

Celiac disease, phylloid hypomelanosis and autoimmune thyroiditis: a case report

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Pigmentary mosaicism is a term used to encompass all of these different types of pigmentary patterns. Among these mosaic patterns, there have been only a few reports of the phylloid presentation in the literature. On the other hand, autoimmune disorders can be associated with neurocutaneous markers and syndromes. A fifteen-year-old girl was presented for chronic diarrhea and abdominal pain. Her physical examination had determined multiple hypopigmented patches. Finally, she was diagnosed phylloid hypomelanosis together with partial trisomy 13 accompanying celiac disease and autoimmune thyroiditis.

Key words: phylloid hypomelanosis, partial trisomy 13, celiac disease, autoimmune thyroiditis.

Phylloid hypomelanosis (PH) has been described as a neurocutaneous syndrome that is characterized by the phylloid pattern of skin pigmentation associated with development delay or mental retardation¹.

Celiac disease (CD) can be defined as a chronic immune-mediated enteropathy against ingested gluten in genetically predisposed people². Several skin diseases are described in CD patients²⁻⁵. The association of dermatitis herpetiformis and CD is well known²⁻⁴. Here, we present the first case of partial trisomy 13 due to t (X;13) translocation with PH and CD.

Case Report

A 15-years old girl was admitted to the hospital with complaints of chronic diarrhea and abdominal pain for six months. She was the sixth child of a consanguineous couple. There was not a reliable history about her natal and postnatal period. On examination, the patient had a body mass index (BMI) of 17.4, which was at the 3rd-15th percentile. She had coarse facial features and mental retardation. Her neurological and ophthalmological examinations were normal. She had abnormal skin lesions consist of multiple hypopigmented patches

over her trunk and extremities (Figs. 1,2). It was learnt that she had lesions since her birth. Complete blood count showed an iron-deficiency anemia (Hb: 7.7 g/dl, Hct: 25.5 %, MCV: 60 fl, RDW: 17.3 %, RBC: 4240x10³/mm³ and Fe: 23 ug/dl). Ferritin level was detected very low. Vitamin B₁₂, folic acid, hemoglobin electrophoresis, serum electrolytes, transaminases and urinalysis were normal. Her thyroid-stimulating hormone (TSH) (15 mU/L) and her antimicrobial antibodies (180 IU/ml) were high, but her FT3 was 1.6 pg/ml (normal range; 1.9-4.9 pg/ml) and her FT4 was 0.8 ng/dl (normal range: 0.8-1.9 ng/dl). Her thyroid ultrasonography showed widespread hypoechoic areas. She had autoimmune thyroiditis. Anti-gliadin IgA (300 IU/ml) and anti-tissue transglutaminase IgA (125 IU/ml) were positive. Gastrointestinal endoscopy was performed. In duodenal biopsy, total villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytes were observed; these findings were consistent with celiac disease. The human leukocyte antigen (HLA) was positive for HLA DQ2. Magnetic resonance imaging of the brain and electroencephalogram were normal. The patient's IQ according to Stanford-Binet intelligence scale was 62.



Fig.1. Phylloid pattern of hypopigmentation. Oblong macules are noted on the back.



Fig. 2. Phylloid pattern of hypopigmentation. Peculiar leaflike depigmented macules are noted on the leg

There was not abnormality on her dental examination. Bone survey graph was normal. Her chromosomal analysis suggested 46, XX t(X;13) (q13 → qter, qter).

Discussion

Celiac disease is an autoimmune disorder that occurs in genetically predisposed individuals as the result of an immune response to gluten. It is very common especially in the eastern of Turkey⁵. The classic symptoms of CD include chronic diarrhea, abdominal pain, fatigue, weight loss, iron deficiency anemia, and failure to thrive². Several studies have shown a positive association between celiac disease and an increased prevalence of autoimmune thyroid antibodies but not clinically overt disease⁶. Similarly, she had autoimmune thyroiditis associated with CD. Both HLA DQ2 and DQ8 are common both in thyroid disease and celiac disease and patients with overlapping disease are often HLA DQ2 positive⁶. In accordance with literature, in our patient who presented autoimmune thyroiditis together with celiac disease, was HLA DQ2 positive.

