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Changes in the digestive system in patients suffering from psoriasis

Zmiany w przewodzie pokarmowym u chorych na łuszczycę

Literature published in the recent years provides more evidence for psoriasis being a disease which involves the whole organism. In the course of the disease not only the skin, but also numerous cells and internal organs are affected (1, 2, 3, 6-12, 15, 17, 20). Despite long effort of many research teams, the etiopathogenesis of the disease has remained unknown. Among many suppositions about the cause of psoriasis the one put forward at the Third Psoriatic Congress in Stanford deserves special attention. It suggests that the starting point of the disease are kinetic disturbances of the digestive system (15). This system takes part in decomposition, modifications and synthesis of many organic compounds, including lipids, and disturbances of its function can be reflected in all the metabolic routes. In psoriatic patients structural and functional abnormalities of the digestive system were found in nearly all its segments (1-4, 6-8, 10, 12, 15, 17, 20).

However, changes revealed in the alimentary tract by means of accessory examinations were hardly ever accompanied by any complications of the system. Long-term observations of a big group of psoriatics carried out in our clinics confirm the absence of subjective symptoms in these patients.

The most common anatomopathologic abnormalities in psoriasis are prelipidophilia and palatal lipidophilia, inflammatory changes in the mucous membrane of the stomach and duodenum (*gastritis chronica superficialis* and *duodentis chronica nature*), as well as changes in the structure of the hepatic lobule and intestinal villi (1, 2, 3, 10, 12, 15, 17, 20).

BOWELS, STOMACH, DUODENUM AND PSORIASIS

To emphasize a close relationship between certain dermatoses and abnormal intestinal absorption Shuster and Marks coined the term of dermatogenic enteropathy (12, 15). The term refers to the following diseases: widespread eczema, exfoliating dermatosis, atopic disease and psoriasis (12, 15). Some studies on intestinal absorption and examinations of the biopsies confirmed the existence of digestive tract disturbances in patients affected by these diseases (2, 3, 6-8, 10, 12, 15, 17, 20).

Cells of intestinal epithelium covering free mucosal villi showed an inhibition of three membranous enzymes activity: leucinic aminopeptidase, nonspecific alkaline phosphatase and adenosinotriphosphatase (12, 15). Histologic examinations revealed partial atrophy of intestinal villi. The degree of exacerbation of intestinal changes was closely correlated with the extent of dermal changes (12, 15). Chapman et al. (12, 15) found in a group of psoriatics the deficiency of aryl hydrocarbon hydroxylase occurring in healthy skin, liver, and mucous membrane of the small intestine. They presume that this deficiency can result from a congenital genetic defect. These findings were not confirmed by Finnen et al. (12, 15). Shuster and Marks believe that psoriatic enteropathy is characterized by fatty diarrhoeas (12, 15). Brenner's team present the view that psoriasis can involve malabsorption syndrome of various severity (12, 15). Kurowska-Madejska in an examined group of male patients found statistically significant decrease of intestinal absorption of fats (12, 15). M i c h a e l s s o n et al. (5) observed that in six patients with psoriasis and one with palmoplantar pustulosis, with discovered gluten intolerance, a gluten-free diet had a remarkable effect on the skin lesions. In 16% out of 302 patients with psoriasis they showed serum antibodies to gliadin-IgA AGA levels above the 90th percentile value of the reference group.

M i c h a e l s s o n et al. In 1995 (6) have observed 33 patients with IgA and IgG antibodies to gliadin, with values above the 90% of the reference values. Patients underwent gastroduodenoscopy and duodenal biopsy. There was a significant correlation both between the biopsy score (degree of intraepithelial lymphocyte infiltration) and the number of intraepithelial gamma/delta $^{++}$ T lymphocytes. The serum IgA AGA levels were significantly correlated with the duodenal biopsy score, the number of intraepithelial gamma/delta $^{++}$ T lymphocytes and the number of CD 3+ intraepithelial T lymphocytes. Most patients had no, or only mild gastrointestinal symptoms.

In 1996 M i c h a e l s s o n et al. (7) have investigated biopsy specimens of duodenal mucosa and skin from 39 patients with psoriasis. They had a pronounced increase of EG2+ cells (positive eosinophils) in their duodenal stroma. Ig E+cells were present in most duodenal specimens, and in some specimens there were > 100 IgE+ cells/section. The number of EG2+ cells was increased in lesional skin, and, in some patients, also in non-involved skin, but there was a more pronounced increase in EG 2 reactivity in the duodenal than in the skin specimens. IgE reactivity was increased both in non-involved skin and was significantly related to the number of IgE-positive cells in the duodenal stroma. Because psoriasis patients have increased numbers of tryptase-positive mast cells not only in involved skin but also in non-involved skin the increased number of EG 2+ and IgE+cells might be linked to mast cells both in the skin and the intestinal tract. The results of this study indicate that the gastrointestinal tract and the eosinophil granulocyte might be involved in psoriasis in a hitherto unknown way.

