Do you know this syndrome? *

Você conhece esta síndrome?

Fernanda de Oliveira Viana[1]
Luíza Helena dos Santos Cavaleiro[1]
Clívia Maria Moraes de Oliveira Carneiro[2]
Maraya de Jesus Semblano Bittencourt[3]
Renata Silva Barros[4]
Diana Mendes da Fonseca[1]

RELATO DO CASO

Dermatological examination of a male child, 2 years and 10 months old, revealed brownish macules (some keratosic and interspersed with hypopigmented patches) on the the face and with bleeding papulo-erythematous lesions on the upper lip, together with pinpoint hyperchromic, reddish-brown macular lesions on the abdomen and limbs (Figures 1 and 2). Clinical examination showed significant retardation of growth and development, microcephaly, generalized hypotonia with hyporeflexia, photophobia, hypogonadism and abdominal distension. Head circumference 38.5 cm, chest 38 cm and abdomen 40 cm (Figures 2 and 3). Seizures experienced since birth. Anato-pathological exam of lip lesion showed pyogenic granuloma. Cranial CT scan showed right-sided open-lip schizencephaly, periventricular calcifications, absence of septum pellucidum and dilatation of the lateral ventricles. A brain MRI showed supratential dilatation, schizencephaly, agenesis of the septum pellucidum and septo-optic dysplasia. Ophthalmologic evaluation: positive and symmetric red reflex, poor response to light and changes in pupillary reflexes. Normal ECG and echocardiogram. Normal karyotype, 46XY. Upper GI endoscopy: sliding hiatal hernia. USG of the scrotum did not find the testicles and epididymis. No ectopic testis. Serology for HIV, herpes, toxoplasmosis and cytomegalovirus (CMV) negative. The clinical and laboratory tests were compatible with the DeSanctis-Cacchione syndrome.

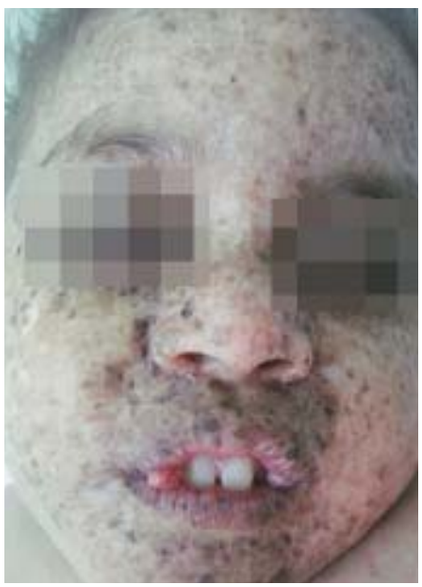

FIGURE 1: Brownish macules (some keratocystic) interspersed with hypopigmented macules on the face. Papuloerythematous bleeding lesion on upper lip

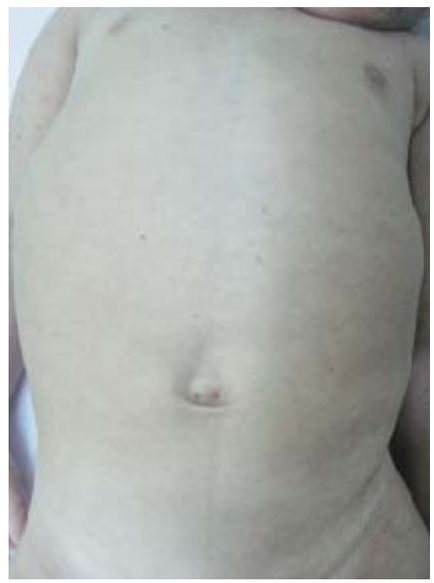

FIGURE 2: Punctiform hypopigmented macules and abdominal distension

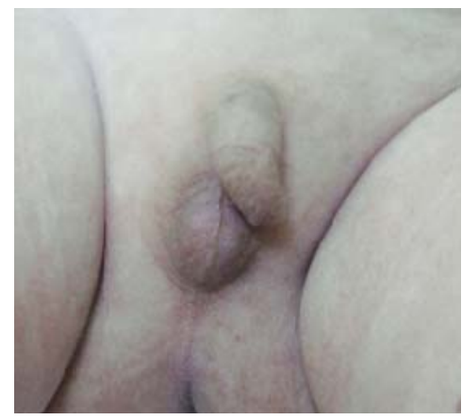

FIGURE 3: Hypogonadism

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[1] Resident of the Dermatology Department, Federal University of Pará (UFPA), Belém (PA), Brazil.
[2] Masters Degree in Tropical Diseases awarded by the Federal University of Pará (UFPA), Adjunct-Professor at Dermatology Department, Federal University of Pará (UFPA), Belém (PA), Brazil.
[3] Masters Degree in Tropical Diseases awarded by the Federal University of Pará (UFPA), MD at the Santa Casa de Misericórdia do Pará Medical Foundation, Belém (PA), Brazil.
[4] Chief Dermatology Resident at the Federal University of Pará (UFPA), Belém (PA), Brazil.