Phylloid hypomelanosis is a neurocutaneous disease, and it could be found associated with autoimmune diseases. Until now, the association of PH and CD was not reported. Various forms of pigmentary dysplasias have been described occurring along the lines of Blaschko, in a checkerboard pattern, phylloid pattern, patchy pattern without midline separation and lateralization pattern. Phylloid pattern is characterized by peculiar leaf-like or oblong macules. A strict midline separation is not always present. This pattern is characteristic, although not pathognomonic, of PH⁷. Characteristic skin findings described for PH were present in our case (Figs. 1,2).

The phylloid pattern was delineated as a distinct form of pigmentary mosaicism characterized by an arrangement of pigmentary lesions reminiscent of floral ornaments or art nouveau paintings. This pattern is composed of various elements such as round or oval patches, lesions resembling the asymmetrical leaves of a begonia, large pear-shaped areas or oblong macules^{8,9}. PH has been found to be predominantly associated with abnormalities in chromosome 13^{1,7-9}. PH has autosomal lethal mutation surviving by mosaicism, so-called

genomic mosaicism. Genomic mosaics are generally not inheritable, with the exception of paradiagnostic traits that sometimes show a familial aggregation⁷.

Gonzales-Ensenat, et al.⁹ presented two cases and showed the characteristic phenotypic and cytogenetic features of PH. In the first patient, typical defects such as mental deficiency, syndactyly, and clinodactyly were noted. In second patient, epileptic seizures and mental deficiency were typical features of syndrome. Two of the patients were girls. All typical cases of PH reflecting mosaic trisomy 13 reported to date have been in girls. Exceptional cases of PH in which no trisomy 13 can be found also may occur. In our patient, there was partial trisomy 13 due to t (X; 13) translocation.

The most important differential diagnosis is pigmentary mosaicism of the Ito type. This Blaschko line hypopigmentation may be associated with extracutaneous anomalies⁹. Hypomelanosis of Ito is a clinical umbrella term that includes many different states of mosaicism, whereas PH appears to be an etiologically rather uniform neurocutaneous trait^{7,9}. In our patient the pigmentary disturbance does not follow Blaschko lines. This observation fits with type 3 of Happle's proposed classification of pigmentary patterns associated mosaicism⁷. As in our patient, phylloid pattern (type 3 of Happle's) has leaf-shaped patches of hypo- or hyperpigmentation with a dorsal and ventral midline separation¹⁰.

Patients with PH suffer from mental retardation, absence of corpus callosum, conductive hearing loss, choroidal and retinal coloboma, and craniofacial defects as well as brachydactyly, clinodactyly, camptodactyly or various skeletal anomalies^{7,9}. Our patient had mental retardation with her IQ being 62, but did not have any additional anomalies.

The other differential diagnosis was vitiligo disease. Some authors have described some cases of vitiligo in patients affected by CD. Vitiligo is a specific, common, often heritable acquired disorder characterized by well-circumscribed milky white cutaneous macules devoid of identifiable melanocytes. This disease appears to be more commonly observed in parts of body exposed to the sun and in darker skin types and may develop at any age². In our patient, hypopigmented lesions were seen in

parts of her body not exposed to the sun and were present since birth therefore it was not considered as Vitiligo disease.

In conclusion, the possibility of CD is high in patients with autoimmune diseases and skin diseases. Our patient had classic symptoms for CD. Moreover, the patient had autoimmune thyroid disease and a neurocutaneous syndrome. To the best of our knowledge, she is the first patient with CD and PH. The association of these two diseases have never been reported earlier. Finally, CD should be kept in mind in skin disorders.

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