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Psoriasis in the pediatric population: comorbidities with psoriasis

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The clinical picture, management and quality of life assessment in psoriasis in the paediatric population are discussed in another article: Szczegielniak M, Lesiak A, Narbutt J. Psoriasis in the pediatric population: clinical presentation, management and quality of life assessment. Forum Derm 2023; 9(2): 71–74; DOI: 10.5603/FD.a2023.0009

ABSTRACT

Psoriasis is a chronic, non-infectious, immune-mediated inflammatory skin disease with periods of exacerbation and remission. Adult patients with psoriasis are predisposed to developing cardiovascular diseases, metabolic syndrome and its components, type 2 diabetes, and inflammatory bowel disease. In almost one-third of patients, the first symptoms of psoriasis occur in childhood. Early identification of risk factors for comorbidities or their detection at an early stage of progression can reduce the likelihood of their development in adulthood. Psoriasis can adversely affect mental health, quality of life as well as functioning in the school community and peer environment. This paper reviews the current state of knowledge on comorbidities of psoriasis in the pediatric population.

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Keywords: psoriasis, children, comorbidities

INTRODUCTION

Psoriasis is a chronic, non-infectious, immune-mediated disease. In recent years, there has been an increase in the incidence of moderate to severe psoriasis in children. As a systemic inflammatory disease, psoriasis predisposes to the development of comorbidities such as metabolic syndrome, cardiovascular diseases, psoriatic arthritis, inflammatory bowel disease, non-alcoholic fatty liver disease, and coeliac disease, which was confirmed in the adult population. In children and adolescents, studies are still underway to confirm comorbidities or the presence of risk factors for comorbidities of psoriasis in adulthood. Comorbidities of psoriasis are presented in Table 1. Laboratory tests performed on patients with psoriasis are listed in Table 2.

PSORIATIC ARTHRITIS

Psoriatic arthritis (PsA) is included in the spectrum of juvenile idiopathic arthritis (JIA). It represents 6–8% of all JIA. There are two peaks of incidence: in the second and third years of life and in the tenth and twelfth years of life. In 80% of children with PsA, inflammatory changes in the joints precede the appearance of skin lesions by 2–3 years [1–3]. The disease process may involve peripheral joints

Table 1. Comorbidities of psoriasis

Classical diseases comorbid with psoriasis	Psoriatic arthritis
	Inflammatory bowel diseases
	Mental disorders
	Uveitis
	Cardiovascular diseases
	Arteriosclerosis
	Metabolic syndrome
	Non-alcoholic fatty liver disease
	Lymphomata
	Sleep disorders
	Chronic obstructive pulmonary disease
	Osteoporosis
	Coeliac disease
	Parkinson's disease
	Sexual disorders
Treatment-related diseases	Hypertension (cyclosporine)
	Neurotoxicity (cyclosporine)
	Hepatotoxicity (methotrexate)
	Skin cancers (PUVA)
	Dyslipidemia (acitretin)

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Table 2. Laboratory tests performed in patients with psoriasis

Laboratory tests and measurements performed in patients with psoriasis	Complete blood count
	C-reactive protein
	Lipid profile
	Liver tests
	Fasting blood glucose test
	Uric acid
	Arterial blood pressure
	Waist circumference

(asymmetric inflammation of both large and small joints is typical), spinal and sacroiliac joints, and tendon attachments. Isolated inflammation of the fingers is also possible. The most common symptoms reported by patients include morning stiffness, pain, and joint swelling. In younger children, especially girls, the lesions mainly affect single joints, while in older children, especially boys, enthesitis and spinal involvement are more commonly observed [4, 5]. Uveitis may coexist with psoriatic arthritis. It is recommended that the patient be asked about joint pain and mobility problems at every dermatological visit, which may facilitate earlier diagnosis of the disease and the implementation of appropriate systemic treatment as well as improve patients' quality of life and prevent permanent complications [6–8].

METABOLIC SYNDROME IN PATIENTS WITH PSORIASIS

Metabolic syndrome is the co-occurrence of obesity, hypertension, carbohydrate, and lipid disorders. The risk of metabolic syndrome in the adult population is at least twice as high in patients with psoriasis [9–11]. Psoriasis and metabolic syndrome share many pathogenic pathways. Both diseases are associated with chronic inflammation, vascular endothelial dysfunction, and oxidative stress [12–16]. The components of the metabolic syndrome represent a group of risk factors for atherosclerosis, cardiovascular diseases, and type 2 diabetes (T2D). The severity of psoriasis in both adults and children is related to the co-occurrence of metabolic syndrome [17]. Therefore, early diagnosis of the disease and effective treatment of psoriatic lesions can prevent the development of dangerous long-term sequelae and complications in adulthood [18–27].

In a 2017 meta-analysis by Pietrzak et al. [28] involving a total of 965 children with psoriasis, the majority of subjects had reduced HDL cholesterol levels and abnormal fasting blood glucose compared to controls. However, there were no abnormalities in triglyceride levels, waist circumference, or blood pressure values. The occurrence of the above abnormalities does not meet the criteria for the diagnosis of metabolic syndrome but may be an early stage of it or a risk factor for its development in adulthood [29, 30].

