

Bazex-Dupre-Christol syndrome – A memorable family

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Abstract Bazex-Dupre-Christol syndrome (BDCS) is clinically characterized by multiple basal cell carcinomas of the face occurring mainly during the second and third decade of life, follicular atrophoderma predominantly of the dorsum of hands and feet and generalized hypotrichosis, sometimes with pili torti and trichorrhexis nodosa. Common associated features are milia, hypohidrosis and calcifying epithelial tumours. We herein report four members of one family with BDC syndrome, a mother and her three daughters. In the mother and one daughter, the clinical picture was very typical with all major features, whereas in the others only follicular atrophoderma, milia and hypotrichosis were present. BDCS is a hereditary multiple BCC syndrome whose pattern of inheritance is thought to be X-linked dominant, which implies that all daughters of the affected mothers should have this disease. In this case three out of four daughters are suffering from BDCS but one is totally asymptomatic. To our knowledge, this is the first report of a family with BDC from Pakistan.

Key words

Basal cell carcinoma, hypotrichosis, follicular atrophoderma.

Introduction

Bazex-Dupre-Christol (BDC) syndrome is an X-linked dominant multiple basal cell carcinoma (BCC) syndrome, clinically characterized by follicular atrophoderma, multiple milia, hypotrichosis and multiple basal cell carcinomas. Other multiple BCC syndromes include Gorlin syndrome and Rombo syndrome. BDC is considered as a primary disorder of hair follicle by some authors while other considers it as an ectodermal dysplasia by others. BDC is inherited as X linked dominant disorder whose gene has been mapped to Xq24-q27 which encodes a protein involved in repair of UV damaged DNA. Few families have been described so far, since the first description of

syndrome by Bazex in 1964.¹ We report a family of BDC syndrome where a mother and her three daughters are suffering.

Case report

A 45-year-old woman from lower socioeconomic group presented to our OPD with progressively increasing asymptomatic pigmented lesions on face for last 20 years. She also complained of decreased hair density over scalp and eyebrow along with reduced sweating over upper half of the body. There were no systemic complaints and no comorbidity. She was married to her maternal cousin with four daughters and two sons. She reported similar complaints in three of her daughters except that the pigmented lesions were present only on the face of her elder daughter. Clinical examination revealed multiple pigmented papules and nodules (from 0.2cm to 2cm in dimension) symmetrically distributed over her face (**Figure 1**). A darkly pigmented annular plaque was

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Figure 1 Multiple pigmented BCCs on face of the patient.



Figure 4 Follicular atrophoderma over knee in one of daughters.



Figure 2 Follicular atrophoderma on thigh and knee,



Figure 3 Pigmented papules on the face of 20-year-old daughter.

noted below her right eye with beaded borders. A detailed body examination revealed multiple ice-pick marks on dorsum of hands, feet, extensor aspects of elbows and knees

(**Figure 2**). Scalp hair and eyebrows were sparse without any underlying erythema, scaling and scarring. Her elder daughter (20-year-old) showed multiple milia, hypotrichosis and a few pigmented mole-like papules on face with prominent ice pick marks on dorsum of hands, feet and extensors of limbs. Two of her younger daughters (9- and 6-year-old) showed similar ice pick marks and multiple milia over face, but there were no pigmented papules. There was no skeletal deformity, bluish discoloration of fingers and lips, telangiectasias. One daughter (13-year-old) and both sons were physically normal on examination.

A clinical diagnosis of Bazex-Dupre-Christol syndrome was made keeping in view multiple BCC, follicular atrophoderma, hypotrichosis and hypohidrosis and a positive family history. Histopathology of pigmented papules was consistent with a well-differentiated pigmented basal cell carcinoma (BCC). Genetic analysis could not be done due to non-availability of assays. Surgical excisions of BCCs were done as stage procedure. Patients were advised strict sun protection and a regular follow-up of her daughters so as to identify early malignancy. A detailed genetic counselling was offered to the whole family.