In 1997 duodental biopsy specimens from 37 patients with psoriasis and 22 patients with irritable bowel syndrome (IBS) were examined by M i c h a e l s s o n et al. (8) regarding the presence of tryptase + mast cells. Patients with psoriasis had 131+58 mast cells/mm^2 (mean+-SD) and those with IBS 28+-18. There were no signs of stromal inflammation except in one psoriasis patients. No relationship was found between degree of severity of psoriasis and number of mast cells. The authors put forward a hypothesis that there are at least two types of abnormalities in the duodenal mucosa in psoriasis, one type that is present in most psoriasis patients and characterized by an increase in mast cells and eosinophils, and another that is present in a subgroup of patients with antibodies to gliadin and an increased number of duodenal intraepithelial lymphocytes. The mechanismus underlying the increase in the number of mast cells and its relevance are not yet known (8).

The coexistence of psoriasis with enteritis, Leśniowski-Crohn's disease and colitis ulcerosa was also described (12, 15). Hartman et al. (12, 15) described a case of psoriatic arthritis with coexisting segmental pseudomembranous inflammation of intestines, chronic diarrhoea, malabsorption syndrome and intestinal pseudoobstruction.

In a study by H e n d e l et at. (2) six of 15 patients with psoriasis had abnormal jejunal histology, with short villi. A xylose excretion test was abnormal in three of these six patients, and in three who had normal jejunal histology. In another study H e n d e l et al.(2) found an increased labelling index with tritia-

ted thymidine in jejunal biopsy specimens from five patients with psoriasis compared with specimens from five control individuals.

Examinations of passive permeability of the small intestine performed by Hamilton et al. (12, 15) using the cellobiose/mannitol differential sugar absorption test showed that urinary recovery of these substances in psoriatics was normal, and cellobiose/mannitol ratio was abnormal in only 7 out of 29 examined patients. The authors thought that passive intestinal permeability of the intestine in most psoriatic patients with atopic dermatosis was normal. In 1991 Humbert et al. (3) examined passive intenstinal permeability using EDTA absorption test marked with Cr and eliminating its metabolites with urine. They showed a statistically significant $p<0.05$) permeability increase in 15 psoriatic patients as compared to a healthy control group.

The role of microorganisms living in the lumen of the digestive tract in the pathogenesis of psoriasis still remains unclear. Soyeur et al. (18) showed in 93% out of 39 examined patients the presence of *Candida albicans* in stool samples. This indicates a possibility of considerable contribution of *Candida* to the colonization of the digestive tract. However, clinical signs of candidiasis were found in none of the examined patients. Similar results were obtained by Kliem (4), who showed the presence of *Candida albicans* in over 80% in stool samples of psoriatic patients.

LIVER AND PSORIASIS

The organ that plays the crucial role in the metabolism of many substances, including lipids, is the liver. Among other processes there occurs synthesis of bile acids, ketones, phospholipids, enzymes, apoproteins, conversion of unsaturated fatty acids into saturated ones. The liver takes part in the synthesis and secretion of very low density lipoproteins (VLDL) and high density lipoproteins (HDL). This organ is also responsible for the elimination of cholesterol and final products of lipid decomposition from the circulatory system (12, 15).

Numerous papers described morphologic changes in the liver in the course of psoriasis (1, 10, 12, 15, 17, 20). Zachariae et al. (20) found frequent occurrence of hepatocyte steatosis, periportal inflammatory infiltrations and focal necrosis in liver biopsies. These changes were markedly more often in psoriatic patients than in the compared control group. The authors suggest that liver lesions can be related to psoriasis despite the presence of additional factors, such as obesity, taking medicines, alcohol abuse. Nyfors and Poulsen (10),

R o e n i g k et al. (17) similarly stated in their prospective projects that psoriatic patients proved all degrees of liver pathology including normal livers, cellular necrosis, fatty metamorphosis, periportal inflammation, fibrosis and cirrhosis. Ruszczak et al. (12, 15) carried out similar studies among the Polish population. In a group of 40 psoriatics they found frequent occurrence of coarse-droplet type fatty degeneration with fatty cyst formation, dystrophic changes, less often they stated the injury of hepatic parenchyma with accompanying inflammatory reaction and in single cases they discovered fibrosis of portal zones of the hepatic lobule. The most intense changes were found in cases of generalized psoriasis. It should be emphasized that liver injury occurred even in patients under 30 years of age. Some authors suggest that psoriasis has its etiopathogenic source in metabolic disturbances of hepatic origin. Dargel (12, 15) points to the fact that hepatic injury is often evidenced by disturbances in serous lipids and lipoproteins. On the contrary, R o e n i g k et al. (17) believe that the liver is often abnormal in psoriatics, but whether these abnormalities are due to psoriasis, an excessive alcohol intake, other diseases, nutritional factors or systemic therapy for psoriasis, especially methotrexate (MTX), it has never been explained.

