

Photosensitivity Skin Disorders in Childhood

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ABSTRACT

Photosensitivity in childhood is caused by a diverse group of diseases. A specific sensitivity of a child's skin to ultraviolet light is often the first manifestation or a clinical symptom of photodermatosis. It might indicate a serious underlying systemic disease such as lupus erythematosus or dermatomyositis, or a rare group of genetic skin disorders like Xeroderma pigmentosum, Cockayne syndrome, Trichothiodystrophy, Bloom syndrome, Rothmund-Thomson and Kindler syndrome as well as metabolic disorders and cutaneous porphyria. Photosensitivity secondary to topical or systemic agents may also cause photosensitivity in children. Early recognition and prompt diagnosis may prevent complications associated with unprotected exposure to sunlight and avoid actinic injuries that can lead to malignant skin changes.

Key words: photosensitivity, skin disorder, childhood

Introduction

Light induced skin eruptions are not a common problem in pediatric dermatology. The incidence of photosensitivity disorders in the pediatric age group is much lower than in adults¹. In contrast to adults, the bulk of photosensitive children are included under the group of metabolic and genetic disorders and pose a diagnostic challenge². Most childhood photodermatoses are sufficiently characteristic that history and examination often suffice to identify a probable diagnosis. A systematic approach with a detailed history of the age of onset, the chronological order of appearance of symptoms associated with clinical examination and investigations are helpful in such cases³. The age of onset of photosensitivity and related skin lesions helps in diagnosis different disorders. Most of the genodermatoses and a few rare types of porphyrias manifest during infancy. Idiopathic photodermatoses usually affect older children. Genodermatoses and metabolic disorders may have associated systemic involvement. Systemic abnormalities such as neurologic dysfunction, mental retardation, and hepatosplenomegaly may be associated features of several photosensitivity syndromes of children⁴.

Classification of photodermatoses

Classification of the photodermatoses is based on the cause of the disorder and on the pathology of cutaneous

response. Observation of the clinical patterns of reactivity of the skin and the timing of the response helps the clinician to classify this disorders⁵. Photodermatoses can be classified into five general categories: 1) immunologically mediated photodermatoses, or idiopathic, including polymorphic light eruption (PMLE), actinic prurigo (AP), hydroa vacciniforme (HV) and solar urticaria (SU); 2) photodermatoses which are secondary to exogenous agents, including phototoxic and photoallergic reactions; 3) photoexacerbated dermatoses, including autoimmune disease, infectious conditions, and nutritional deficiencies; 4) photodermatoses secondary to endogenous agents, mainly the porphyrias; and 5) genodermatoses⁶.

Immunologically mediated photodermatoses (idiopathic)

The immunologically mediated photodermatoses (IMP, previous term: idiopathic photodermatoses) represent a heterogenous group of disorders presenting with pathologic skin reactions caused by optical radiation, particularly in the UVA wavelength region⁷.

Polimorphous light eruption (PLE) is the commonest photodermatosis in childhood, with prevalence of as high as 10–20%. PLE lesions usually appear 2 hours to 3 days following sun exposure and persist for several days or weeks. PLE is characterised clinically by the occurrence of

non-scarring, pruritic, erythematous papules, papulovesicles, vesicles or plaques on sun-exposed skin areas^{8,9}. Currently, a delayed-type immunoreaction induced by ultraviolet radiation (UVR) and maintained by defective immunoregulatory mechanism is proposed as the pathogenesis of PLE¹⁰. A particular type of PLE in 5–12 year-old boys is previously termed „juvenile spring eruption«. Here, recurrent episodes of an itchy papulo-vesicular eruption occur over the helices of the ears, followed by crusting and healing without scarring¹¹. There are no diagnostic laboratory tests available for PLE, thus laboratory examinations are usually performed to exclude other dermatoses such as photosensitive lupus erythematosus or erythropoietic protoporphyria. Persistent plaque-type of PLE must also be differentiated from Jessner-Kanof's lymphocytic infiltration of the skin⁹. Pruritus occurring within hours with the same time course as polymorphous light eruption (PLE) has been described PLE sine eruptione¹².

Solar urticaria is a rare, acute urticarial reaction on both sun-exposed and covered skin areas, which appears soon after exposure to sun or artificial lighting¹³. Typical urticarial wheals appear within seconds to minutes following sun exposure. They generally resolve within 1–2 hours of avoidance of sun exposure¹⁴. Sunlight induced urticaria may be a symptom of erythropoietic protoporphyria (EPP), but the latter starts at an earlier age, family history is often positive and the skin lesions are painful¹⁵. In solar urticaria, the proposed pathogenesis is an immediate-type hypersensitivity reaction. A precursor (chromophore) is activated by electromagnetic irradiation, thus forming a photoproduct (photoallergen). Specific IgE directed against the photallergen is bound to the surface of mast cells¹⁰.

