Dowling–Degos Disease with Hidradenitis Suppurativa and Inflammatory Arthritis in Two Generations

Abstract

Dowling–Degos disease (DDD) is a rare autosomal dominant genodermatosis characterized by reticulate brown-to-black pigmentation of the flexures, pitted perioral acneiform scars, and comedo-like follicular papules on the flexures. The diagnosis is based on characteristic clinical and histopathological features. DDD has been found to occur in association with hidradenitis suppurativa (HS), arthritis, epidermoid cysts, keratoacanthomas, and squamous cell carcinoma. To date, there is only one report of DDD associated with HS and polyarticular arthritis.

Keywords: *Arthritis, familial Dowling–Degos disease, hidradenitis suppurativa, reticulate*

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Introduction

Reticulate pigmented anomaly of the flexures or Dowling–Degos disease (DDD) is a rare autosomal dominant genodermatosis characterized by reticulate brown-to-black pigmentation of the flexures, pitted perioral acneiform scars, and comedo-like follicular papules on the flexures. DDD is often associated with other conditions such as hidradenitis suppurativa (HS).[1] Other associations include arthritis,[2] epidermoid cysts, keratoacanthomas,[3] squamous cell carcinoma,[4] seborrhoeic keratoses, and Haber's syndrome.[5,6]

Case Report

A 38-year-old lady presented with hyperpigmented lesions on the face and flexures since childhood, gradually progressing over the past 5 years along with onset of pustulonodular lesions on the axillae and groins since 1 year. She also gave history of pain and stiffness involving multiple large joints and small joints of hands for 3 years. There was no history of dactylitis or deformities. A similar pattern of pigmentation with symptoms of arthritis and HS were present in both her father and brother.

Cutaneous examination revealed discrete and confluent reticulate hyperpigmented macules and few papules on the face, chest, inframammary areas, neck, axillae, and groins [Figures 1 and 2]. Multiple open comedones and few nodules were present in the axillae and groins with healed scars [Figure 3]. Pitted scars were observed on the nape of the neck and upper back [Figure 4]. There were no fluid-filled lesions or erosions. Tongue showed scattered pigmented macules. X-ray of the hands and wrist did not show any significant abnormality. Musculoskeletal examination showed features suggestive of polyarticular arthritis. There was no axial joint involvement. Her rheumatoid factor levels, anti-cyclic citrullinated peptide (CCP) enzyme-linked immune sorbent assay (ELISA), and antinuclear antibody (ANA) were also negative. C-reactive protein test (CRP) was 6.4 mg/L (normal <3 mg/L) at presentation. ESR (erythrocyte sedimentation rate) and HLA (human leukocyte antigen) B27 tests were not done. Histopathological examination of the pigmented area revealed basket weave hyperkeratosis of the epidermis, preserved granular layer, regular acanthosis with elongated slender finger-like projections of rete pegs and increase in pigmentation of basal keratinocytes. Mild perivascular lymphohistiocytic infiltrate was present in the superficial dermis [Figure 5]. There were no fungal microorganisms. She was diagnosed as DDD associated with HS and polyarticular arthritis based on the

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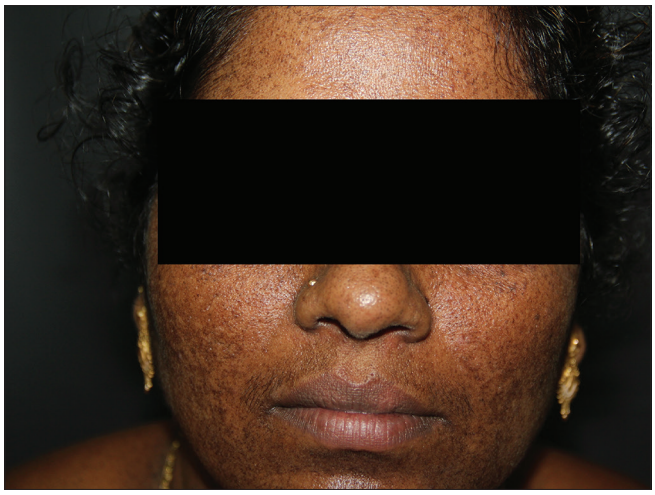

Figure 1: Reticulate hyperpigmented macules on the face of the patient

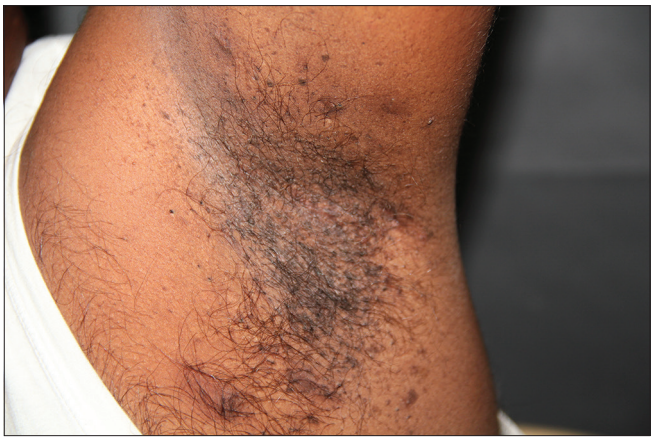

Figure 2: Sibling with hyperpigmented macules, papules, comedones in the axilla, and minimal scarring suggestive of quiescent HS

