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# Cutis Tricolor

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*Cutis tricolor is characterized by the coexistence of congenital hyperpigmented and hypopigmented patches in the context of normally pigmented skin. We report the case of a 13-year-old white adolescent girl with cutis tricolor. We analyze other reported cases of cutis tricolor as well as other cases characterized by coexistent hyperpigmented and hypopigmented patches. Cutis tricolor seems to be a rather unique cutaneous manifestation and occurs either in isolation or in association with internal manifestations. Labeling any other case characterized by hyperpigmented and hypopigmented patches as cutis tricolor, regardless of the distribution pattern, is inappropriate in our opinion.*

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Cutis tricolor, first identified in 1997 and found to be possibly associated with extracutaneous abnormalities, is characterized by the coexistence of congenital hyperpigmented and hypopigmented patches in the context of normally pigmented skin.[1] We describe a new case and analyze previously reported cases of cutis tricolor as well as others characterized by long-lasting hyperpigmented and hypopigmented patches.

## Case Report

A 13-year-old white adolescent girl who was otherwise healthy was referred to us for the appearance of brown spots within a white congenital skin lesion. On physical examination a 12×6-cm (approximately rectangular), sharply demarcated, hypopigmented patch was observed on the right lower chest (Figure 1). The patch was obliquely oriented and was composed of several smaller lesions of irregular shape surrounded by a 1- to 2-cm hyperpigmented border. The patch was light pink in color, as in solar erythema, and innumerable light brown, 1- to 3-mm, flat macules, similar to lentigines, were scattered throughout the patch. Both findings relatively spared the central portion of the hypopigmented patch, which allegedly was more protected from the sun. An additional 1×2-cm hypopigmented patch was present on the right anterior abdomen approximately 1 cm from the umbilicus, and a 12×4-cm (nearly rectangular), sharply demarcated, hyperpigmented patch was found on the medial aspect of her right arm. The lesion on the arm was longitudinally oriented and was composed of 2 rhomboidal-shaped and strictly juxtaposed hyperpigmented patches separated by unaffected skin (Figure 2). There were no other notable skin findings and a diagnosis of cutis tricolor was made. She was recommended to engage in careful sun protection and periodic follow-up.

## Comment

Twenty-four cases[1-13] labeled as cutis tricolor were retrieved from the literature using the search terms *cutis tricolor*, *nevus depigmentosus*, *achromic nevus*, *linear and whorled nevoid hypermelanosis*, and *pigmentary mosaicism*, according to a method described

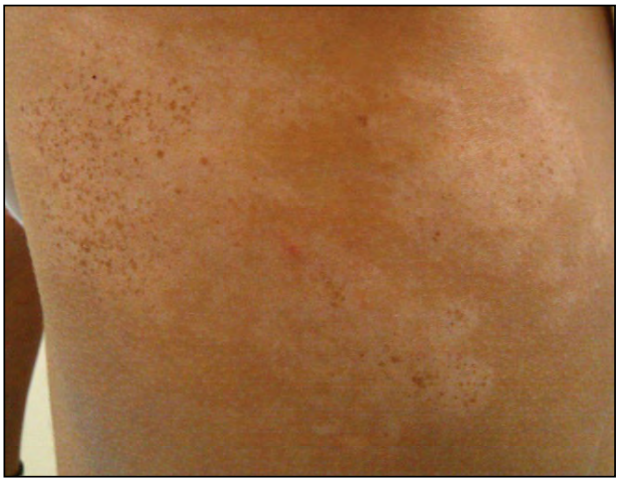

**Figure 1.** Hypopigmented patch on the right chest with visible lentigines in the posterior and anterior portion of the hypopigmented area.

