

Case presentation

Isolated benign primary cutaneous plasmacytosis in an adult Indian male

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Abstract

Primary cutaneous plasmacytosis (PCP) is an uncommon reactive lymphoplasmacytic disorder of uncertain etiology. It has been mainly described in patients of Japanese descent, with only few reports in Caucasians and Chinese. We present a case of isolated benign PCP in a 45-year-old man, who clinically manifested with a localized ulcerated nodule overlying a hyperpigmented plaque on the upper back. To the best of our knowledge, PCP from India has not been described before.

Keywords: Plasmacytosis, cutaneous, systemic, benign

Introduction

The proliferation of plasma cells in skin may be monoclonal as in neoplastic conditions like multiple myeloma, cutaneous plasmacytoma, and plasma cell leukemia or polyclonal as in benign inflammatory and infectious processes. Polyclonal plasma cell disorders are further classified into primary and secondary plasmacytosis. Primary cutaneous plasmacytosis (PCP) is a rare entity characterized by benign plasma cell infiltrate in the skin with associated polyclonal hypergammaglobulinemia in the absence of an underlying disease. Isolated benign PCP has been described as a distinct entity, albeit in children only [1,2,3,4]. We report the first case of isolated benign PCP from India in a 45-year-old gentleman with an unusual presentation of a localized ulcerated nodule overlying a hyperpigmented plaque.

Case synopsis

A 45-year-old man presented with a solitary growth on the upper back of 3 years duration, which had become painful with purulent discharge and surrounding redness over 3-4 months. In the past one month, he had also developed multiple itchy erythematous papules in the vicinity of the growth. There was no history of trauma, insect bite, fever, loss of weight or appetite, joint or bone pains, or any other systemic symptoms. Muco-cutaneous examination revealed a hyperpigmented, indurated plaque with irregular margins topped with a single skin colored nodule measuring 2 cm in diameter, showing superficial ulceration with purulent discharge and adherent yellowish- brown crust. The nodule was surrounded by crusted papules measuring 0.5-1 cm in size (Figure1). Mucosa was not involved. There was no lymphadenopathy or hepatosplenomegaly. A skin biopsy was performed from the nodule and the surrounding plaque with the differential diagnoses of leishmaniasis, cutaneous B or T- cell lymphoma, and angiolymphoid hyperplasia with eosinophilia. Histopathological examination from the nodule, hyperpigmented plaque, and crusted papule showed similar findings including acanthotic

epidermis and dense perivascular and periadnexal infiltrate of mature plasma cells without atypia in the dermis. A few lymphocytes and histiocytes were interspersed among plasma cells (Figure 2). Immunohistochemistry showed plasma cells positive for CD 38 and both kappa and lambda light chains in the ratio of 1:1 indicating polyclonality (Figure 3). Giemsa, Warthin–Starry, and Congo red stains were negative. Leishmania culture was also negative. Complete blood count, liver and renal function tests, and total protein levels were within normal limits. Serum protein electrophoresis was normal with absence of M band and serum immunoglobulin levels were within normal range. Bence-Jones proteins were not detected in urine electrophoresis. Serological tests for syphilis, borrelia, hepatitis virus types B and C, HIV, and anti-nuclear antibodies were negative. The serum level of interleukin-6 (IL-6) was normal. Chest X-ray and ultrasonography of abdomen did not reveal any lymphadenopathy or hepatosplenomegaly. Skeletal survey showed no abnormality. Bone marrow biopsy was not performed as the patient did not give consent. Based on the above findings, a diagnosis of primary cutaneous plasmacytosis was made. The patient was started on amoxicillin and clavulanic acid 625 mg thrice a day for 1 week and subsequently on clobetasol propionate 0.05% cream twice a day, which led to significant improvement in both the papules and plaque in 4 weeks. The nodule also decreased in size and subsequently was excised. Histopathology of the excised specimen showed a moderately dense perivascular and periadnexal, mature lymphoplasmacytic infiltrate in the dermis. The patient has shown no activity of the treated site and no new lesions after 2 years of follow-up (Figure 4).



Figure 1. Solitary ulcerated nodule surrounded by a well-defined hyperpigmented plaque with irregular margins and overlying crusted papules on left upper back.

