Linear unilateral hamartomatous basal cell naevus with glandular and follicular differentiation

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Summary

Mosaicismss are characterized by genetic or functional differences between ≥ 2 cell lines in one person, derived from a single zygote. Of the various clinical patterns of cutaneous mosaicism, linear lesions following Blaschko’s lines are probably the most commonly encountered. Several cases of multiple basal cell carcinomas or basaloïd hamartomatous lesions distributed in a segmentary distribution and following Blaschko’s lines have been described. The various terms of ‘linear unilateral basal cell naevus with comedones’, ‘linear unilateral basaloïd follicular hamartoma’, ‘linear unilateral basal cell naevus’, and ‘basal-cell and linear unilateral adnexal hamartoma’ have been used to define this apparently heterogeneous group of disorders. We report a 66-year-old woman with a linear unilateral lesion that appeared during puberty and that histologically showed an adnexal hamartomatous lesion with multiple superficial and nodular basal cell carcinomas. Focal areas of glandular and follicular differentiation were also noted. Molecular studies from these lesions ruled out loss of heterozygosity or mutations in patched gene.

Mosaicismss are characterized by genetic or functional differences between ≥ 2 cell lines in one person, derived from a single zygote, and linear lesions following Blaschko’s lines are probably the most commonly encountered pattern. We report a woman with a linear unilateral lesion that first appeared during puberty and that showed an adnexal hamartomatous lesion with multiple superficial and nodular basal cell carcinomas.

Report

A 66-year-old woman was referred to our department for evaluation of an asymptomatic, unilateral and linear lesion on the left arm that had appeared during puberty. Her medical history was not relevant, except for Sjögren’s syndrome. There was no family history of consanguinity and no similar skin lesions or basal cell carcinomas (BCCs) had developed in other members of the family.

On physical examination a solitary linear plaque, 200 × 30 mm in diameter, was found, extending from the outer aspect of the left arm to the elbow and following a segmental distribution (Fig. 1). Within this plaque, several (10–20) erythematous, tiny keratotic and waxy papules, 1–4 mm in diameter, were noted. The rest of the physical examination was unremarkable and no similar lesions were noted elsewhere.

Several skin biopsies were taken from the lesions. The histopathological features of the papular lesions were characteristic of multifocal superficial or nodular BCCs (Fig. 2). In some of these lesions, areas of unequivocal glandular differentiation showing tubular structures with an eosinophilic cuticular border were noted (Fig. 2, inset). The adjacent epidermis and follicular structures showed hamartomatous changes (Fig. 2b). Focal areas showing a superficial and plaque-like proliferation in the

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papillary dermis presenting connections with the overlying epidermis (showing histopathological features resembling a tumour of the follicular infundibulum) were also observed. In another area, a solitary lesion showing histopathological features consistent with a trichilemmoma was also present. Immunohistochemical studies revealed cellular immunoreactivity for epithelial membrane antigen and carcinoembryonic antigen in tubular and glandular structures. Radiological studies excluded the presence of jaw cysts or other associated osseous lesions.

Surgical excision of some lesions was performed. In addition, treatment with an erbium laser was given, and a good clinical response was obtained. No recurrences have been observed after a 2-year follow-up.

We analysed loss of heterozygosity (LOH) using four microsatellite markers involving and flanking the patched (PTCH) gene on chromosome 9q22.3. DNA from matched normal and lesional tissues was amplified by PCR using the microsatellite markers D9S287, D9S1690, D9S1776 and D9S283 (ABI Prism Linkage Mapping Sets; Applied Biosystems, Foster City, CA, USA) following the manufacturer's instructions. PCR products were analysed by capillary electrophoresis in an automated DNA sequencer (ABI Prism 3100; Applied Biosystems). A heterozygous pattern was obtained for all four microsatellite markers in both lesional and normal skin (Fig. 3), indicating the absence of LOH.

Genomic DNA was isolated from both involved and uninvolved skin. Exons 1–23 of PTCH were amplified with primers described in the PTCH mutation database (http://www.cybergene.se/PTCH/ptch_primer_table.html) and exons 1–12 of the SMO gene were analysed with primers described by Xie et al. Analysis of the exonic and intronic boundary sequences of PTCH and of the smoothened (SMO) gene by PCR and heteroduplex analysis did not show any abnormality in any of the studied samples.

Adnexal tumours or hamartomatous lesions can occasionally show a segmentary or lineal distribution. Several examples of basaloid tumours or basaloid hamartomatous proliferations following Blaschko’s lines have rarely been reported. These include multiple linear trichoepitheliomas, linear infundibulomas, linear unilateral basaloid follicular hamartomas, linear unilateral basal cell naevus with comedones, and basal-cell and linear unilateral adnexal hamartoma. All these adnexal hamartomatous lesions may show an almost identical clinical picture, and only the characteristic histopathological data permit establishment of the diagnosis. Unilateral naevoid BCC syndrome is an uncommon condition clinically characterized by numerous unilateral, papulonodular, yellow or brown lesions arranged in a zosteriform pattern showing the characteristic histopathological features of BCCs. Some authors have suggested that these lesions may correspond to either an hamartomatous non-genetic entity or a segmentary (mosaic) form of a hereditary disorder showing a tendency to develop multiple BCCs, specifically Goltz–Gorlin

Figure 1 Linear plaque, 200 × 30 mm in diameter, with multiple erythematous, shiny and keratotic papules, following Blaschko’s lines.

Figure 2 Slightly acanthotic epidermis showing follicular hamartomatous changes and multiple superficial basal cell carcinomas. H-E × 4. (Inset) Basal cell carcinoma with glandular differentiation. H-E × 10.
syndrome (naevoid BCC syndrome). A patient with a congenital unilateral lesion on the right flank showing histological findings strongly suggestive of BCC has recently been reported. Interestingly, the authors did not find any inactivating mutations of **PTCH** nor activating mutations of **SMO** and they concluded that their case corresponded to a linear basal cell naevus with no link to Gorlin’s syndrome (GS).

Several genetic disorders other than GS, characterized by the late development of multiple BCCs (BCC) in nonexposed areas, have also been reported. Multiple hereditary infundibulocystic BCCs is a rare disorder apparently unrelated to GS. In Bazex–Dupre–Christol syndrome and Rombo, syndrome, the combination of folliculosebaceous hamartomas and BCCs are noted. To our knowledge, no segmentary forms of these disorders have been identified.

Our patient showed linear erythematous lesions following Blaschko’s lines from puberty. The histopathological examination showed multiple superficial and nodular BCCs with occasional unequivocal glandular and follicular differentiation. In addition, adnexal hamartomatous changes in the adjacent epidermis were noted. We consider that this lesion corresponds to an hamartomatous follicular–sebaceous–apocrine lesion showing a tendency to the development of multifocal BCCs. This ‘linear unilateral hamartomatous basal cell naevus’ should be included within the spectrum of other similar lesions reported under the terms ‘linear unilateral basal cell naevus with comedones’, ‘congenital linear unilateral basal cell naevus’ and ‘basal-cell and linear unilateral adnexal hamartoma’. Molecular studies ruled out mutations in the **PTCH** and **SMO** genes, as well as LOH in 9q22.3, thus suggesting that these lesions are probably not genetically related to GS. The possible participation of other genes that are not located in chromosome 9q may be hypothesized.

Further studies are warranted in order to elucidate the pathogenic mechanism implicated in the development of these lesions, and their possible relationship with other hereditary disorders associated with multiple BCCs.

References

