



Cyanotoxins: a dermatological problem

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SUMMARY

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*Cyanobacteria (blue-green algae), that are common inhabitants of water and terrestrial environments throughout the world, produce a broad spectrum of secondary metabolites – biologically active products that could be toxic (cyanotoxins). Scientific literature data unequivocally showed adverse effects of cyanotoxins on animal and human health, above all their hepatotoxic and neurotoxic activities. However, the cutaneous adverse effects of cyanobacteria and their cyanotoxins are often under-diagnosed, misdiagnosed or under reported together with a long-standing lack of knowledge about it, not only amongst primary healthcare providers, but also amongst dermatologists. The seaweed dermatitis is the first described cutaneous adverse effect that occurred after contact with marine waters in cyanobacterial toxic bloom condition. This acute irritant dermatitis was connected with the benthic marine filamentous cyanobacterium *Lyngbya majuscula* (Gomont) and its toxins (debromoaplysiatoxin, aplysiatoxin and lyngbyatoxin A). Apart from irritant cutaneous adverse effects, the hypersensitivity immune responses were reported as well, i.e. allergic contact dermatitis due to cylindrospermopsin from *Cylindrospermopsis raciborski*. Aside from direct or indirect (airborne dermatitis) local effects of cyanotoxins on the skin and/or mucous membranes, a severe systemic manifestations were also diagnosed, such as hay fever, asthma and generalized urticarial rash, as well as ocular symptoms and signs e.g., itchy edematous eyelids associated with conjunctivitis. Potentially toxic cyanobacteria and their toxins are present in water resources of the Republic of Serbia, which means that an adequate, relevant and more-coordinated monitoring of all water environments is crucial for preventing human exposure to cyanobacteria and their toxins. A significant role in all of these could and should be taken by dermatologists, above all in the identification of the cyanobacterial adverse effect on skin and mucous membranes, as well as in diagnostic allergy testing.*

Key words: Cyanobacteria; Bacterial Toxins; Dermatitis, Contact

INTRODUCTION

Cyanobacteria (blue-green algae) are common inhabitants of water (fresh, brackish, and marine) and terrestrial environments throughout the world. Under favorable conditions, a massive growth of certain cyanobacteria develops, forming a dense biomass on the water surface – cyanobacterial blooms and scums of planktonic species as well as mats and biofilms of benthic species. Cyanobacteria produce a broad spectrum of secondary metabolites – biologically active products, which could be toxic (cyanotoxins). Their adverse effects have been known for more than 120 years, when the farm animals died after drinking water during algal bloom (1).

Since the 1950s, the growing scientific literature data unequivocally showed adverse effects of cyanotoxins on animal and human health. Their hepatotoxic and neurotoxic activities have been well known and published (1-3). The recreational and occupational exposure to freshwater cyanobacteria has also been assessed (4, 5). However, the cutaneous adverse effects of cyanobacteria and their cyanotoxins are often under-diagnosed. Various freshwater microbial agents may cause signs and symptoms that resemble those attributed to contact with cyanobacteria. Thus, an acute illness caused by exposure to cyanobacteria or cyanotoxins in recreational waters could be misdiagnosed (4). Since the majority of cases associated with recreational contact with cyanobacterial blooms (if recognized at all) are present with short termed non-specific signs and mild symptoms, which are mostly self-limited, they are under-reported as well. Moreover, it happens mostly on a small scale (6), that is why the reports hardly reach primary journals (1).

Consequently, there is still a long-standing lack of knowledge regarding cutaneous adverse effects of cyanobacteria and their cytotoxins. This happens not only amongst primary healthcare providers, but also amongst dermatologists. Moreover, even in the leading dermatological textbooks, many details about cutaneous effects of cyanobacteria are rather obscure.

SKIN MANIFESTATIONS

Pruritic skin rashes after recreational or occupational exposure to cyanobacteria in association with exposure to freshwater cyanobacteria and their cytotoxins are infrequently reported. In the medical and scientific literature these are published mostly as anecdotal and case reports (4). Seaweed dermatitis is the first described cutaneous adverse effect, which could be seen after contact with marine waters in cyanobacterial toxic bloom condition. (7, 8). Basically, it is a contact dermatitis (histopathologically verified), with gradual onset of itching and burning and progressing to visible dermatitis with reddening, blistering and deep desquamation, leaving moist, bright red, tender and painful areas over the genital and perianal regions (9). Bathing suits and particularly diving suits tend to aggravate such effects by accumulating algal material and enhancing disruption of cells and liberation of cell content (10).