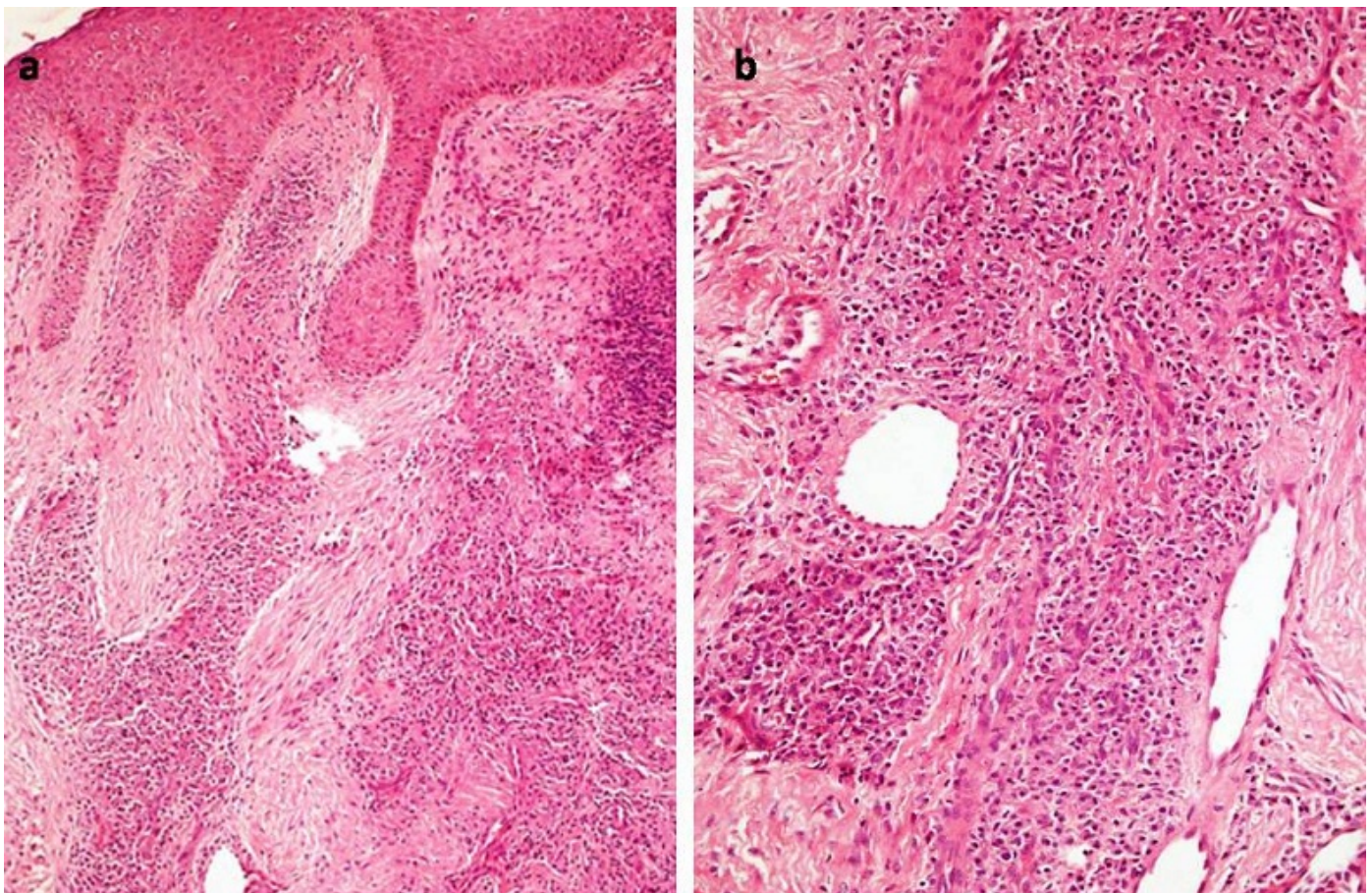


Figure 2 (a) Acanthotic epidermis with dense mononuclear cell infiltrate in superficial and deep dermis (H&E x10X), (b) Moderately dense perivascular, nodular aggregates of mature plasma cells without atypia, admixed with few lymphocytes and histiocytes in the dermis (H&E x 20X).