In the pediatric population, overweight and obesity are among the most commonly observed metabolic disorders that lead to metabolic syndrome. In recent years, there has been an increase in the prevalence of excess body weight in both adults as well as children, and adolescents. The link between psoriasis and obesity is explained by the presence of chronic inflammation typical of the diseases mentioned. In psoriasis, there are high levels of pro-inflammatory cytokines such as TNF-α, IL-6, IL-1, which leads to stimulation of the hypothalamic-pituitary-adrenal axis and, through this pathway, contributes to the development of central obesity [31–34]. Adipose tissue is hormonally active, which leads to increased production of pro-inflammatory mediators and may contribute to the exacerbation of psoriatic lesions and, according to some authors, be a risk factor for the development of skin lesions [35–39]. The above association was confirmed in a multicentre study among Turkish children with psoriasis and in a study conducted at a center in Padua involving 107 pediatric patients with psoriasis. It was found that the prevalence of overweight or obesity was higher than in the control group and increased with the duration of skin lesions. A multicentre study by Paller et al. also observed an increased prevalence of central obesity in children with psoriasis compared to controls [40–42].

A population-based study by Koebnick et al. [43] and a multicentre study among French children found that obesity often precedes the appearance of the first skin lesions, indicating an increased predisposition of obese children to develop psoriasis. There is also a more severe course of the disease in obese individuals and a poorer response to treatment. Children with psoriasis with comorbid obesity are more likely to have lipid disorders [44]. Weight reduction may improve skin conditions in psoriasis patients [45–48].

ATHEROSCLEROSIS AND CARDIOVASCULAR DISEASES

The clinical manifestations of atherosclerosis become apparent in adulthood, although it is a process progressing from childhood [49, 50]. Inflammatory cells and the mediators they produce both contribute to the development of psoriatic lesions and play a role in vascular endothelial damage and atherosclerotic plaque formation [51–65]. In multicentre studies of psoriasis patients in the adult population, cardiovascular disease was found to be an important source of mortality. This was also confirmed by a UK population-based epidemiological study using the General Practice Research Database [66–76]. A Danish population-based study revealed that patients with severe psoriasis have an increased risk of myocardial infarction [77]. An Iraqi study screening for cardiovascular risk factors in children with moderate to severe psoriasis reported an increased prevalence of overweight, obesity, atherogenic

lipid profile, and hypertension [78]. A US-based analysis of patients hospitalized in the years 2002–2012, which included 4,884,448 children aged 0–17 years, confirmed that childhood psoriasis is associated with an increased risk of cardiovascular disease and its risk factors such as hypertension, obesity, and abnormal glucose tolerance [79]. One study assessed carotid artery intima-media complex (cIMT) thickness in children with psoriasis using ultrasound (US) Doppler. It was found that the cIMT value was significantly higher in the psoriasis group compared to the control group and positively correlated with disease duration and other metabolic disorders, indicating a higher risk of developing early cardiovascular disease [80–84].

HYPERTENSION

Patients with psoriasis are at increased risk of developing hypertension. Moreover, patients with moderate to severe forms of psoriasis tend to have hypertension resistant to hypotensive treatment. Hypertension may be a risk factor for the development of psoriasis, mainly due to patients' use of blood pressure-lowering drugs such as β-blockers [85]. Abnormal activation of inflammatory cells with overexpression of pro-inflammatory cytokines in psoriasis set in motion an immune cascade, leading to vascular endothelial damage, collagen deposition in arteries, vascular stiffening, and the appearance of elevated blood pressure [86–92]. Children with psoriasis also have an increased incidence of hypertension. A study in Italy recruited children with mild to severe psoriasis without concomitant overweight, obesity, or other metabolic diseases. It was found that children with psoriasis had elevated blood pressure values compared to the control group. Patients with psoriasis should be routinely screened for the presence of hypertension [93].

DIABETES

There is an increased prevalence of T2D among adult patients with psoriasis [94–98]. Several meta-analyses revealed that the risk of diabetes is particularly increased in moderate to severe psoriasis [99–101]. Patients with psoriasis were also found to have a higher risk of insulin resistance compared to controls, implying that psoriasis may be a pre-diabetic condition. This justifies the need for screening in children and adolescents with psoriasis, especially with comorbid obesity and overweight [102–105]. The increased risk of glycemic disorders is associated with the systemic inflammatory process present in psoriasis and many common pathogenetic pathways of both diseases [106–109]. Psoriasis can also coexist with T1D [110–113]. The co-occurrence of diabetes and psoriasis was found to accelerate the development of complications in the form of micro- and macroangiopathies. At the same time, blood glucose normalization contributes to the resolution of psoriatic lesions [114, 115].

