Primary angioplasmacellular hyperplasia with multiple lesions showing a dramatic response to isotretinoin: a case report

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Primary angioplasmacellular hyperplasia is a scarce clinical dermatologic condition presenting different skin lesions diagnosed through biopsies indicating vascular proliferation with perivascular plasma cell infiltrations. In the current case presentation, a 40-year-old healthy male was referred to our outpatient dermatologic clinic with concurrent limbs and trunk erythematous vascular lesions for five years. The chief complaint of the patient was intermittent pruritus and relative irritation for years. Multiple biopsies were derived from the lesions, and vascular proliferation of capillaries with intensive perivascular infiltration of plasma cells was detected in the pathological specimen that finally led us to the final diagnosis of primary angioplasmocellular hyperplasia. Treatment with isotretinoin was initiated, and the patient responded to the treatment protocol dramatically. Given the rarity of reported cases, this report is considered the first case of primary angioplasmacellular hyperplasia with numerous lesions scattered and the first experience of successful treatment with isotretinoin.

Keywords: primary angioplasmacellular hyperplasia, vascular proliferation, plasma cell

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INTRODUCTION

Angioplasmacellular hyperplasia is a rare clinical condition presenting with skin lesions diagnosed through biopsies, which indicate vascular proliferation with perivascular plasma cell infiltrations [1]. This condition was primarily explained in two adults with solitary skin nodules on their trunks [2]. This disorder is a distinct skin disorder diagnosed through skin biopsies presenting perivascular reactive plasma cell infiltration; thus, a correct early diagnosis of primary angioplasmacellular hyperplasia due to its probable violent presentation and its distinction from other vascular skin lesions [3].

The current study presents a case with skin lesions without an apparent diagnosis for five years that finally was diagnosed as primary angioplasmacellular hyperplasia.

CASE PRESENTATION

A 40-year-old male was referred to the outpatient dermatology clinic with the presentation of concurrent limbs and trunk erythematous lesions since five years ago. The chief complaint of the patient was pruritus and irritation of the lesions. The lesions were located on the trunk with a size of 3-10 mm with no epidermal change or scar formation. A medical and family history was taken from the patient, presenting no previous medical history and no further similar lesions or

other skin diseases among his first-degree family members. He referred to dermatologists five years ago, skin biopsies were taken, and the pathology reports only described the lesion without any net diagnosis. So, the patient did not continue to follow up and was treated with antihistamine remedies to control pruritus. This trend went on as lesions were stable. Given the progression of the lesions over the preceding two years, he was referred for another skin biopsy with differential diagnoses of Kaposi sarcoma, angioendotheliomatosis, and lichen planus.

The histopathologic survey showed mild acanthosis, vascular proliferation of capillaries with varying numbers of plump endothelial cells, and abundant perivascular plasma cell infiltrations in the dermis. Diagnosis of Kaposi sarcoma was ruled out due to the lack of atypia in endothelial cells and promontory sign, and negative result of PCR for detecting human herpes simplex virus 8 (HHV8) antigen in the specimen. Based on the patients' clinical features, further evaluations were requested, including cardiac echocardiography, abdominopelvic ultrasonography, and complete blood count; all were normal. Considering the mentioned clinical and laboratory findings, the diagnosis of primary angioendotheliomatosis was made for him. Therefore, treatment with isotretinoin was considered, but its initiation was postponed until the subsequent biopsy was derived from the lesions.

In follow-up assessments, the patient underwent another skin biopsy from trunk and limb lesions. Considering the vascular proliferation of capillaries with varying numbers of plump endothelial cells and intensive perivascular infiltration of plasma cells detected in pathological findings of biopsies, the final diagnosis of angioplasmocellular hyperplasia was made. Thus, treatment with isotretinoin (Zahravi Co., Iran), a daily regimen of 20 milligrams on odd days and 40 milligrams on even days, was started. The patients' response to treatment was notable as the pruritus was well-controlled, the prominent lesions were flattened, the vascular lesions turned to post-inflammatory hypopigmentation (PIH), and some of the lesions completely disappeared. Moreover, in physical examination, patchy rippled pigmentation was detected on the back, confirmed in the histological assay as macular amyloidosis, which was treated topically with mild improvement.

The patient had withdrawn his medical remedy arbitrarily, which caused new lesions formation within seven months. He returned; isotretinoin therapy was started again and continued for eight months to the total dose of 120 mg/kg. After completing the treatment course, the patient was followed for eight months. During this period, some of the lesions were eliminated, vascular ones turned to PIH, and no new lesions were found (Figures 1 and 2). The last obtained biopsy revealed considerably less vascular proliferation and sparse perivascular plasma cell infiltrations compared with the previous specimen (Figure 3).