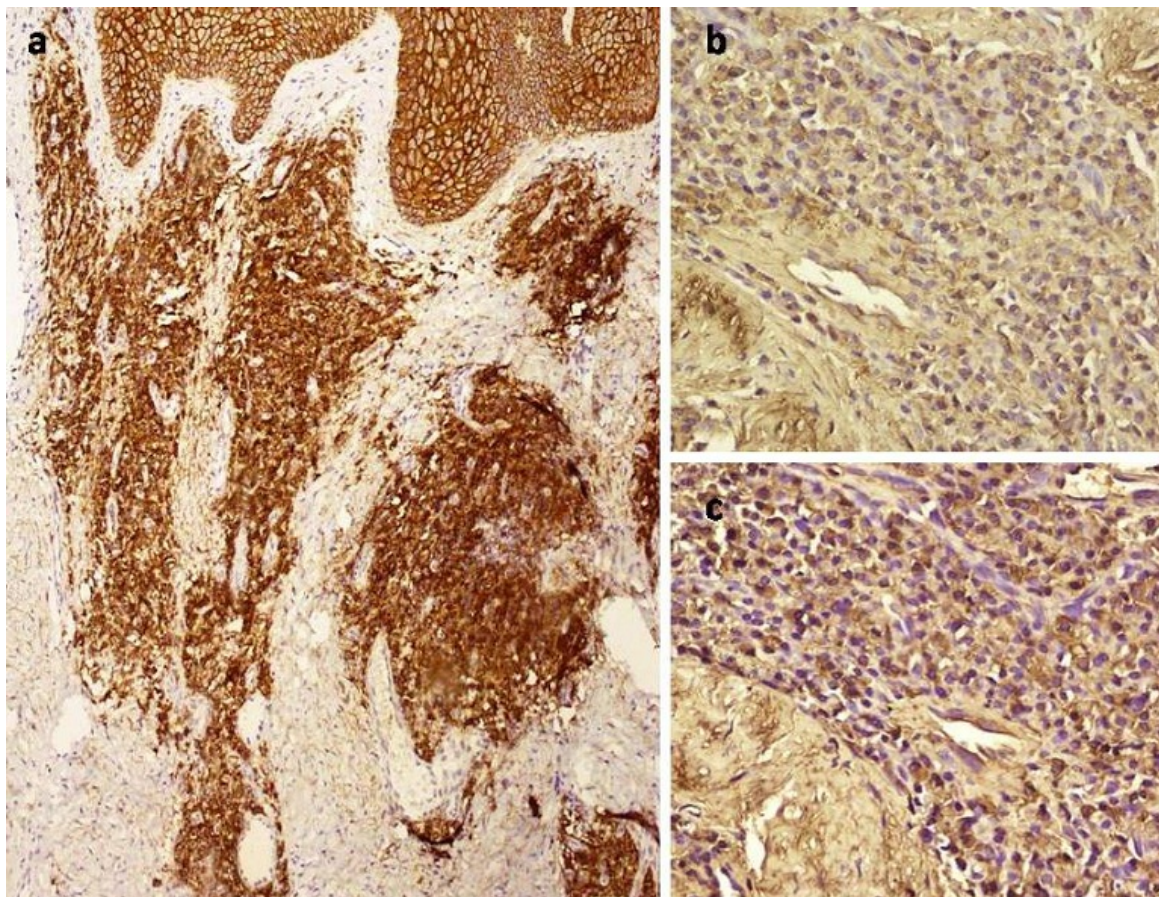


Figure 3. (a) Immunohistochemistry shows plasma cells strongly positive for CD 38, (b) with no restriction of either kappa or (c) lambda light chain (1:1 positivity) (IHC x 20X).

