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The levels of C3 and C4 components of the complement in the sera of relapsing-remitting multiple sclerosis patients (RR-MS) treated by 2-CDA (cladribine)

Poziom składnika C3 i C4 układu dopełniacza w surowicy krwi pacjentów z zaostrzająco-zwalniającą postacią stwardnienia rozsianego leczonych 2-CDA (kladrybina)

Multiple sclerosis is a presumed autoimmune disease of the CNS with focal inflammation and demyelination as the major pathological features. The pathogenesis of CNS lesions consists of series of events. The immune mechanisms then occurring involve T cells, macrophages and antibodies. The complement, a complex of plasma proteins, represents a major element in the system of immunity and plays an important role as a mediator of many immune reactions (1, 3, 9). The sera of the multiple sclerosis patients were found to have a normal or reduced level of the C3 and C4 components (5, 8). The reduction seems to be genetically conditioned. Franciotta et al. (2) reported that patients with RR SM had a significantly higher frequency of C4 AQO allele than primary progressive patients. Moreover, a structural gene deletion was present in 45% of RR SM patients with the C4 AQO allele. One should also consider the binding of the complement by the immunological complexes which are always present in the sera of the majority of the multiple sclerosis patients, also in those in remission. The lowest values of the complement components were observed during the attack of the diseases, whereas their increase and stabilization are connected with the period of remission (5, 8).

OBJECTIVE

1. The examination of the levels of C3 and C4 complement components in the blood of the remitting-relapsing multiple sclerosis patients.
2. The evaluation of the changes in the levels of C3 and C4 complement components in the blood of the remitting-relapsing multiple sclerosis patients during immunosuppressive treatment with 2-CDA.
3. The analysis of the levels of C3 and C4 complement components according to the Kurtzke scale (4), duration of the disease and number of attacks.

MATERIAL AND METHODS

The study included 17 patients (14 women, 3 men) with the remitting-relapsing multiple sclerosis. The diagnosis was made on the basis of Pozer criteria (7). The patients were aged 26 to 48, the mean equalled 35.28 ± 6.2. The duration of the disease was from 2 to 22 years, with the mean 9.37 ± 5.67 years; the number of attacks during the disease was 2 to 8, with the mean 4.5 ± 1.88 per person. EDSS before treatment was started equalled 2 to 7 points, with the mean 4.1 ± 2.02 points. All the patients were in the state of remission. They received the immunosuppressant, 2-deoxyadenozine (2-CDA), in doses 0.07 mg/kg/day, administered subcutaneously for 4-6 days. The same course was repeated 6 times, every 5 weeks. The levels of C3 and C4 components of the complement were examined by means of the turbidimetric method in all the patients. The examination was carried out before treatment and after the 1st, 3rd and 6th course of treatment. Statistical analyses were performed using Wilcoxon's rank sum test and Spearman's test.

RESULTS

The assumed clinical norm of the C3 levels in blood serum equals 80-140 mg% (6). In the group under study before treatment with 2-CDA four patients (23.5%) were found with the C3 level below the norm. The assumed clinical norm of the C4 levels in blood serum equals 20-50 mg% (6). In the group under study before treatment with 2-CDA five patients (29.4%) were found with the C4 level below the norm. The table depicts our results. When immunosuppressive treatment with 2-CDA was started in the remitting-relapsing multiple sclerosis patients, the levels of the C3 and C4 components in the patients' sera increased. Most probably this increase occurred immediately after treatment had started, since the highest mean values of the complement components were observed after the first cycle of treatment. In the case of the C4 the difference was statistically

significant (p = 0.002). After the third cycle of treatment the levels of the complement components was also higher than before the treatment (for the C4 the difference was statistically significant and p = 0.05), yet we observed a tendency for the parameters in question to become lower. Between the third and the sixth cycle of the treatment we observed a decrease in the levels of both C3 and C4, yet in the case of the C3 it was statistically significant (p = 0.03), whereas for the C4 it was minimal. Despite some fluctuations in the levels of the complement components during treatment with 2-CDA, the levels of C3 and C4 before the treatment were not essentially different from those after six cycles of the treatment. No statistically significant relationships between the C3 and C4 levels before treatment and the patients' age, duration of the disease, number of attack or punctuation according to the EDSS scale were found. Positive correlation, however, was found between the C3 and C4 levels before the treatment with 2-CDA. In the patients with a low level of the C3 in their sera the level of the C4 was low as well (p = 0.04). After the first cycle of treatment the C3 and C4 levels most obviously increased in the same patients. This relationship appeared statistically significant p = 0.004).

CONCLUSIONS

The multiple sclerosis patients were found to havea decreased level of the complement components, especially C4. The administration of 2-CDA does not cause any change in the levels of the complement components in the sera of multiple sclerosis patients. The stabilisation of the levels of the complement components may reflect the clinical stabilisation of the patients during the examination.

Table 1. The levels of C3 and C4 components of the complement in the sera of RR MS patients treated by 2-CDA (cladribine)

Components of the complement	Mean	Minimum	Maximum	SD
C3 - 0	87.51	63.8	108.0	20.15
C3 - 1	98.03	55.5	118.0	17.29
C3 - 3	95.45	60.1	138.0	22.63
C3 - 6	82.25	55.3	120.0	30.73
C4 - 0	28.85	15.4	47.5	8.10
C4 -1	35.80	15.6	67.9	13.33
C4 - 3	32.39	20.4	54.5	9.16
C4 - 6	31. 23	15.1	52.1	7.51

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STRESZCZENIE

Składowe układu dopełniacza biorą udział w procesie demielinizacji. W pracy przedstawiono poziom składników C3 i C4 układu dopełniacza u chorych ze zwalniającą postacią stwardnienia rozsianego, leczonych lekiem immunosupresyjnym kladrybiną. Stwierdzono stabilizację poziomu składowych dopełniacza po 6-miesięcznych kursach leczenia. Wskazuje to na stabilizację stanu klinicznego pacjentów.