This acute irritant contact dermatitis was primarily connected with the benthic marine filamentous cyanobacterium *Lyngbya majuscula* (Gomont) and its toxin (debromoaplysiatoxin) (7, 11, 12), and subsequently verified by human skin patch testing. This blue green alga is spread throughout the world in tropical and subtropical estuarine and coastal waters, loosely attached to sea grass, sand and rocky outcrops from intertidal zone to a depth of 30 m (13).

Further research revealed that other dermatotoxins (aplysiatoxin and lyngbyatoxin A), originating from various cyanobacteria might be recreational and occupational health hazard for acute irritant contact dermatitis (14, 13, 11). Other studies also confirmed the potential of cyanobacteria to provoke skin irritation after recreational water exposure, but it turned out to be small, causing mild reaction that resolved without treatment (5, 15).

Apart from irritant cutaneous adverse effects, hypersensitivity immune responses were reported as well, primarily regarding the highly water soluble cyanotoxins from fresh water species of the cyanobacterial genera (*Cylindrospermopsis* from *Cylindrospermopsis raciborskii*). Thus, an irritant, allergic contact dermatitis may also develop (16).

Moreover, the allergic contact type dermatitis due to cutaneous sensitivity to cyanobacterial (Anabaena) pigment phycocyanin was registered in a form of erythematous papulovesicular dermatitis and confirmed by positive skin patch testing (17).

Aside from the direct or indirect (airborne dermatitis) local effects of cyanotoxins on the skin and/or mucous membranes, severe systemic manifestations were also diagnosed, such as hay fever, asthma and generalized urticarial rash (18, 5). Ocular symptoms and signs e.g., itchy edematous eyelids associated with conjunctivitis, are frequently seen (17, 5). Various studies (19-22) support the opinion that cyanobacteria and algae have allergenic potential and act also as inhalant allergens in Type I hypersensitivity reactions.

Most recently, it has been shown that cyanobacterial allergenicity exists in non-toxin-containing parts of these organisms (23).

DIAGNOSIS

Both, the anamnesis and clinical investigation are crucial for the diagnosis, but certain cutaneous tests (*in vivo*) are valuable as well. When positive, epicutaneous patch testing with cyanobacterial extracts confirms respiratory allergy.

Without relevant *in vitro* allergy testing (determination of specific IgE in sera), to confirm other e.g., respiratory allergy, current data (which are primarily based on clinical manifestations and skin tests), lead us to the following questions: to what extent these organisms may influence the human health; does atopy influence the clinical course; whether photo sensitivity or photo allergy present the risk factors (24). Searching for the answers to these questions traces the path, which should be followed.

EPIDEMIOLOGICAL SITUATION IN THE REPUBLIC OF SERBIA

Potentially toxic cyanobacteria are known to be present in water resources of the Republic of Serbia (25). A recent research showed in Vojvodina region (Northern Serbia) freshwater ecosystems a massive occurrences of some, potentially toxic species that belong to the cyanobacterial genera *Microcystis*, *Aphanizomenon*, *Anabaena*, *Oscillatoria* and *Planktothrix*. During the period of investigation, it was detected that these toxins were permanently present in almost all investigated ecosystems. (26).

CONCLUSION

An adequate, relevant and more-coordinated monitoring of all water environments is *conditio sine qua non* for all crucial actions introduced for preventing human exposure to cyanobacteria and their toxins. A

significant role in all of these could and should be taken by dermatologists. They will be the leading actors in identification of the cyanobacterial adverse effects on skin and mucous membranes, as well as in diagnostic allergy testing.

Future epidemiological investigations in this field are important prerequisite for better understanding of the magnitude and seriousness of this problem. Keeping in mind the global climate changes, it is to be expected that the problem of "cyanobacterial contamination" of waters would be more present in the future. In that respect, a proactive global action is necessary.

Conflict of interest

We declare no conflicts of interest.

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