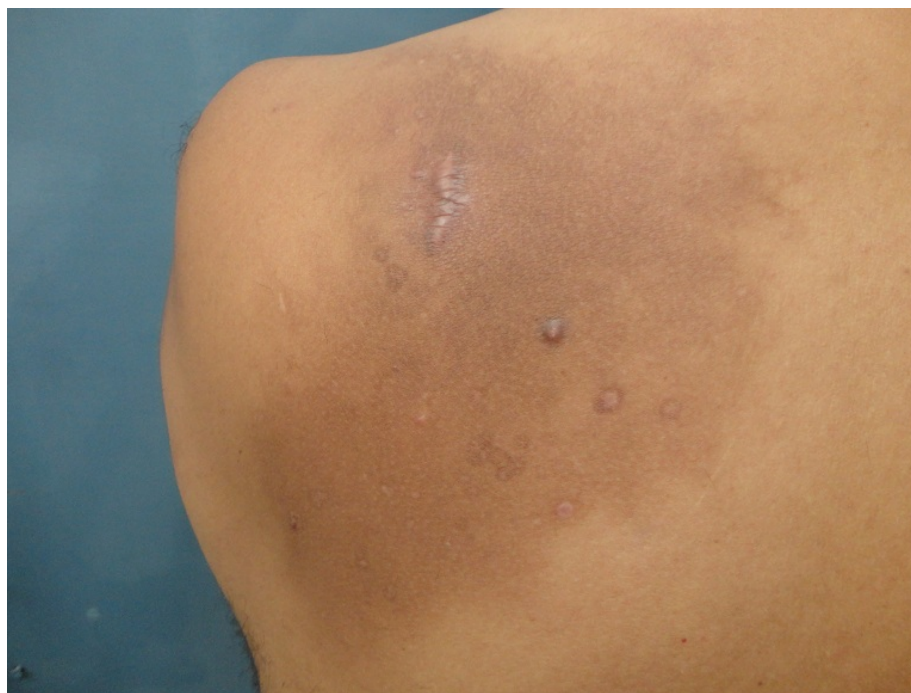


Figure 4. Linear scar at the excision site of nodule and residual post-inflammatory hyperpigmentation at 2 years of follow-up

Discussion

Primary cutaneous plasmacytosis (PCP) is an uncommon disorder classified under the group of reactive plasma cell hyperplasia in skin. It usually affects middle aged to elderly individuals and rarely children [1,2,3,4], with a male to female ratio of 1: 0.6. The typical presentation consists of multiple, mostly asymptomatic, erythematous to brown macules, nodules and plaques distributed on the face, neck, trunk, and extremities in individuals of Asian, particularly Japanese origin and infrequently in Koreans, Chinese, and Caucasians [1,5,6]. Systemic plasmacytosis is characterized by involvement of more than 2 organs (skin, lymph node, bone marrow, lung), accompanied with polyclonal hypergammaglobulinemia [7]. Polyclonal hypergammaglobulinemia is an associated finding in both cutaneous and systemic variants but may be absent in 10% of the cases. Lymphadenopathy is the commonest extracutaneous presentation in systemic plasmacytosis. Other systemic manifestations include hepatosplenomegaly, lymphoid interstitial pneumonia, mesangioproliferative glomerulonephritis and

periureteric retroperitoneal masses [8,9]. Although it was earlier termed as cutaneous plasmacytosis, the nomenclature has been revised to cutaneous and systemic plasmacytosis (CSP) to emphasize the high incidence of occult involvement of organs other than skin even in asymptomatic cases [10]. PCP in children has been recognized as a distinct entity, also known as isolated benign cutaneous plasmacytosis, because of younger age at presentation, single skin lesion, proliferation of mature plasma cells confined to the skin, and absence of hypergammaglobulinemia, lymphadenopathy and hepatosplenomegaly [1,2,3,4].

The exact pathogenesis of cutaneous plasmacytosis is not completely known. Genetic and infective factors may have a role. Elevated levels of IL-6, which plays a role in differentiation of B-lymphocytes to plasma cells, have been described [9]. It has therefore been suggested that cutaneous plasmacytosis might be a variant of multicentric Castleman disease (MCD), which is characterized by reactive lymphadenopathy with increased levels of IL-6 produced by cells latently infected with human herpes virus (HHV)-8. However, Jayaraman *et al* showed negative HHV-8 expression in cutaneous plasmacytosis [11]. Mutations in genes encoding for signalling molecules that regulate plasma cell function may also contribute to the pathogenesis [12]. The plasma cell infiltrate represents a reactive inflammatory response to an underlying infection, malignancy or friction [6,10,13]. Friction and subsequent infection might have been the triggers in our case as well.