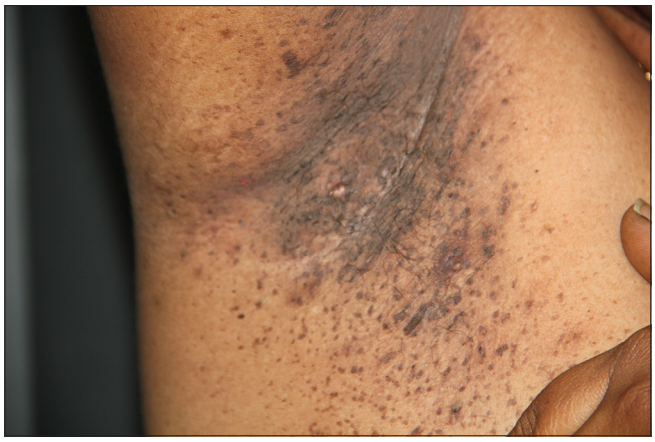

Figure 3: Hyperpigmented macules, papules, multiple open comedones, and few nodules in the axillae of the patient with healed scars

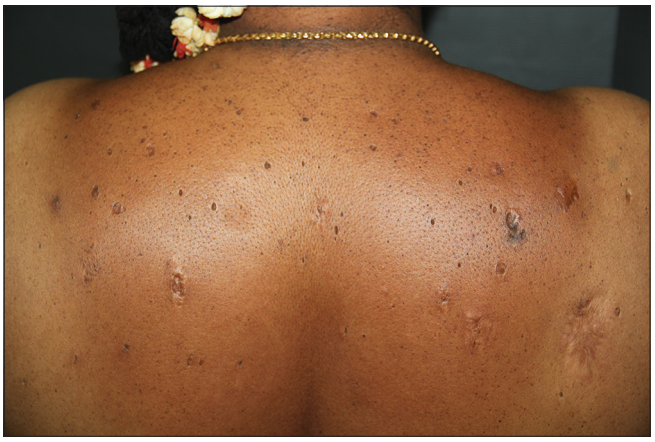

Figure 4: Pitted scars and comedones on the nape of the neck and upper back of the patient

clinical, histopathological findings, and a positive familial occurrence. Ciclosporine was initiated at 2 mg/kg body weight with which she had significant improvement of HS and a partial resolution of pigmentation. She was lost to further follow-up.

Discussion

The occurrence of DDD and HS is well-known. There is only one previous report of DDD, HS and inflammatory arthritis in two successive generations.[2] Our patient also had a similar presentation with familial DDD, HS, and arthritis in her father and brother. Both DDD and familial HS are autosomal dominant genetic disorders that can coexist in the same person. DDD has been shown to result from mutations in at least three genes, keratin 5 (KRT5), protein O-fucosyltransferase 1 (POFUT1), and protein O-glucosyltransferase 1 (POGLUT1).[7] Recent reports have shown that mutations in presenilin enhancer, gamma-secretase subunit (PSENEN) gene which encodes the protein presenilin enhancer gamma-secretase subunit, results in altered Notch signaling. Appropriate Notch signaling is important in maintaining the integrity of inner and outer root sheath of hair follicles and cutaneous appendages. Decreased Notch activity is associated with mutations in POFUT1, seen in DDD. In familial HS, loss-of-function mutations of components of the γ-secretase (GS) complex leads to decreased protease cleaving activity, which in turn compromises Notch signaling. In DDD, PSENEN and POGLUT1 expression have also been found to be down-regulated in keratinocytes.[8] A recent report describes a DDD sub phenotype in PSENEN mutation carriers which increases the susceptibility for HS.[9]

Our patient had arthritis in addition to HS and DDD. There is an increase in the prevalence of inflammatory arthritis in patients with severe HS, including reactive arthritis. Although the exact mechanism is not known, hypersensitivity to bacterial antigens and dysregulated immune response have been proposed.[10,11] In a study by Liu *et al*., it was found that sustained Notch activation in adult joint cartilage results in progressive osteoarthritis which could be the reason for associated familial arthritis in this scenario.[12]

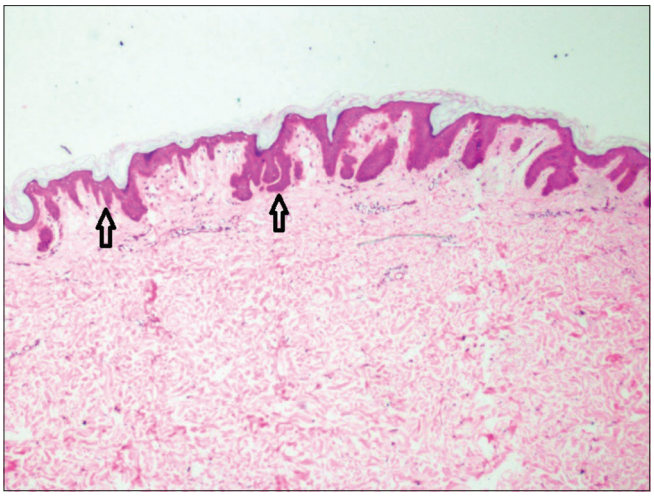

Figure 5: Epidermis with mild acanthosis and slender finger-like projections (broad arrows) of rete pegs (H and E 40x)

Conclusion

Mutation analysis was not done in our patient due to financial constraints. However, we would like to highlight the association of familial DDD, HS, and arthritis which may be linked to the PSENEN mutation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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