Bazex-Dupre-Christol syndrome: A case report

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Bazex-Dupre-Christol (BDC) syndrome is clinically characterized by multiple basal cell carcinomas of the face that mainly occur during the second and third decade of life, follicular atrophoderma predominantly of the dorsum sides of the hands and feet and generalized hypotrichosis; sometimes with pili torti and trichorrhexis nodosa. Features commonly associated with BDC are milia, hypohidrosis and calcifying epithelial tumours. In this study, four members of one family with BDC syndrome, a mother and her three daughters were reported. The major clinical features of BDC were very typical in the mother and one of the daughters whereas only follicular atrophoderma, milia and hypotrichosis were present in the other two daughters. Bazex Dupre Christol Syndrome is a hereditary multiple basal cell carcinoma (BCC) syndrome whose pattern of inheritance is thought to be X-linked dominant, which implies that all daughters of affected mothers should be having this disease. In this case report, among the four daughters, only three were suffering from BDCS while one is totally asymptomatic. Based on the literature review, this appears to be the first report of a family with BDC from Pakistan.

Keywords: basal cell carcinoma, Bazex-Dupre-Christol syndrome, follicular atrophoderma, hypotrichosis

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INTRODUCTION

Bazex-Dupre-Christol (BDG) syndrome is an X-linked dominant multiple basal cell carcinoma (BCC) syndrome, clinically characterized by folicular atrophoderma, multiple milia, hypotrichosis and multiple basal cell carcinomas. Other multiple BCC syndromes include Gorlin and Rombo syndromes. BDC is considered as a primary disorder of the hair follicle by some authors while others consider it as an ectodermal dysplasia. BDC is inherited as an X-linked dominant disorder whose gene has been mapped to Xq24-q27 encoding a protein which is involved in the repair of UV damaged DNA. Since the first description of the syndrome by Bazex in 1964 [1], only few families have been described so far. Herein, a family, a mother and her three daughters, suffering from Bazex-Dupre-Christol syndrome was described.

CASE REPORT

A 45 years old woman from a lower socioeconomic group was presented to us. She has progressively increasing asymptomatic pigmented lesions on her face since the last 20 years. She also complained of decreased hair density on her scalp and eyebrows along with reduced sweating over the upper half of her body. There were no systemic complaints or co-morbidity. She was married to her maternal cousin with four daughters and two sons (Figure 1). She reported similar complaints in three of her daughters except that pigmented lesions were only present on the face of her elder daughter. Clinical examination revealed multiple pigmented papules and nodules (from 0.2 to 2cm in dimension) symmetrically distributed over her face. A darkly pigmented annular plaque was also noted below her right eye with beaded borders. A

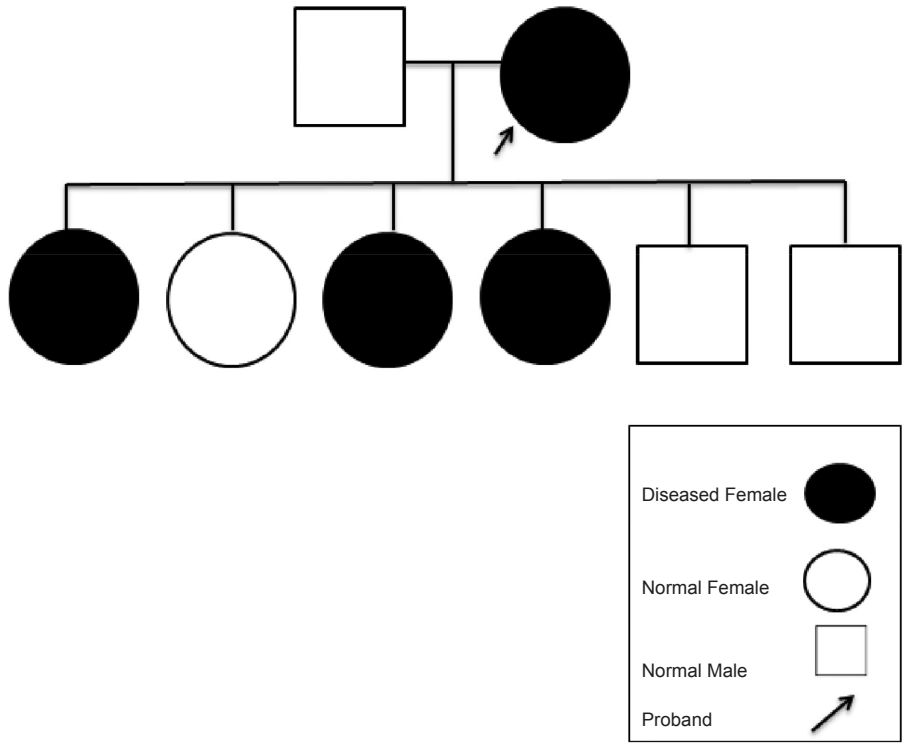

Figure 1. The pedigree of disease inheritance in this family

detailed body examination revealed multiple ice pick marks on the dorsum side of the hands, feet, extensor aspects of the elbow and knee. Hair scalp and eye brows were sparse without any underlying erythema, scaling and scarring. Her family members were called for clinical examinations. Her elder daughter (20 years old) showed multiple milias, hypotrichosis and few pigmented papules on her face with prominent ice pick marks on the dorsum side of the hands, feet and limbs extensor surfaces. Two of her younger daughters (6 and 9 years old) were having similar ice pick marks and multiple milias over their faces, but there were no pigmented papules. There was no skeletal deformity, bluish discoloration of fingers and lips, telangiectasia. One of the daughters (13 years old) and the two sons were physically normal on examination.