There is, however, a shortage of accurate enough and repeatable methods estimating liver efficiency. Therefore, in many papers we come across reports on various biochemical abnormalities, which tend to be interpreted as the evidence for some liver damage. As early as in 1940, Incedaye and Ottenstein thought that an increase of lipids level and cholesterol level as well as a decrease of free to esterized cholesterol ratio observed in psoriatics resulted from a disurbance or hepatic esterification function (12, 15). In 1964 Cainnelli and Petruzzelis using the reographic method found a reduction of hepatic blood flow in psoriatic patients (12, 15). Mingrone et al. (12, 15) proved that in psoriasis occurs a raised lipid synthesis in the liver. Its expression is found in an increased incorporation of C14 marked acetylocoenzyme A to hepatic lipids. Zlatkov et al. (12, 15) observed in 60 patients with generalized psoriasis a fall of arachidonic and linolenic acid concentrations, rise of palmitic and stearic acid concentrations and also an increase of hepatic enzymes activity analogous to the changes occurring in fatty degeneration of the liver. A l t m e y e r et al. (1) found that psoriatics are characterized by an acceleration of Tc99 marked albumins elimination from circulation by macrophages resident in the liver and spleen. Macrophages activity got normalized during the treatment with aromatic retinoids. Bienias et at. (12, 15) investigated in patients with generalized psoriasis the effectiveness of the hepatic metabolism reflected by drug biotransformation using the antipyrine test.

The findings sugested an impairment of the hepatic metabolic efficiency reflected by drug biotransformation in psoriatics.

PANCREAS AND PSORIASIS

The pancreas is another vital organ of the digestive tract. It influences, to a considerable degree, the carbohydrate balance in the body, secreting two hormones regulating blood glucose concentration i.e., insulin and glucagon. The first reports on the coexistence of hyperglycemia and psoriasis were published in 1938 by Incedaye, who in 19% examined psoriatics and found an abnormal diabetic curve and in 46% the presence of hyperglycemia (12). Later studies of other authors showed the presence of hyperglycemia in 1.8-5.7% of psoriatic patients (15). Subsequent papers of Jucci et al. stated that in psoriatics diabetes occurs more frequently than in healthy population (15).

No reports concerning extrasecretory function of the pancreas in the course of psoriasis have been found in current literature. Investigations of T o r u n i o w a et al. have shown that in psoriatic patients pancreatic lipase concentrations (EC 3.1.1.3) in blood serum are higher than in analogous healthy control groups (13). Psoriatic patients are known to consume considerable amounts of alcohol (12, 15, 16). Psoriasis appears characterized by an especially disadvantageus cumulation of changes in the liver and pancreas caused by alcohol (15) and active psoriatic process. Heller's investigations have shown that in the group of obese psoriatic patients abusing alcohol acute pancreatitis occurs more often than in the remaining part of the population (15).

For the last few years the Lublin group has carried out the investigations of disturbances of lipid balance in psoriasis. They pointed to the existence of many abnormalities that can indirectly reflect disturbances of hepatocyte function in the course of psoriasis. The decrease in cholesterol and phospholipid concentration connected with HDL fraction appeared essential. Next comes the increase in concentrations of triglycerides and apolipoproteins A and B in the serum (12, 13, 14, 19).

Although many recent reports dealt with the pathogenesis of psoriasis the cause of this disease remains unknown. The results of studies on the functions of the digestive system in the course of psoriasis are unclear and often contradictory. Basing on them it is impossible to definitely confirm or preclude the possibility of alimentary etiopathogenesis of psoriasis. However, numerous reports

on disturbances in the digestive system suggest one should be very careful about using drugs in psoriatics, and especially potentially hepatotoxic ones.

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STRESZCZENIE

Gromadzone od wielu lat obserwacje wydają się wskazywać na to, że łuszczyca jest schorzeniem ogólnoustrojowym. W licznych pracach opisywano współistnienie łuszczycy i różnorodnych nieprawidłowości w budowie lub funkcji narządów wewnętrznych. W niniejszej pracy przedstawiono przegląd piśmiennictwa dotyczący zaburzeń budowy bądź funkcji przewodu pokarmowego w przebiegu łuszczycy. Dane te odniesiono do własnych obserwacji i badań dotyczących występujących w tej dermatozie zaburzeń metabolizmu lipidów, które być może są pośrednim wykładnikiem upośledzenia funkcji przewodu pokarmowego.