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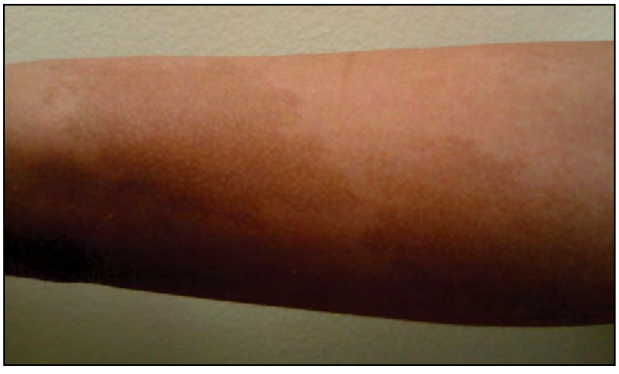

**Figure 2.** Two rhomboidal hyperpigmented patches on the medial aspect of the right arm.

elsewhere.[14] Thirty-one cases of congenital hyperpigmented and hypopigmented patches that were not diagnosed as cutis tricolor also were identified.[15-31] The clinical presentation was highly variable, and regrettably, a complete analysis was not possible, as neither an iconographic nor a detailed written description of the skin lesions was available in several of the patients.[17] At least 4 types of presentation of hyperpigmented and hypopigmented patches were identified: (1) large, grossly polygonal with bizarrely arranged sharp edges, mostly crossing the midline and involving the trunk and proximal extremities (Table 1); (2) blaschkolinear, involving the trunk and/or limbs unilaterally or bilaterally; (3) lateralized and blocklike with midline demarcation; and (4) small irregularly shaped or oval macules, mostly localized on the trunk. These patterns were isolated or specifically associated with a spectrum of similar extracutaneous manifestations. The first variant was observed exclusively in patients with Ruggieri-Happle syndrome; the second and fourth variants were noted in the setting of severe malformations, often with an underlying mosaic state; and the third variant was found in association with a telangiectatic nevus (Table 2).

In the earliest reports, cutis tricolor was framed as a homogeneous condition that was characterized by the presence of large hyperpigmented and hypopigmented patches on a background of normally pigmented skin.[1,5,6] Skin lesions also were found to be associated with characteristic extracutaneous abnormalities. This unique description was named Ruggieri-Happle syndrome after the main authors of the first 2 reports[1,5] and eventually was confirmed to be a congenital and sporadic disorder characterized by multisystem involvement.[3,4] As shown in Table 3, most of the extracutaneous anomalies involve the face, musculoskeletal system, and central nervous system. Additionally, the main cutaneous abnormality was interpreted as the result of allelic twin spotting and therefore represented a skin mosaic. However, the distribution of lesions could not be categorized into one of the prototypical patterns of cutaneous mosaicism (eg, blaschkolinear, blocklike). In fact, lesions consisted of 1 or few large patches that intermingled with other skin areas of different color and featured a quadrangular shape, sharp margins, and some tendency to lateralize, even if the midline often was not respected. More case reports as well as genotypic and phenotypic studies hopefully will help physicians to understand if Ruggieri-Happle syndrome actually is an expression of gene mosaicism.

Eventually, cases characterized by the coexistence of hyperpigmented and hypopigmented patches or macules have been labeled as cutis tricolor, regardless of the distribution pattern over the body. Other similar cases that were reported either before or after the identification of cutis tricolor had been labeled with various and often generic terms, such as *pigmentary anomalies*. However, according to the serendipitous rule that a given type of skin mosaic only follows one mosaic pattern, these cases might have represented different entities from cutis tricolor, as originally described. Hence, cases following a bilateral, narrowband, blaschkolinear pattern are likely a trichromic variant of mosaic hypomelanoses or hypermelanoses, as confirmed by several similar instances reported in the literature under other denominations.[4,5,7,15,18,19,21-24,29,31] However, in 2 cases that were associated with telangiectatic nevi, the hypopigmented lesion was arranged in a blocklike pattern, thus probably representing a full-blown achromic nevus, and contributed to the formation of an unusual variant of phacomatosis pigmentovascularis, as suggested by the authors.[5,13] Lastly, the presence of multiple scattered macules often was a hint of a complex disorder featuring prominent central nervous system abnormalities.[9,16,18,27,30]