The clinical diagnosis of Bazex-Dupre-Christol syndrome was made keeping multiple BCC, follicular atrophoderma, hypotrichosis, hypohydrosis and a positive family history in view. Histopathology of pigmented papules was consistent with a well differentiated pigmented 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 to consider strict protection from the sun and a regular follow-up 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 elaborated in 1964 a new syndrome in six affected members of one family [1,2]. 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. All daughters of affected mothers are usually affected, but in the family used for this study, three out of the four daughters are suffering from the disease while the fourth is physically normal. The gene responsible for BDC 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, which has been mapped to Xq24-q25 [3]. A large number of families with BDCS originated from Central Europe, mostly from Belgium and France. However, to the best of our knowledge,

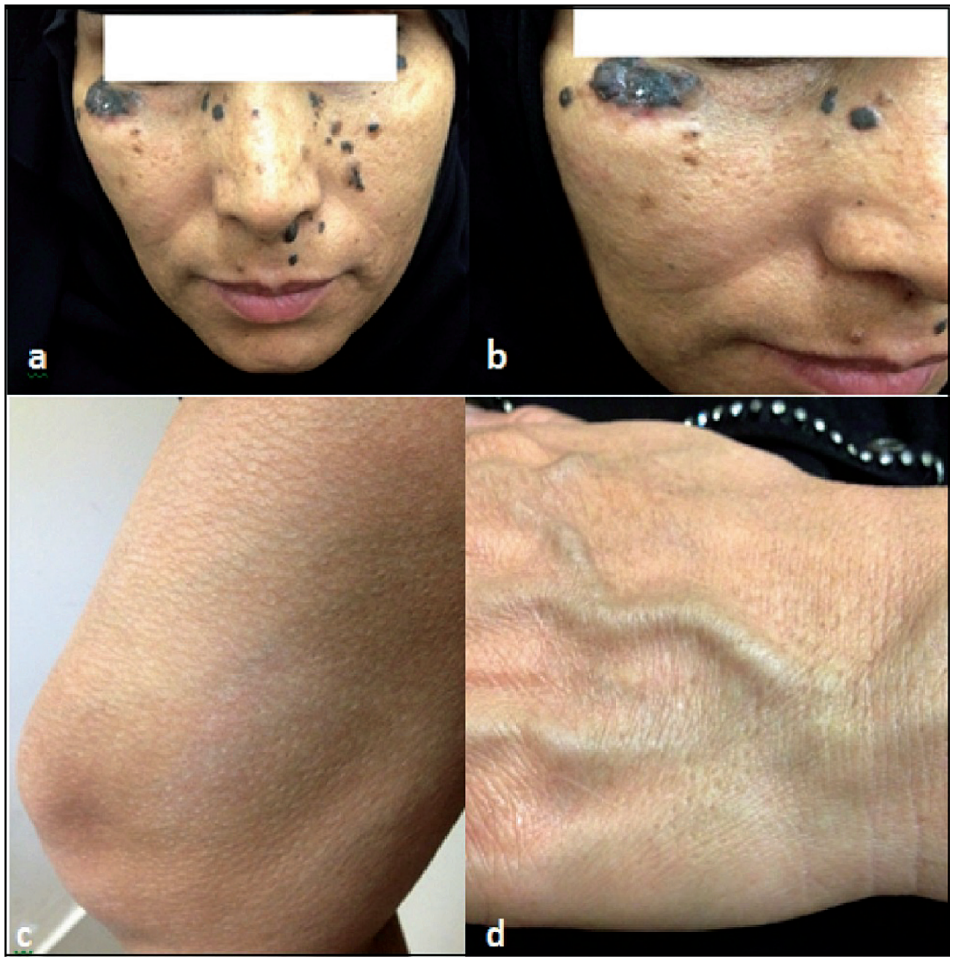

Figure 2. a,b: multiple pigmented BCCs; c,d: follicular atrophoderma of knee and the dorsum of the hand

the family described in this study is the first family reported from the subcontinent [4,5].

The primary features of BDCS consist of follicular atrophoderma, hypotrichosis, milia, basal cell carcinomas, and hypohidrosis [4-6]. Follicular atrophoderma appears in approximately 80% of patients, and may be present at birth or it may appear later. It usually affects the dorsal side of the hands and feet, the extensor surfaces 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 regions of the body. It appears in about 85% of patients and may vary in severity [7]. Hypotrichosis may be confined to the scalp or may also affect the eyebrows; all patients were having uniform hypotrichosis of the scalp and eyebrows. It starts in infancy and has been described to improve with age. Hair shaft anomalies have also been reported, consisting of pili torti and trichorrhexis nodosa [8]. On electron microscopy, cuticular scales were completely absent in one family [4]. Milia appear in about 70-75% of patients, usually affecting the face, limbs and trunk. It has been postulated that milia 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. They are mostly 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]. The presence of hypohidrosis has been reported in about 55% of patients which may affect only the face or may be widespread.

Sweat glands were found to be absent in 9 out 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 with multiple BCCs are Gorlin syndrome, which shows multiple carcinomas basal cell nevi, and X-linked dominant chondrodysplasia punctata, which shows prominent follicular atrophoderma. Rombo syndrome also resemble 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 the family used for this study has developed basal cell carcinomas, unlike BDCS. Oley et al [17] described a possibly new syndrome with basal cell carcinomas, milia and decreased hair density but it is now accepted that Oley syndrome is infact BDCS.

Close follow-up is mandatory for patients with BDCS, to enable early surgical intervention of BCC. Cryosurgery and curettage with electrocautry may be useful in some cases. Imiquimod is helpful for early BCC. Radiotherapy for BCC is not recommended and exposure to the sun should be strictly avoided. Retinoids may be of great 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, wherever available.

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