ABNORMAL GLYCOSAMINOGLYCAN EXCRETION IN SYRINGOMYELIA PATIENTS

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Syringomyelia is a neurologic disease accompanied by degeneration of the spinal cord. Although this disease was described about 150 years ago its pathogenetic basis is still unknown. Hydrodynamic hypotheses of the pathogenesis of syringomyelia, or those based on the dynamics of the cerebrospinal fluid (CSF) [3, 5, 7, 11, 13], are essentially phenomenologic, and do not explain the primary cause of the disease. The "status disraphicus" which as a rule typifies the syringomyelia patient suggests that investigation of the state of the connective tissue in this disease may be promising. The urinary excretion of glycosaminoglycans (mucopolysaccharides), the main structure-forming components of connective tissue, is a sufficiently informative indicator of its metabolism. Mainly hyaluronic acid and chondroitin sulfate, and to a lesser degree dermatan sulfate and heparan sulfate are excreted [1, 2, 9]. In the mucopolysaccharidoses, rheumatic fever, various types of arthritis, and certain other diseases significant changes take place in glycosaminoglycan excretion [1, 10, 12].

The aim of this investigation was to study excretion of glycosaminoglycans (GAG) in patients with syringomyelia.

EXPERIMENTAL METHOD

The 24-hourly urine specimen was collected from patients and normal individuals (aged from 28 to 50 years). Aliquots of urine (3 ml) were treated with 3 volumes of ethanol containing 0.1 M potassium acetate, mixed, and allowed to stand for 10 min at 4°C. The samples were centrifuged for 5 min at 1500*g*. The supernatant was drawn off and the GAG concentration, as uronic acids, was determined in the residue, consisting of the polymeric fraction of urine, by the reaction with carbazole [4]. Heparin sulfate was used as the standard substance.

EXPERIMENTAL RESULTS

Since the state of the connective tissue and, consequently, GAG metabolism are under hormonal control, and primarily of growth hormone [6, 8], GAG excretion was determined in the course of 1 year. Altogether 128 patients and 109 normal individuals were tested. On average 10-11 patients and 9-10 normal subjects were tested during 1 month, and the latter were chosen so that their age composition corresponded to that of the first group.

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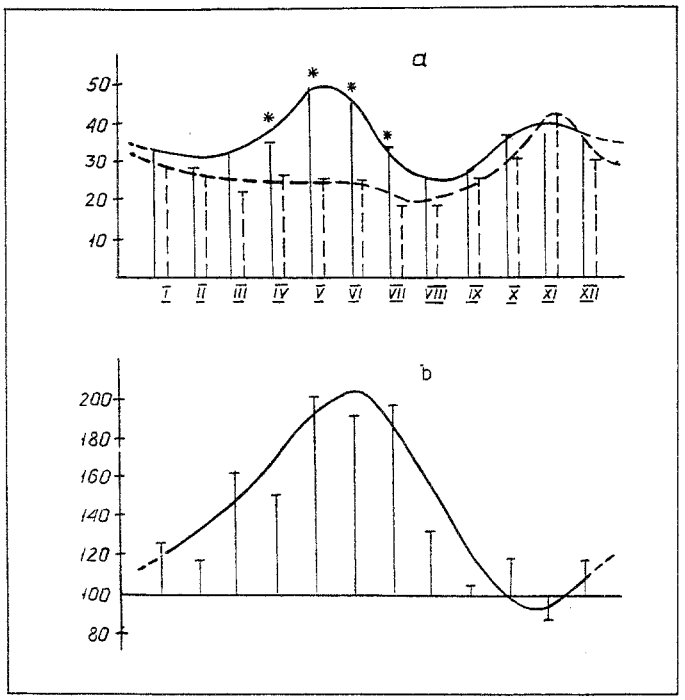

Fig. 1. Glycosaminoglycan excretion of syringomyelia patients (continuous line) and normal individuals (broken line) by months during the year. a: Abscissa, I-XII denotes months (January-December); ordinate, quantity of GAG excreted with urine (in mg/day); b: the same results expressed as percentages of control (normal individuals); *$p < 0.05$.

The results of this investigation are given in Fig. 1a. GAG excretion in healthy individuals is maintained at approximately the same level from March through September, namely 20-25 mg/day, rising to 30-40 mg/day in the fall and winter (October-February). A basically different picture was found in the patients: a sharp rise of GAG excretion in the spring-summer season (March-July; up to 50 mg/day in May-June), which was twice as high as the control level for the same period. The second maximum corresponds to that found in healthy individuals (October-December). The clearest differences in the patients' GAG excretion were observed when the results were expressed as percentages of the control, i.e., of normal individuals (Fig. 1b).

Thus, during most of the year (January-August) the patients excrete significantly more GAG than normal individuals. An increase in GAG excretion is theoretically possible in the following cases: 1) activation of their synthesis, 2) disturbance of their hydrolysis in lysosomes in the presence of a genetic anomaly of the utilization enzymes (for example, in the case of mucropolysaccharides), 3) a decrease in their binding by connective tissue. When the status disraphicus of syringomyelia patients is analyzed, the first of these possibilities must be excluded in this case. The sinusoidal character of the curve of GAG excretion in patients as a function of the season of the year, and the virtually identical level in patients and normal individuals in October-December effectively rule out the second possibility, for GAG excretion is constantly increased in mucopolysaccharidoses. The most likely cause is disturbance of GAG storage in the connective tissue in syringomyelia. The well defined seasonal dependence of GAG excretion by the patients suggests that the effect is mediated through a hormonal anomaly.

The phenomenon thus brought to light brings with it the hope that it will eventually be possible, along this road, to find an approach to the study of the molecular basis of syringomyelia.

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FREE-RADICAL MECHANISM OF THE ANTIMICROBIAL ACTION OF XANTHINE OXIDASE AND LACTOPEROXIDASE

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Human and animal milk contains a group of antimicrobial factors of specific (immune) and nonspecific nature, intended to protect the newly born offspring against bacteria and viral infections [4, 10]. Among the nonspecific antimicrobial factors of milk an important role is played by the enzymes xanthine oxidase (XO) and lactoperoxidase (LP), which are involved in the generation and utilization of active forms of oxygen.

The mechanism of action of LP is based on oxidation of the thiocyanate ion, which is constantly present in milk, with the aid of hydrogen peroxide, with the formation of bactericidal intermediates [7, 10]. XO in milk catalyzes oxidation of xanthine and other purines to uric acid, with the formation of the superoxide anion-radical $O_2^{\cdot-}$. The antimicrobial action of LP [3, 5, 8, 9] and XO [1, 11] on different species of microorganisms has been demonstrated. The possibility of including XO and LP in a single common system, on functional grounds, and of their interaction with antioxidant systems of the pathogenic agents of intestinal infections has not previously been considered.

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