Actinic prurigo (AP) is commoner in girls and manifests by 9–10 years of age as pruritic excoriated papules and nodules on exposed parts. Associated conjunctivitis and actinic cheilitis are characteristic^{8,16}.

Hydroa vacciniforme (HV) is a very rare condition mostly seen among young boys in a sun exposed distribution which tends to heal spontaneously during adolescence^{1,13}. Recurrent crops of vesicles with surrounding erythema appear on exposed body parts within 1–2 days after sun exposure and heal with pock-like scars¹³. HV is a rare childhood disorder mainly induced by UVA. The major differential diagnosis includes EPP, vesicular PLE, AP, Hartnup's disease and bullous LE^{17,18}. PLE, SU, AP and HV have overlapping clinical pictures but can be distinguished easily³.

Photosensitivity secondary to exogenous agents

In general, childhood photosensitization by external chemicals or internal medication is rather rare¹⁹.

Phototoxic dermatitis is caused by external agents either systemic, or topically applied which predictably lower threshold for abnormal UVR (ultraviolet radiation)

responses¹³. In the most common phototoxic dermatitis with erythema, edema and sometimes blisters, the provoking agents in childhood are usually psoralen-containing plants (phytophotodermatitis)^{1,13}. Citrus fruits, lime juice, mango and extracts of a few common weeds containing furocoumarins are common sensitizing agents in school-going children¹³.

Pseudoporphyria is a bullous photosensitivity disorder that clinically and histologically mimics porphyria cutanea tarda (PCT), with no demonstrable porphyrin abnormalities^{20,21}. Pseudoporphyria is clinically characterized by increased skin fragility, erythema, and the appearance of tense bullae and erosions with scarring on sun-exposed skin²¹. Pseudoporphyria is a common side effect with facial scarring of naproxen therapy in children with juvenile rheumatoid arthritis²².

Drug-induced photosensitivity reactions refer to the development of cutaneous disease as a result of the combined effects of a drug and light (mostly spectrum within the UVA and visible light range or UVB range). Drugs such as furosemide, nalidixic acid and quinolones produce often blistering in sunlight²³.

Photoallergic disorders are skin lesions occur following sun exposure, and are characterized by activation of immunological mechanisms, involving photosensitizers and photoallergens that can cause photosensibilization in some individuals¹³. They are less common than phototoxic reactions and are determined by either delayed hypersensitivity responses or more rarely immediate hypersensitivity reactions mediated by IgE in response to UVR. Several therapeutic agents may give rise to both phototoxic and photoallergic reactions. Many disorders develop photoadaptation; thus, the patient and clinician may be misled by the fact that the face is unaffected, but sites only occasionally exposed to the sun are worst affected⁵.

Photoexacerbated / aggravated disorders

The diverse group of photoexacerbated/aggravated disorders occur independently of environmental UVR exposure, but may be worsened by exposure to UVR; such as cutaneous lupus erythematosus (LE) and dermatomyositis^{1,24}. Cutaneous LE is frequently photoaggravated, this is usually associated with positive Ro and La antibodies. These keratinocyte-expressed nuclear antigens are exteriorized by UVR, and cytotoxic antibodies directed against the Ro antigen react directly with the antigen leading to cell death and inflammation. Many patients with LE exhibit a rash identical in morphology to PLE. Thus, the only way of determining whether a patient has PLE is by excluding LE on serology, by checking anti-nuclear antibody (ANA), extractable nuclear antigen (ENA), complement (C3,C4) and by direct immunofluorescence^{25,26}.

Cutaneous porphyrias

Porphyria is a predominantly inherited metabolic disorder, resulting from a deficiency of an enzyme in the heme production pathway and overproduction of toxic heme precursors²⁷. It is the most common inherited cause of photosensitivity, which can arise in childhood²⁸.

Erythropoietic protoporphyria (EPP) is the most common childhood porphyria manifested in early infancy, and usually transmitted in an autosomal dominant manner. A heterogeneous group of mutations in the gene of ferrochelatase has been detected²⁹. Immediate photosensitivity manifest as a painful swelling with erythema, urticaria or blisters healing with scars. With the progression of the disease, characteristic chronic skin symptoms (waxy thickening of the sun-exposed skin and orange peel appearance of the nose) appear³⁰.

Porphyria cutanea tarda (PCT) results from decreased hepatic uroporphyrinogen decarboxylase (UROD) activity. In the majority of patients, the disease is sporadic (S-PCT or type I) and the enzyme deficiency is limited to the liver. The principal clinical manifestation of PCT are cutaneous photosensitivity leading to blistering in areas exposed to sun, skin fragility, hyperpigmentation and hypertrichosis³¹. Familial porphyria cutanea tarda (F-PCT or type II) may arise in the first decade of life, similar to its extremely rare homozygous form called *hepatoerythropoietic porphyria (HEP)*³². F-PCT is observed in 20–30% of patients in whom mutations on one allele of the UROD gene reduce UROD activity by approximately 50% in all tissues³³.

