 3 – Erythema with scale on dorsa of the hands, edema of perionychium and nail dystrophy

The patient suffered from psoriasis vulgaris for 30 years and has been treated with topical corticosteroids, keratolytics and psoralen-ultraviolet A (PUVA) therapy. The diagnosis of psoriasis was made on clinical and histological basis.

Except for increased erythrocyte sedimentation rate, cholesterol, triglycerides, lactate dehydrogenase and decreased values of glycemia, other routine laboratory analyses were within normal limits. C-reactive protein, antinuclear antibodies and cryoglobulins were negative. The cytological analysis of sputum performed by direct microscopy did not reveal any acidoresistent bacilli. Veneral Disease Research Laboratory (VDRL) test was negative. Mycological examinations performed on finger nail plaques as well as perionychium of both hands were negative. Histopathological examinations of the involved skin of the elbow, knee, ear lobe and chin were nonspecific. Histology of the skin lesions showed hyperkeratosis, parakeratosis and spongiosis in the epidermis and mixed inflammatory infiltrate in the dermis. There were not elements for psoriasis vulgaris. The chest X-ray was normal. The abdominal sonography was normal, except for a 28 mm cyst in the left kidney. Otorhinolaryngologic, neurologic, urologic, hematologic and endocrinologic investigations showed no abnormalities. Bronchoscopy was normal.

Esophagoscopy revealed ulcerovegetant lesion of the esophageal mucous membrane, at least 2 cm in diameter, localized 30 cm from the teeth. Mild esophageal stricture was noticed. The gastroduodenoscopy disclosed normal gastric and dudenal mucosa. Histology of the ulcerovegetant lesion showed squamocellular invasive carcinoma, histologicaly defined as nonkeratinizing, moderately differented carcinoma with ulcerated surface and evident invasion. The grade of histologic malignancy was G-3, NG-2.

The total tumor removal was recommended as the main therapy. This was done by esophageal resection, subtotal esophagectomy and transmediastinal esophagogastroplastic procedure. According to the tumor node metastases (TNM) classification tumor was in the second stadium. Among 18 lymph nodes, none was affected and there were no evidence of metastasis, lymphoid and venous dissemination (T2 No (0/18) Mx Lo Vo).

Dermatologic therapy consisted of systemic antibiotics and corticosteroids (prednisone 0.5 mg/kg which was slow tapered over a month and discontinued), topical corticosteroids, antibiotics and emollients.

Two weeks after the surgery complete resolution of cutaneous lesions, except for elbow and nail lesions, was noted. Unfortunately, four months after the tumor removal, violaceous erythema, edema, erosions and yellowish crusts appeared on ear lobes, as well as erythema and scale on dorsa of hands. Body weight was reduced by 12 kg comparing to the period before the surgery. The presence of metastasis of esophageal carcinoma was identified. The patient was followed in relevant surgery unit.

Discussion

Acrokeratosis paraneoplastica was first described by Gougerot and Rupp in 1924, but the disease was named after the Bazex who published several cases of APB in French dermatologic journal in 1965 [5].

The disease is rare, belongs to a group of obligate paraneoplastic dermatoses and most frequently is associated with squamous cell carcinoma of upper aerodigestive tract or metastatic cervical lymphadenopathy. Several cases of the association between APB and adenocarcinoma have been published, only two of them were adenocarcinoma of the colon [6–8]. The association of APB with multiple genitourinary tumors, namely adenocarcinoma of the prostate and undifferentiated bladder cancer has been reported [9]. Bazex syndrome has also been described in patients with Hodgkin disease and neuroendocrine tumor [10, 11]. It can be associated with other paraneoplastic diseases, as in the case of simultaneous appearance of APB and acquired ichthyosis in a patient with lymphoma [10]. The concurrent presence of AP, vitiligo and alopecia areata in a patient with cutaneous SCC pointed to possible pathogenesis of AP; serial detection of SCC antigens showed the correlation of serum concentration of SCC-Ag with the severity of clinical picture of APB. Authors directed to a possible role of immune mediated mechanisms in development of APB [12].

Bazex syndrome affects mainly Caucasian males after the age of 40 [1]. A small number of affected females have been reported, APB associated with breast cancer is especially rare among them [1, 13].

Skin lesions of APB are similar to psoriasis vulgaris, but histological picture is nonspecific. It correlates with clinical picture and most frequently shows hyperkeratosis, parakeratosis, acanthosis, focal spongiosis and mixed dermal cell infiltrate [4]. Histological features of psoriasis vulgaris such as acanthosis with elongation of the rete ridges, focal collection of neutrophils in the stratum corneum and papillomatosis were not present. Diagnosis of APB in our patient was based on the appearance and acral location of skin lesions and nonspecific histology.

According to the literature and Medline search, about 160 cases of APB have been published thus far. Only one larger study which included 113 patients (105 males, 8 females) has been published [2]. In that study, in 67% of the patients psoriasiform lesions preceded the diagnosis of malignancy, in 15% of the patients cutaneous lesions appeared after the establishing the diagnosis of neoplasm, and in the rest of the patients cutaneous lesions emerged simultaneously with symptoms of malignancy. In 93% of the patients cutaneous lesions significantly regressed after the tumor removal/treatment, or they remained unchanged if the underlying disease persisted [2].

Conclusion

Skin lesions characteristic for APB in our patient that lasted for three months brought suspicion to the presence of malignancy, and detailed investigations and examinations conducted led to the revelation of invasive squamous cell carcinoma of esophagus and its removal. Four months after the surgery the relapse of extensive cutaneous lesions suggested the presence of metastases of primary esophageal carcinoma which was confirmed by further investigations. The course of the disease in our patient proved that APB is a specific marker of underlying malignancy.

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