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Cytogenetic Studies of a Patient with Chronic Myelocytic Leukemia and his Nonleukemic Identical Twin

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One of our patients with chronic myelocytic leukemia has a twin brother. The twins, 31 years old, show similar physical appearance. Both have blue eyes, brown hair and are right-handed. Anthropometric measurements and fingerprint patterns are matching. Blood group antigens, serum factors and PTC tasting are identical. Blood group antigens of the parents have also been determined. It has been calculated that the probability that the twins are MZ is higher than 99.8%.

The twins were the result of an uncomplicated pregnancy. There are no other siblings. No family history of consanguinity, hematological disorders or cancer was given. They spent their childhood on a farm. Both have not been exposed to drugs, benzene or radiological procedures, apart from routine X-ray films of the chest.

Our patient, who is still working on his farm, had been referred to a hospital in June 1959, because of a knife wound of the chest with a myocardial laceration and pericardial tamponade. White blood cell count at that time was 22 300 with 3% basophils.

In April 1962, the diagnosis of chronic myelocytic leukemia was established. Findings included hepatosplenomegaly, leukocytosis with a marked shift to the left, hyperplasia of granulopoiesis in the bone marrow and diminished leukocyte alkaline phosphatase activity. In the following years the patient was treated with cyclophosphamide, splenic irradiation and busulfan. Busulfan is continued at present at low doses. He is in good conditions and the disease is still in its chronic phase.

The identical twin is an electrician, has had no serious illnesses, and states that he is in perfect health. He is married and has two healthy children. Physical examination in August 1969 revealed normal findings, liver and spleen were not palpable. Hematological data concerning peripheral blood, bone marrow and leukocyte alkaline phosphatase activity were within normal limits.

Cytogenetic studies in the leukemic twin revealed a diploid mode of 46 chromosomes in peripheral blood cells and bone marrow cells. All bone marrow metaphases scorable for G group chromosomes contained a typical Philadelphia chromosome and presented a 46,XY,Ph^1 karyotype. Hypodiploid cells had scattered losses of chromosomes due to preparation.

In the peripheral blood, stimulated with phytohemagglutinin, a minor cell line

was present, showing radiation-induced structural aberrations. These cells, negative for a Philadelphia chromosome, were presumably lymphocytes. The healthy twin was found to have only normal diploid cells in both tissues. Karyotypic analysis revealed a normal male 46,XY complement. In November 1967 and in August 1969 five normal G group chromosomes were observed in 125 and 97 bone marrow metaphases respectively.

Cytogenetic data are now available in seven sets of MZ twins, so far discordant for chronic myelocytic leukemia (Goh and Swisher, 1965; Jacobs et al, 1966; Goh et al, 1967; Woodliff and Onesti, 1967; Lapin and Wolterink, 1968; Kosenow and Pfeiffer, 1969). In all of them a Philadelphia chromosome could only be demonstrated in the leukemic twin. It was absent in all bone marrow cells from nonleukemic cotwins. Therefore it was assumed to be an acquired postzygotic abnormality. However, recently, Hirschhorn (1968) and Tokuhata (1968) reported on two families with high incidence of chronic myelocytic leukemia and Philadelphia chromosome, suggesting an inherited tendency to develop a Philadelphia chromosome. In Hirschhorn's family the Philadelphia chromosome was demonstrated in a male patient with chronic myelocytic leukemia, in his daughter and in two grandchildren, who all three occasionally run a leukocytosis of 12000-15000. Chronic myelocytic leukemia was present in the patients brother, sister and son and two further children show splenomegaly and leukocytosis.

In Tokuhata's family, in three brothers, including a pair of MZ twins, chronic myelocytic leukemia was detected within a span of three months. All three were Philadelphia positive, a daughter of one of the twins showed a normal karyotype in phytohemagglutinin stimulated peripheral blood cells. Unfortunately, other tissues were not investigated. A history of common mutagenic events could not be evaluated.

Concordance rate of chronic myelocytic leukemia in identical twins cannot be determined because the number of studies on twins has been limited. From nine discordant (Goh and Swisher, 1965; Woodliff and Onesti, 1967; Lapin and Wolterink, 1968; Osgood, 1968; Bernard, 1969; Kosenow and Pfeiffer, 1969) and two concordant pairs (Aleksandrowicz and Blicharski, 1960; Tokuhata et al, 1968) reported in the literature, one can only estimate a concordance rate of 18%. Cytogenetic studies on healthy cotwins made by Goh and ourselves (1969) cover periods of 7½ and 10 years. Osgood (1968) has observed a healthy cotwin for 20 years and Bernard (1969) has followed another healthy cotwin for 19 years.

Therefore, long term follow-up examinations are needed as well as further observations of MZ and DZ twins affected with leukemia. And all cases should be reported, whether they are concordant or not.

ADDENDUM

In October 1969 the patient underwent blastic crisis with generally enlarged lymph nodes. Death occurred in November 1969. Analysis of 213 metaphases derived from a direct preparation of lymph node material revealed a hyperdiploid stemline with duplication of the Philadelphia chromosome and a 51, XY, Ph^1, Ph^1, C+, D+, 2F+ karyotype.

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