Table 1. The previously reported cases

Authors	Patient characteristics	Site of the lesion(s)	Treatment
Dhali *et al.* [1]	65-year-old male	A single nodule on the back	Excision with no recurrence
Hsiao *et al.* [6]	10 cases (4 males and 6 females)	Nine had a single and one had two lesions on the face, scalp, neck, trunk, and leg. The lesions were papules or nodules	-
González *et al.* [2]	A 55-year-old male and a 20-year-old female	Both presented a nodule on the trunk	-
Kumar *et al.* [11]	A 62-year-old male	A nodule on the back of the neck	-
Wang *et al.* [3]	A 35-year-old male and a 39-year-old female	The male with a nodule on the lower back The female with a nodule on the chest	-
Ide *et al.* [7]	A 50-year-old male	A single movable nodule in oral cavity	-
Tobias *et al.* [12]	An immunocompromised HIV-positive patient	A cutaneous involvement of herpes simplex virus infection compatible with angioplasmacellular hyperplasia	-
Ramírez-Santos *et al.* [8]	A 40-year-old male	An erythematous-violaceous nodule on the chest	-
González-González *et al.* [13]	A 28-year-old male	A single oval-shaped purplish erythematous nodule with defined edges, with small ulcerated areas and blood crust on the surface nodule	-

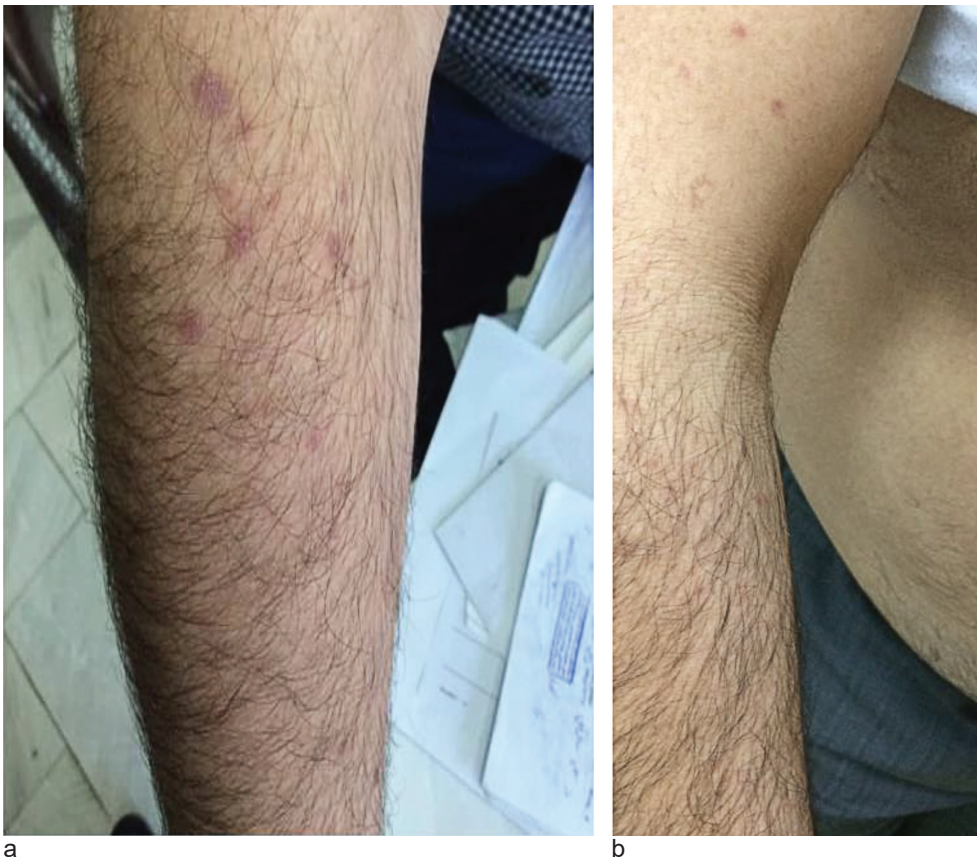

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Figure 1. (a)The limb lesions before the treatment; (b) the improvement in the limb lesions following the administration of isotretinoin.