Our case seems to belong to the original cutis tricolor pattern. Although the dyschromic lesions were clearly lateralized and somehow followed a mosaic pattern, giving the impression of an incomplete form of blaschkolinear or blocklike pattern, they were composed of oddly arranged, grossly quadrangular patches and had no relation with the midline. The appearance of lentigines on sun-exposed areas of the patch is not surprising, as this phenomenon has been previously reported in hypopigmented nevi.[32] The main hyperpigmented and hypopigmented lesions were similar in shape, size, and orientation, and were localized on distant body parts that faced each other. This mirror image somehow is reminiscent of divided or kissing nevi, involving adjacent portions of 2 mobile body parts so that they are composed of 2 lesions but appear as a single one when such parts are juxtaposed.[33] Also, this peculiar arrangement may further represent evidence that cutis tricolor is caused

Table 1.

## Main Features of True Cases of Cutis Tricolor

| Reference(s) | Age, y | Gender | Hyperpigmented Lesion | | Hypopigmented Lesion | | Other Manifestations |
|---|---|---|---|---|---|---|---|
| | | | Shape | Location | Shape | Location | |
| Happle et al[1]; Ruggieri et al[2]; Lionetti et al[3]; Ruggieri et al[4] | 17 | M | Bizarre, polygonal | Right neck, shoulder | Bizarre, polygonal | Right neck, shoulder | Ruggieri-Happle syndrome |
| Ruggieri et al[2]; Lionetti et al[3]; Ruggieri et al[4]; Ruggieri[5] | 11 | M | Quadrangular patch | Left anterior chest, back, right abdomen, right neck, face | Quadrangular patch | Right chest, neck, shoulder | None |
| | 6 | M | Quadrangular patch | Most of anterior trunk, back, proximal arms, right lateral thigh, neck, left face | Quadrangular patch | Left chest, most of back, shoulders, buttocks, thighs, left ankle | Ruggieri-Happle syndrome |
| Ruggieri et al[2]; Lionetti et al[3]; Ruggieri et al[4]; Ruggieri et al[6] | 11 | F | Quadrangular patch | Most of arms, left back, abdomen | Quadrangular patch | Most of trunk, posteromedial arms | Ruggieri-Happle syndrome |
| Froes et al[11] | 16 | M | Elongated patch | Right chest, axilla | Elongated patch | Right chest, axilla | None |
| Lionetti et al[3]; Ruggieri et al[4] | 2 | F | "Patches" | Trunk, legs | "Patches" | Trunk, legs | Ruggieri-Happle syndrome |
| | 2 | M | "Linear, patches" | Trunk | "Linear, patches" | Trunk | Ruggieri-Happle syndrome |

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Table 1. (continued)

| Reference(s) | Age, y | Gender | Hyperpigmented Lesion | | Hypopigmented Lesion | | Other Manifestations |
|---|---|---|---|---|---|---|---|
| | | | Shape | Location | Shape | Location | |
| Lionetti et al[3]; Ruggieri et al[4] (continued) | 5 | F | "Macules" | Trunk, legs | "Macules" | Trunk, legs | Ruggieri-Happle syndrome |
| | 8 | M | "Linear, patches" | Trunk, face, legs | "Linear, patches" | Trunk, face, legs | Ruggieri-Happle syndrome |
| | 10 | F | "Patches" | Trunk, arms, legs | "Patches" | Trunk, arms, legs | None |
| | 11 | M | "Bizarre" | Trunk | "Bizarre" | Trunk | Ruggieri-Happle syndrome |
| | 14 | F | "Linear, patches" | Trunk, arms, legs | "Linear, patches" | Trunk, arms, legs | Ruggieri-Happle syndrome |
| | 14 | M | "Patches" | Trunk, arms, legs | "Patches" | Trunk, arms, legs | Ruggieri-Happle syndrome |
| | 17 | M | "Bizarre" | Trunk, face | "Bizarre" | Trunk, face | None |
| | 22 | F | "Macules" | Trunk | "Macules" | Trunk | None |
| Molho-Pessach and Schaffer[13] | NP | NP | Macule | NP | Macule | NP | None |
| Current report | 13 | F | Elongated patch | Right arm | Elongated patch | Right chest | None |