INTESTINAL DISEASES

Inflammatory bowel diseases (IBDs) such as Crohn's disease and ulcerative colitis often coexist with psoriasis [116–120]. It was found that there was a common pathogenetic link (basis) for the mentioned diseases at the genetic and immunological level and in relation to disturbances in the skin and gut microbiome. In terms of immunology, a particularly important role is played by the elevated levels of IL-17, which largely accounts for intestinal and skin manifestations. The common genetic basis is supported by the *locus* on chromosome 6p21, where psoriasis and inflammatory bowel disease susceptibility genes are located. In recent years, there has been an increase in the incidence of IBD. Crohn's disease and ulcerative colitis are 3–4 times more common in children with psoriasis compared to controls. Follow-up for these diseases in psoriasis patients is recommended, particularly in the case of gastrointestinal complaints, impaired growth, and unintentional weight loss [121–124].

COELIAC DISEASE

Patients with psoriasis are more likely to suffer from coeliac disease. This is due to common pathogenetic mechanisms including an inflammatory background and the presence of shared *loci* for genes [125, 126]. A UK study found that patients with psoriasis have a higher prevalence of the disease. Studies in Italy, the Czech Republic, and India confirmed an increased prevalence of coeliac disease in psoriasis [127–141]. There are also isolated reports that do not confirm the association of psoriasis with coeliac disease or the presence of elevated celiac-specific antibodies, suggesting the need for further follow-up of patients [142, 143]. In light of the evidence presented, it is important to bear in mind the possibility of co-occurrence of psoriasis and coeliac disease and ask patients diagnosed with psoriasis, both adults and children, about the presence of symptoms of the coeliac disease such as the presence of gastric symptoms, as well as iron deficiency anemia and hair loss. Moreover, the level of anti-endomysium antibodies, anti-gliadin antibodies, and anti-tissue transglutaminase IgA antibodies should be checked in these patients, and a gastroenterology consultation should be performed.

NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease (NAFLD) is described by lipid accumulation in hepatocytes in the absence of a history of excessive alcohol consumption. Over the past two decades, NAFLD has become one of the most common chronic liver diseases [144]. Compared to the general population, patients with psoriasis are at increased risk of NAFLD and of developing non-alcoholic steatohepatitis (NASH), as well as cirrhosis and liver fibrosis. In psoriasis, there are increased

blood levels of pro-inflammatory cytokines such as TNF-α, IL-6, IL-17 and of pro-hyperglycemic adipokines, resulting in inflammation, insulin resistance, and thereby an increased risk of NAFLD and, later, NASH [145–150]. Also, comorbidities of psoriasis such as metabolic syndrome, being overweight and obesity can contribute to the development of NAFLD. This disease may exacerbate psoriatic lesions due to secreted pro-inflammatory cytokines. On the other hand, NAFLD is more common in patients with moderate to severe psoriasis and its course is then more severe [151–153]. Several studies revealed that psoriasis is an independent risk factor for liver diseases [154–169]. All patients with psoriasis, including children and adolescents, should have NAFLD screening and be appropriately consulted by a hepatologist to detect the first symptoms early and prevent further liver damage. This relationship should also be borne in mind when selecting systemic therapy in psoriasis.

MENTAL DISORDERS IN PSORIASIS

Chronic and recurrent skin diseases, especially psoriasis, may increase the risk of mental disorders. The co-occurrence of psoriasis with depressive disorders, anxiety disorders, bipolar affective disorder, and schizophrenia was reported. There are numerous reports indicating a higher risk of these disorders in psoriasis than in other skin diseases [170–173]. One center in the USA conducted a long-term follow-up of several thousand children and adolescents under 18 years of age with psoriasis and observed that patients with psoriasis were at significantly higher risk of developing mental disorders compared to controls [174]. A study in a Danish center highlighted that children with psoriasis were at increased risk of developing eating disorders, alcohol abuse, and drug abuse. There was a significant increase in the use of psychopharmacology compared with children without skin lesions [175].

Early onset of the diseases and the associated negative self-perception has a significant impact on personality formation and on increasing the risk of mental disorders in adulthood. The onset of the disease in childhood may have a greater negative impact on mental health than the disease duration. Longer duration of the disease also positively correlates with an increased risk of depressive disorders and reduced quality of life. Early intervention and consultation with a psychologist are important [176–179]. Mental disorders and increased emotional stress play an important role in the development of the first symptoms and the initiation of the onset of the disease, as well as in the occurrence of exacerbations in the course of an already existing disease.

Emotional disorders in the form of increased anxiety, depression, and reduced quality of life are also present in caregivers of sick children [180–184].

CONCLUSIONS

Psoriasis is a systemic process that affects the functioning of the entire body and is not limited to the skin. Many population-based studies proved the association of this disease with an abnormal metabolic profile and other diseases. In a population of children and adolescents with psoriasis, abnormalities in the lipid profile are found in laboratory tests, indicating that psoriasis is an independent risk factor for future atherosclerosis and cardiovascular diseases. The treatment of psoriasis does not only involve conventional medications, but it also requires modifications in the lifestyle and implementation of preventive measures for comorbidities associated with psoriasis. It is important to keep this in mind when taking care of young patients with psoriasis.

Conflict of interest

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