Case Report

Chronic Arthritis Associated with Chromosome Deletion 22q11.2 Syndrome

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ABSTRACT. We describe 3 children with chromosome deletion 22q11.2 and chronic arthritis. The onset of arthritis occurred between the ages of 8 and 17 months. The disease course has been polyarticular in all 3. Neither iridocyclitis nor antinuclear antibody positivity was present. On the basis of the findings in these 3 patients and 9 reported in the literature, chronic arthritis in the 22q11.2 deletion syndrome seems to be characterized by very early onset and severe polyarticular course. Based on our findings the prevalence of chronic arthritis in patients with del 22q11.2 is estimated to be 25-fold compared to that in the general population. (J Rheumatol 2002;29:2648-50)

Key Indexing Terms: CHROMOSOME DELETION

Recently, chronic arthritis has been described in association with the deletion of chromosome 22q11.2. The phenotype of the deletion is variable, but most cases of DiGeorge anomalad and velocardiofacial syndrome have this deletion. The acronym CATCH 22 refers to some of the principal features of the phenotype: cardiac anomalies, abnormal facies, thymic aplasia or hypoplasia (sometimes manifesting as an immune deficiency), cleft palate, and hypocalcemia. More than half of patients have language related learning difficulties. Altogether 9 patients with del 22q11.2 and arthritis have been reported. We describe 3 new patients with this association and review the rheumatological findings of the patients reported previously.

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In the 3 patients, a microdeletion of chromosome 22 was verified by the fluorescent in situ hybridization (FISH) test at the ages of 8 months, 2 days, and 6 months, respectively. The FISH test was negative in the parents of Patients 1 and 2; the parents of Patient 3 have not been tested. The findings with the deletion of chromosome 22q11.2 syndrome in each patient are given in Table 1. For Patients 1 and 2; the parents of Patient 3 have not been tested. The findings related to the del 22q11.2 syndrome in each patient are given in Table 1. For evaluation of immune deficiency, mitogen responses (Patients 1, 2, and 3) and lymphocyte subsets (Patients 1 and 2) were studied, and serum immunoglobulin concentrations were followed sequentially.

Rheumatological findings. Onset of arthritis was at the age of 8 months (Patient 1), 13 months (Patient 2), and 17 months (Patient 3). Pertinent rheumatological findings in our 3 patients and in the 9 patients reported so far are given in Table 2. We also studied patients’ synovial fluid in samples taken in association with intraarticular injections, but found the cell counts were not different from those seen in patients with juvenile idiopathic arthritis (JIA) in general: in knee joint aspirates obtained from the 3 patients the white blood cell counts were 11.1 × 10^12/l (58% mononuclear cells, Patient 1), 6.96 × 10^12/l (51% mononuclear, Patient 2), and 10.2 × 10^12/l (42% mononuclear, Patient 3).

DISCUSSION

The clinical features of arthritis associated with del 22q11.2, summarized in Table 2, are based on findings in 12 patients. The disease set in very early, before 6 years of age in 10/12 patients, and 6/12 had onset in infancy. This contrasts with patients with JIA, in whom onset before the age of 6 years occurs in about 40%. All the patients have shown a polyarticular course, whereas in a 10 year followup study nearly 50% of patients with juvenile rheumatoid arthritis/JIA remained oligoarticular. Iridocyclitis complicates the course of one in 6 patients with JIA, but so far no patient in the small group with del 22q11.2 has been reported to have iridocyclitis. Four of the patients have shown antinuclear antibody positivity and one has been rheumatoid factor positive; these data correspond to those in the JIA population in general.

In a cohort of 80 patients with del 22q11.2, Sullivan, et al. found the frequency of polyarthritis to be 50-fold compared with that in the general population. Our 3 patients represent all the cases with del 22q11.2 and chronic arthritis known to pediatric rheumatologists in Finland, with a population of around one million children under 16 years of age and with a prevalence of JIA of 1:1250. We sent an inquiry to the 7 laboratories using the FISH technique to find del 22q11.2 in this country. During the 6 year period 1994–99, the number of new diagnoses of the 22q11.2 deletion in children below 16 years of age was 98. This gives the estimated prevalence of 2 cases of chronic arthritis in 100 children with del 22q11.2 syndrome (about 1:50). In one of our patients, the diagnosis of del 22q11.2 syndrome was made prior to the study period. Thus, the prevalence of chronic arthritis in...
children with the deletion is about 25-fold that in the general population. Admittedly, the phenotypic variation of the 22q11.2 deletion, which may leave some cases undiagnosed, limits the accuracy of this estimate. The median age at diagnosis of del 22q11.2 was 4 years. The number of live births during the same 6 year period was 363,032. As the majority of the tests are made in early childhood, a prevalence of 1:3700 in Finnish children can be estimated, which corresponds closely to the reported 1:4000 prevalence of 22q11.2 deletion in the general population.

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REFERENCES


