

Becker's Naevus Syndrome with Breast Aplasia Due to Postzygotic Mutation of *ACTB*

Jeanne RAMSPACHER¹, Virginie CARMIGNAC², Pierre VABRES² and Juliette MAZEREEUW-HAUTIER^{1*}

¹Dermatology Department, Reference Centre for Rare Skin Diseases, Larrey Hospital, 24 Chemin de Pouvoirville, FR-31400 Toulouse, and

²French National Reference Centre for Rare Diseases of the Skin and Mucous Membranes of Genetic Origin), Dermatology Department, Dijon University Hospital, Dijon, France. *E-mail: mazereeuw-hautier.j@chu-toulouse.fr

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Becker's naevus (BN) is a common benign lesion with an estimated prevalence of 0.52% and a male predominance (1). BN manifests during childhood, sometimes after a sun rash, as a hyperpigmented well-demarcated unilateral hairy patch, sometimes with papulopustules and comedones, mostly located in the scapular, pectoral and deltoid regions (2). Histologically, BN displays epidermal acanthosis, irregularly dispersed ectopic smooth muscle bundles and increased terminal hair follicles. Becker's naevus syndrome (BNS) is a rare condition reported in approximately 50 cases. It is characterized by a combination of BN with unilateral breast hypoplasia and muscle and skeletal abnormalities (3–5). Mental and development deficiencies, as well as cardiomyopathies, may also be present. Postzygotic mutations in the *ACTB* gene were recently detected in 13 cases of BN and 1 case of BNS (6). We report on a new case of BNS with breast aplasia and postzygotic mutation of *ACTB*.

CASE REPORT

A 17-year-old girl has presented since the age of 11 years with a skin lesion located on the left hemithorax (extending from the breast to the axillary area), associated with severe left breast hypoplasia (Fig. 1). The skin lesion was discrete, made of a light-brown hyperpigmented patch without any skin thickening or hypertrichosis (Fig. 2). Her medical history revealed only atopic dermatitis. Menarches occurred at the age of 13 years and she had regular cycles. Luteinizing and follicle-stimulating hor-



Fig. 2. Hyperpigmented patch without any hypertrichosis or skin thickening.

mones were within normal ranges. An ultrasound scan of the left breast revealed a hypoplastic mammary bud.

Deep next generation sequencing (mean depth: 4,560 reads) of the *ACTB* gene on MySeq (Illumina, San Diego, CA, USA) was performed on DNA from a whole-skin biopsy from the brown patch, without prior microdissection. A postzygotic heterozygous missense *ACTB* variant was detected (chr7:g.5568275G>ANM_001101.3:c.439 C>T p.Arg147Cys, variant allele fraction=4%). No skin biopsy with histological analysis was performed.

DISCUSSION

This is the second reported case of BNS associated with a postzygotic mutation of *ACTB*. *ACTB* encodes beta-actin, an intracellular cytoskeletal molecule, ubiquitously expressed with functions in cell migration, proliferation, signalling, and gene expression (5, 9). Different mutations in *ACTB* have been identified in other conditions (Baraitser-Winter syndrome, juvenile-onset dystonia and neutrophil dysfunction (7–9) that include musculoskeletal abnormalities similar to BNS. The molecular defect responsible for BN and BNS was first identified by Cai



Fig. 1. Hyperpigmented patch of the left hemithorax and marked hypotrophy of the left breast.

et al. (6) in 2017 in 13 cases of BN and 1 case of BNS (clinical presentation similar to our patient). Cai et al. (6) identified 2 recurrent hotspot post-zygotic mutations in the same *ACTB* gene codon: the p.R147C mutation in 11 out of 13 cases of BN and the BNS case, and the p.R147S mutation in the 2 remaining BN.

The current case suggests that BNS is associated with the same recurrent mutation. It also confirms the key role of *ACTB* in the pathophysiology of BNS. Based on laser capture microdissection of tissue from BN and a functional study, Cai et al. (6) hypothesized that *ACTB* mutations associated with BN act in a non-cell autonomous manner, as the mutations were identified only in pilar muscle, but the clinical phenotype involves hyperplasia of the epidermis and hair follicles. BNS may reflect mutation earlier in development, affecting multiple cell lineages compared with isolated BN. The mutation may potentiate Hedgehog signalling, thereby disrupting hair follicle and pilar muscle development.

In conclusion, this new case improves our understanding of this rare syndrome and may contribute to the future development of novel targeted drugs.

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