Abbreviations: M, male; F, female; NP, not provided.

Table 2.

**Relationship Between the Morphology of Coexistent Hypopigmented and Hyperpigmented Lesions and Their Associated Manifestations**[1-13,15-31]

| | No. of Cases | | | |
|---|---|---|---|---|
| Clinical Pattern | Isolated | Ruggieri-Happle Syndrome | Telangiectatic Nevus | Other Associations |
| Bizarre polygonal[a] | 4 | 10 | 0 | 0 |
| Blaschkolinear[a] | 8 | 0 | 0 | 22 |
| Blocklike[a] | 2 | 0 | 2 | 0 |
| Multiple macules or patternless | 2 | 0 | 0 | 5 |

[a]At least 1 of the 2 types of patches (hypopigmented or hyperpigmented).

Table 3.

**Extracutaneous Features of Ruggieri-Happle Syndrome**

| |
|---|
| **Facial Abnormalities** |
| Coarse face, asymmetry, dolichocephaly, frontal bossing, orbital bossing, brushy eyebrows, hypertelorism, epicanthus, deep nasal bridge, large bulbus nose, large nostrils, low-set ears, angulated ears, wide philtrum, thick lips, prominent chin |
| **Musculoskeletal Abnormalities** |
| Clinodactyly, short neck, pectus excavatum, small skull, prognathism, mandible defect, j-shaped pituitary fossa, absent arch of the atlas, scoliosis, kyphosis, lordosis, vertebral scalloping, increased pedicles, altered pedicles, osteosclerosis, rib abnormalities, bowing of long bones, leg discrepancy |
| **Central Nervous System Abnormalities** |
| Delayed development, hypotonia, poor coordination, delayed language, epilepsy, hearing defect, abnormal behavior, mental retardation, white matter anomalies |
| **Other** |
| Cardiac ventricle anomalies, cataract |

by didymosis. Didymosis, or allelic twin spotting, is a peculiar phenomenon in which a genotypically heterozygous and phenotypically normal cell raises 2 different homozygous clones after crossover recombination.[34] These clones ultimately cause the appearance of 2 topographically related but clinically different lesions. The sooner this phenomenon takes place, the larger the lesions will be. In our case, we hypothesize that the crossover recombination took place in the embryo right before the arm buds emerged from the embryonic trunk at approximately 4 weeks' gestation. If the event had occurred much earlier, the 2 distant patches would have been in contact close to the posterior midline; if it had occurred later, both patches would have been localized on the same body part. In cases of Ruggieri-Happle syndrome, we noticed that cutis tricolor was large and crossed the midline, thus suggesting that the mosaic mutation, if any, occurred early and also was able to involve internal structures.

## Conclusion

Cutis tricolor, as originally described, is a unique cutaneous manifestation that occurs in isolation or in association with Ruggieri-Happle syndrome. Labeling other cases characterized by hyperpigmented and hypopigmented patches as cutis tricolor is inappropriate regardless of the distribution pattern, unless one accepts the term *cutis tricolor* to define not a specific clinicogenetic phenomenon but a cutaneous sign that may occur in several different instances of mosaicism.[7]

Knowledge of the existence of cutis tricolor among dermatologists and pediatricians as well as the ability to differentiate this rare disorder from other similarly appearing conditions may improve the management of affected patients with earlier diagnosis and treatment.

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