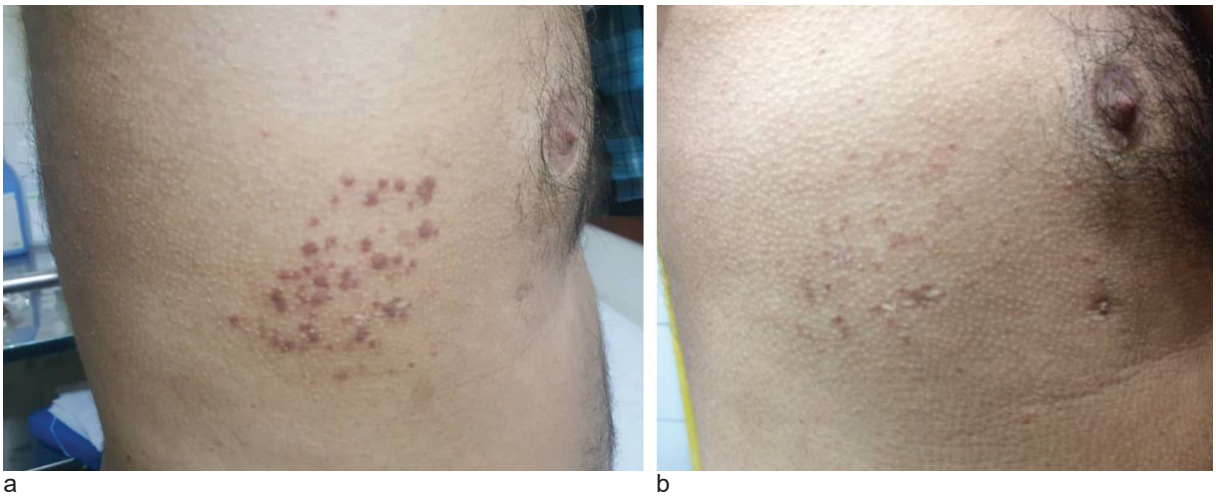

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Figure 2. (a) The trunk lesions before the treatment; (b) the improvement in the lesions following treatment with isotretinoin.

DISCUSSION

Plasma cells are typically located in mucous membranes, and their reactive proliferation in mucous tissues has been well-documented [4]. In rare normal conditions, plasma cells have been detected in the skin, while cutaneous plasmacytosis with mucosal involvement is another pathological