Congenital erythropoietic porphyria (CEP) (CEP, Günther's disease) is an extremely rare autosomal recessive disease, characterized by mutilating cutaneous photosensitivity and abnormal haem synthesis in the bone marrow with reduced activity of uroporphyrinogen III synthase. Clinical manifestations can range from mild to severe and include erythrodontia, reddish-colored urine, and hemolytic anemia that can be mild or severe and may result in splenomegaly³⁴.

All photosensitive children without definitive clinical diagnosis should be evaluated for antinuclear (ANA), anti-Ro(SSA), and anti-La (SSB) antibodies and porphyrin levels. Wood's lamp examination helps in demonstrating erythrodontia in CEP and HEP. Skin biopsy is helpful in idiopathic photodermatoses and porphyrias (deposition of PAS positive porphyrins in a perivascular distribution is characteristic³⁵).

Genophotodermatoses

Hereditary photodermatoses are characterized by an increased photosensitivity caused by an inherited single gene defect. With few exceptions, they manifest in early childhood, reveal heterogeneous clinical symptoms, and are difficult to treat. Although these diseases are rare, it is very important to make an accurate diagnosis on the basis of clinical symptoms, specific diagnostic tests, and direct DNA analysis³⁶. Besides the characteristic skin

symptoms, these disorders are usually associated with an early development of cutaneous and ocular malignancies as well as specific extracutaneous features^{1,19}. Xeroderma pigmentosum (XP), trichothiodystrophy (TTD) and Cockayne syndrome (CS) are rare, inherited neurocutaneous disorders characterized by skin hypersensitivity to sun exposure in association with abnormalities in the nervous system. These autosomal recessive diseases are caused by defects in nucleotide excision repair (NER)³⁷.

Xeroderma pigmentosum (XP) is an autosomal recessive disease, characterized by an abnormal sensitivity to sunlight, freckling, premature skin ageing and multiple neoplasia.

Most patients have a defective NER of UV-damaged DNA due to the lack of specific UV-endonuclease³⁸.

Bloom syndrome (congenital telangiectatic erythema) is a rare autosomal recessive disorder characterized by telangiectases and photosensitivity, growth deficiency of prenatal onset, variable degrees of immunodeficiency, and increased susceptibility to neoplasms of many sites and types³⁹. It is caused by a mutation in the gene designated *BLM*, traced to band 15q26.1. The protein encoded by the normal gene has DNA helicase activity and functions in the maintenance of genomic stability⁴⁰.

Rothmund-Thomson syndrome, or poikiloderma congenitale, is a rare autosomal recessive disorder attributed to mutations of the *RECQL4* helicase gene on 8q24. Key features include early photosensitivity and poikilodermatous skin changes, juvenile cataracts, skeletal dysplasias, and a predisposition to osteosarcoma and skin cancer^{41,42}.

Kindler syndrome is an autosomal recessive genodermatosis characterized by poikiloderma, skin atrophy, trauma-induced skin blistering, mucosal inflammation, and photosensitivity. The molecular pathology of Kindler syndrome involves loss-of-function mutations in a newly recognized actin cytoskeleton-associated protein, now known as fermitin family homologue 1, encoded by the gene *FERMT1*⁴³. Although Kindler syndrome is classified as a subtype of epidermolysis bullosa, it has distinct clinicopathological and molecular abnormalities. During infancy and childhood, there is clinical overlap between Kindler syndrome and dystrophic epidermolysis bullosa (EB)⁴⁴.

Conclusion

The initial step in evaluating a photosensitive patient is based on a directed personal and family history. The morphology of the eruption, phototests, and in some patients, photopatch tests are essential in focusing the diagnosis. Skin biopsies and laboratory investigations, such as antinuclear antibody (ANA) panels and porphyrin profiles, may be required to further confirm the diagnosis. Early recognition and prompt diagnosis may prevent complications associated with unprotected exposure to sunlight and avoid actinic injuries that can lead to malignant skin changes.

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FOTODERMATOZE U DJETINJSTVU

SAŽETAK

Pojava fotodermatoza u djetinjstvu može biti uzrokovana različitim grupama bolesti pri čemu je pojačana specifična senzitivnost dječje kože na ultraljubičasto svjetlo često prvi klinički simptom. Kožne promjene mogu biti prvi znak sistemske bolesti kao što je lupus erythematosus ili dermatomiozitis, ili rijetke grupe genetskih bolesti koje uključuju porfirije, xerodermu pigmentosum, Cockayne sindrom, Bloom sindrom, Rothmund-Thomson sindrom, te Kindler sindrom, kao i metaboličke bolesti sa sistemskim manifestacijama. Fotosenzitivnost može biti i posljedica primjenjenog lokalnog pripravka ili sistemskih lijekova. Rano prepoznavanje i brza dijagnoza mogu spriječiti komplikacije kao posljedice nezaštićenog izlaganja sunčevom svjetlu te spriječiti aktiničku ozljedu kože koja može voditi pojavi zloćudnih kožnih promjena.