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Viana FO, Cavaleiro LHS, Carneiro CMMO, Bittencourt MJS, Barros RS, Fonseca DM

DISCUSSION

Xeroderma pigmentosum (XP) is a rare autosomal recessive disease (one case in 250,000 births), affecting both sexes and all races. [1,2] It is characterized clinically by erythema with scaling and diffuse hyperpigmentation or freckle-like lesions, especially in sun-exposed areas and usually onsets very early in life. The lesions have a high risk of progression to cancers such as basal and squamous cell carcinoma and melanoma. An even greater risk exists of cancers developing in internal organs such as the lung, kidney and brain. It is believed that XP results from a defect in the process of excision and repair of deoxyribonucleic acid. [2,3] Eight types of XP exist, produced by mutations in different genes: A, B, C, D, E, F, G and V. Subtypes A, B, D, F and G are associated with neurological symptoms.3 The most severe form is represented by the DeSanctis-Cacchione syndrome. This is associated with group A and involves changes in the gene located on chromosome 9q22.3 that encodes DNA damage-binding protein 1. [1,4] In the past, anyone with XP and neurological alterations was described as a carrier of DeSanctis-Cacchione syndrome. This term is currently reserved for patients with XP who have severe neurological disease, dwarfism and immature sexual development. The full syndrome occurs in few individuals, presenting as cutaneous manifestations of XP, microcephaly, progressive mental retardation, delayed physical growth and sexual development, hearing loss, corioatetosis, ataxia and in due course quadriparesis. [1-5] Other manifestations of XP may occur, including epilepsy, deafness, spasticity, hyporeflexia or areflexia, paralysis, brain tumors and changes in the electroencephalogram. [6] Since the lesions of the skin, mucous membranes and eyes reflect the harmful effects of sunlight, involvement of the central nervous system signals the heterogeneity and severity of the disease. In our case we diagnosed schizencephaly, defined as a cleft lined with a layer of thick and richly cellular gray matter, extending from the cortex to the ventricle wall and bilaterally symmetrical. [7] Considered to be a neuronal migration anomaly, the malformation may be associated with subependymal nodular heterotopia, incomplete or absent septum pellucidum and hypoplasia or atrophy of the thalamus. The CT findings described in the DeSanctis Cacchione syndrome above include: cortical atrophy, ventricular dilation, olivopontocerebellar atrophy (OPCA) and microcephaly. [1,8-10] The combination of schizencephaly and XP has not to date been reported in the literature. The prognosis of the syndrome is uncertain. It can be life threatening. No specific treatment exists but the patient should avoid sun exposure and other factors that can cause DNA damage. We describe the case of DeSanctis-Cacchione syndrome in a patient who presented with severe neurological and somatic alteration, highlighting the rarity of this form of XP (with only 60 cases reported in international literature) and the association of schizencephaly with XP, which has not yet been described in the literature. [6] ❑

Abstract: Xeroderma pigmentosum is a rare genetic disease characterized by clinical and cellular hypersensitivity to ultraviolet radiation and DNA repair defects. Patients with xeroderma pigmentosum experience sun-induced cutaneous and ocular abnormalities, including cancer. Some develop neurological disorders. We describe the case of a 2 year-old child with DeSanctis-Cacchione's syndrome, with severe neurological deterioration associated with schizencephaly. In the current clinical classification of xeroderma pigmentosum, the term is reserved for cases with severe neurological disorders linked to dwarfism and immature sexual development. The association of *xeroderma pigmentosum* with schizencephaly has not to date been reported in the literature.
Keywords: DNA repair; DNA repair enzymes; Genes, recessive; Xeroderma pigmentosum

Resumo: Xeroderma pigmentoso é uma rara doença genética que se caracteriza por hipersensibilidade à radiação ultravioleta e defeitos da reparação do DNA, que favorece o desenvolvimento de neoplasias cutâneas e anormalidades oculares. Alguns indivíduos apresentam alterações neurológicas. Descreve-se o caso de criança de dois anos de idade a qual apresentava a síndrome de DeSanctis-Cacchione, com deterioração neurológica grave e associação com esquizencefalia. Na classificação clínica atual do xeroderma pigmentoso, este termo é reservado para casos com graves alterações neurológicas, associados a nanismo e desenvolvimento sexual imaturo. A associação de xeroderma pigmentoso e esquizencefalia ainda foi não relatada na literatura.
Palavras-chave: Enzimas reparadoras do DNA; Genes recessivos; Reparo do DNA; Xeroderma pigmentoso

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Mailing address / Endereço para correspondência:
Fernanda de Oliveira Viana
Rua Tibúrcio Cavalcante – 2777 - Ap 702 -
Dionísio Torres
CEP: 60125101 Fortaleza – CE, Brazil
E-mail: nandinhaviana@hotmail.com

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