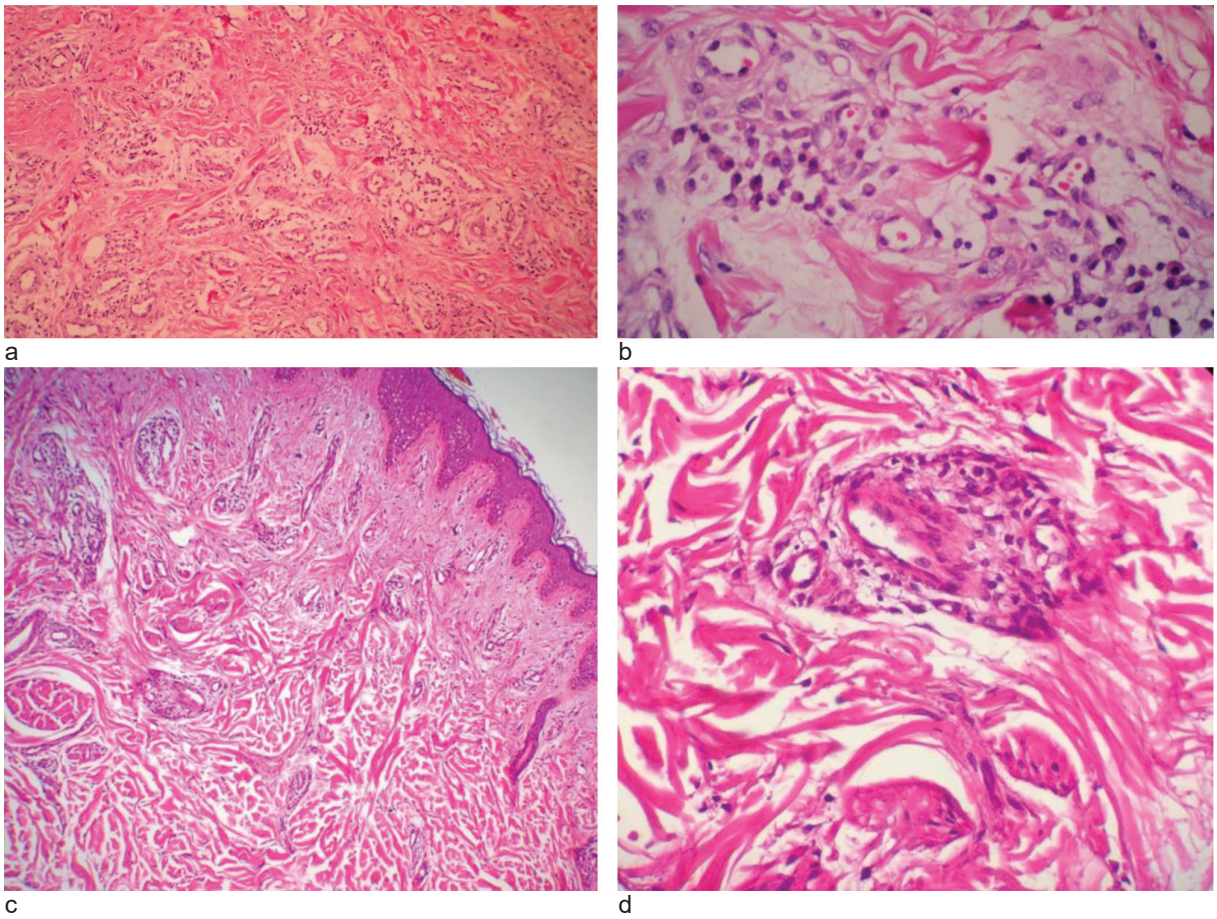

Figure 3. (a) There is a vascular proliferation of capillaries with varying numbers of plump endothelial cells (H & E, ×100); (b) Higher-power view of the lesion with abundant perivascular plasma cell infiltrations (H & E, ×400); (c, d) There is less vascular proliferation and sparse perivascular plasma cell infiltrations after treatment with isotretinoin (H & E, ×100, ×400, respectively).

condition presented previously in a few studies [5].

Primary angioplasmacellular hyperplasia is a non-neoplastic dermatologic condition, clinically known as an asymptomatic, non-ulcerated umbilicated nodule, which may be violaceous or sometimes brownish [3]. The lesions are primarily solitary on the trunk and neck [1], while a report has previously presented a case with two simultaneous lesions [6], and our patient had various lesions on the trunk and limbs. The final diagnosis of mentioned lesions is usually made late because of their asymptomatic nature [1], while our case was referred many times to dermatologists because of irritating pruritus.

The etiopathogenesis of this condition is still a great question. Some previous studies have raised the hypothesis of a hemangioma associated with dense proliferation of plasma cells [7]. Hsiao *et al.* presented ten cases of primary angioplasmocellular hyperplasia and hypothesized the potential encroachment of plasma cells to upper submucosa altering local blood flow accompanying vascular proliferation [2].

While making the final diagnosis of primary angioplasmacellular hyperplasia was a critical challenge for us, Hsiao and colleagues explained that clinical and histopathological findings are adequate for making a direct diagnosis. They declared that a history of the previous injury or being affected by varicella is responsible for reactive inflammatory vascular hyperplasia, though this hypothesis has not been well-established by other authors [6]. The histopathological findings indicating primary angioplasmocelluar hyperplasia is known as dermal vessel dilatation and proliferation accompanying with infiltration of cells, mostly plasma cells for

over 60% of cells with less proportion of other cells such as neutrophils, lymphocytes, and sometimes eosinophils with atypia [8].

To the best of our knowledge, approximately 20 cases with primary plasma cellular hyperplasia have been presented worldwide. Although no conventional treatment has been recommended for this condition, some of the authors preferred surgical excision therapy, and no recurrence was reported [1,6], while we treated our patient with a high dose of isotretinoin and achieved successful clinical and histopathological outcomes. This is the first report representing the efficacy of isotretinoin in treating this rare condition.

Isotretinoin was administered according to case reports in which isotretinoin had a therapeutic effect on skin disorders with benign vascular proliferation in pathology such as diffuse dermal angiomatosis of the breast, a type of reactive angioendotheliomatosis [9,10]. It seems that the improvement in our patients has occurred, possibly due to its antiangiogenic properties.

CONCLUSION

Contrary to the previous studies that presented solitary lesions, primary angioplasmacellular hyperplasia was presented as numerous vascular lesions on the trunk and limbs in our study. The final diagnosis was made through several skin biopsies. Besides, we could successfully treat primary angioplasmacellular hyperplasia using isotretinoin for the first time, which is the current study's hallmark. In order to generalize this therapeutic approach, further studies are strongly recommended.

Conflict of interest: None declared.

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