The histopathology shows dense superficial and deep perivascular and periadnexal infiltrate of mature plasma cells without atypia, admixed with few lymphocytes and histiocytes in the dermis. Less commonly reported features include lymphoid follicles with reactive germinal centers. A clinico-histopathologic analysis of 6 patients with CSP revealed perineural and occasional intraneural plasma cells [14]. Histopathological differential diagnoses include neoplastic, infectious, and autoimmune conditions (Table 1).

Table 1. Histopathological differential diagnoses of plasma cell rich infiltrate in skin

Disease	Key histological features
Primary cutaneous marginal zone B-cell lymphoma	Expanded interfollicular zones by atypical B cells (irregular nuclear contours), plasmacytic differentiation may be seen. Tumor cells show light chain restriction
Primary cutaneous plasmacytoma	Monoclonal proliferation of plasma cells showing atypia, monotypic light chain expression on IHC
Multicentric Castleman's disease (plasma cell variant)	Follicular hyperplasia with polyclonal plasma cells localized to interfollicular region of lymph node
Lupus erythematosus and scleroderma	Few plasma cells in a lymphohistiocytic background
Secondary syphilis	Interface dermatitis, perivascular / periadnexal lymphohistiocytic and plasma cell infiltrate in papillary dermis, endothelial swelling. Warthin- Starry stain positive
Lyme's disease	Superficial and deep perivascular, perineural and periadnexal, predominantly lymphocytic infiltrate admixed with plasma cells in the periphery and eosinophils in the center. Warthin- Starry stain may be positive
Leishmaniasis	Diffuse infiltrate of histiocytes admixed with lymphocytes and plasma cells. Histiocytes filled with Leishman-Donovan bodies. Giemsa stain positive
Cutaneous B-cell lymphomatoid hyperplasia	Top heavy mixed infiltrate in nodular / diffuse pattern, prominent reactive lymphoid follicles, polyclonal light chains on IHC
Nodular amyloidosis	Amyloid deposits throughout the dermis, walls of blood vessels and extending into the subcutaneous fat, surrounded by lymphoplasmacytic infiltrate

IHC: immunohistochemistry

Although the disease runs a prolonged course, it is associated with favorable prognosis in most cases. A wide range of treatment modalities have been employed but there is no consensus on the standard treatment. Various treatments used for cutaneous lesions are oral, topical, and intralesional corticosteroids [1], topical tacrolimus [1], topical psoralen plus ultraviolet-A (PUVA) [15], radiotherapy [8], and photodynamic therapy [16].

The present case was atypical in many ways. Firstly, the clinical presentation as a localized lesion has been reported in children rather than adults [1,2,3,4]. The morphological appearance of PCP as a large nodule is unusual and may somewhat be likened to that of a plasmocanthoma, which is a reactive plasma cell tumor that presents as a verrucous polypoidal mass on the periorificial sites [17]. Ulceration in PCP is also uncommon, though pretibial ulcers showing dense benign plasmacytic infiltrates, in addition to typical papules on the chest have been described in cutaneous plasmacytosis [18]. Secondly, PCP is

classically asymptomatic, whereas our patient had intense pruritus. Thirdly, our patient did not have polyclonal hypergammaglobulinemia, another similarity with childhood cases [1,2,3,4]. Also, this is the first description of PCP in a patient of Indian origin. The course of the disease was benign, with no relapse or systemic involvement after 2 years of follow-up.

Conclusion

PCP, though rare, is an increasingly recognized entity in Asians. An ulcerated nodule overlying a hyperpigmented plaque represents an unusual clinical presentation of PCP and the diagnosis is usually established by histopathology in conjunction with immunohistochemistry. A thorough evaluation for systemic disease should be carried out before labelling as cutaneous plasmacytosis and patients should be followed up to rule out any extracutaneous involvement or malignant transformation.

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