Discussion

Under the terms “basal cell carcinomas, follicular atrophoderma and hypotrichosis,” Bazex *et al.*^{1,2} elaborated in 1964 a new syndrome in six affected members of one family. So far, more than 140 patients have been reported. A dominant X-linked mode of inheritance seems more likely as no male-to-male transmission has been reported so far. Almost all daughters of affected fathers are usually affected, but in our family three out of four are suffering and the fourth one is totally normal. The gene for BDCS has been mapped to the distal part of the long arm of chromosome X, in the Xq24-q27.1 region.³ A culprit gene has been proposed, the UBE2A gene, thought to be involved in DNA repair after ultraviolet-induced damage, and which has been mapped to Xq24-q25.³ A large number of families with BDCS originated from Central Europe, mostly from Belgium and France. Our family is the first one to be reported from Subcontinent.^{4,5}

The primary features of BDCS consist of follicular atrophoderma, hypotrichosis, milia, basal cell carcinomas, and hypohidrosis.^{4,5,6} Follicular atrophoderma appears in approximately 80% of patients and may present at birth or appear later. It usually affects the dorsa of the hands and feet, the extensors of the elbows and knees. Few authors had a view that these depressed lesions are not follicular, and should be named “Ice pick marks.” Hypotrichosis is widespread and diffuse, affecting all body regions. It appears in about 85% of patients and may vary in severity.⁷ Hypotrichosis may get confined to the scalp or may also affect the eyebrows; all of our patients had uniform hypotrichosis of scalp and eyebrows. It starts in infancy and tends to improve with age. Hair shaft anomalies have been reported, consisting of pili torti and trichorrhexis nodosa.⁸ On electron microscopy in

one family, cuticular scales were completely absent.⁴ Milia appear in about 70-75% of patients, usually affecting the face, limbs and trunk. These may precede the development of atrophoderma or basal cell carcinomas. Pathologically, in addition to milia, basaloid proliferations have been reported. Calcified cysts and occasionally trichoepitheliomas have also been described.^{7,8} Basal cell carcinomas develop in about 40-50% of patients during the second or third decade of life, but onset may range from 10 to 50 years. Mostly they are localized on the face, and may clinically resemble melanocytic nevi. BCCs may show aggressive behavior and tendency to relapse.^{5,9} Basaloid proliferations described in patients with BDC are basal cell nevi and trichoepithelioma.⁸ Hypohidrosis has been reported in about 55% of patients which may affect only the face or may be widespread. Sweat glands were absent in 9 of 11 patients in one family). Other features less constantly mentioned in patients with BDC are, comedones, keratosis pilaris,⁹ ichthyosis,¹⁰ joint hyperlaxity,¹¹ osteochondritis,¹² deafness, lingua plicata,¹³ and hyperpigmentation of the forehead.¹⁴

The main differential diagnoses in patients of multiple BCCs are Gorlin syndrome, which shows multiple carcinomas basal cell nevi, and X-linked dominant chondrodysplasia punctata, with prominent follicular atrophoderma. Rombo syndrome also resembles BDCS, such as follicular atrophy, milia-like papules, and basal cell carcinomas, but usually shows cyanotic redness of the hands and lips, redness of the face, telangiectasia, build with short trunk and is inherited as an autosomal dominant syndrome.¹⁵ Inoue *et al.*¹⁶ described a family with perioral pigmented follicular atrophoderma, epidermoid cysts and milia, but no patient in this family has developed basal cell carcinomas, unlike BDCS.¹⁶ Oley *et al.*¹⁷ described a possibly new syndrome with basal cell carcinomas, milia and decreased

hair density but now it is accepted that Oley syndrome is in fact BDCS.

Close follow-up is mandatory for patients with BDCS, to allow for early surgical intervention of BCC. Cryosurgery and curettage with electrocautery may be useful in some cases. Imiquimod is helpful for early BCC. Radiotherapy for BCC is not recommended and sun exposure should be strictly avoided. Retinoids may be of benefit in the prevention of skin cancer in BDCS as they have been found effective in Gorlin syndrome. Detailed genetic counselling should be offered to the patients either by the dermatologist or geneticist.

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