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Trisomy 18 Mosaicism in a 24-Year-Old White Woman With Normal Intelligence and Skeletal Abnormalities

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To the Editor

Recently, Sarigol and Rogers [1994] reported on a 13-year-old white girl with trisomy 18 mosaicism but with normal intelligence, delayed pubertal development, scoliosis, growth failure, and abnormal thyroid function test results. Their patient was the fourth reported individual (all females) with trisomy 18 mosaicism and normal intelligence. Two of the 4 were diagnosed in the third and fourth decades of life after giving birth to malformed stillbirths [Kohn and Shohat, 1987; Gersdorf et al., 1990]. The third was the mother of a trisomy 18 patient, and chromosome studies showed that the mother had trisomy 18 mosaicism [Beratis et al., 1972]. Thus, there is a paucity of reports of individuals with trisomy 18 mosaicism and normal intelligence.

I would like to report another woman with trisomy 18 mosaicism and normal intelligence but with skeletal abnormalities. She was born at term to 24-year-old parents. There were no complications of the pregnancy, labor, or delivery. At the time of delivery, bilateral 5th finger clinodactyly and proximally placed thumbs were observed but the rest of the physical findings were normal. At age 2 weeks, she developed anemia of unknown cause and required a single blood transfusion. She had no subsequent hematological problems. Thereafter she did well with normal psychomotor development. Her growth throughout childhood was normal as were the onset of puberty and menarche. She wore a back brace with success during adolescence because of scoliosis. At the time of evaluation, she was 24 years old and had graduated from college with a degree in public relations. The family history was unremarkable except for a history of miscarriages (mother had 2 miscarriages) and an older brother (26 years old) who was tall (185 cm [95th centile]) with normal intelligence and facial appearance but who had similar hand findings as his sister. He had received blood transfusions during infancy but the reasons for the transfusions was not known. He was treated for anemia with iron supplements at age 12 and again at 14 years. There were no other relatives with skeletal abnormalities. Recently he developed acute myelocytic leukemia.

Because she was under consideration as a bone marrow transplant donor for her 26-year-old leukemic brother, chromosome breakage studies of her peripheral blood lymphocytes were

undertaken using Mitomycin C. The brother was previously studied cyto-genetically because of his leukemia and hand abnormalities in order to rule out Fanconi anemia. No increased chromosome breakage compared with laboratory controls was observed in the brother or sister. However, several structural and numerical abnormalities were observed in a clone cell line from a bone marrow specimen from the brother, including monosomy 7, t(5;12) (q13;p12), and 2 marker chromosomes.

In general, our patient was a cooperative, intelligent 24-year-old woman in no acute distress. Her height was 175 cm (>97th centile) and her weight was 58.1 kg (60th centile). Her blood pressure was 98/64 mmHg and pulse rate was 76 beats/min. Her facial appearance was normal and similar to that of other family relatives. On physical examination she had bilateral small asymmetric fifth fingers (left shorter than right) with clinodactyly, single flexion creases of fifth digits with underdeveloped middle phalanges, bilateral proximally placed thumbs without a normal range of motion or strength, mild clinodactyly of the first digits bilaterally, fourth and fifth cutaneous syndactyly of toes bilaterally, and a 4 × 8 cm nonraised hyperpigmented area on her left lower back. There was no physical evidence of scoliosis. The remaining physical findings were normal. An ECG was also interpreted as normal. Because of her status as a bone marrow donor (e.g., good HLA match), blood was obtained for laboratory studies, including a complete blood count with differential, blood chemistry tests and, as stated previously, chromosome breakage studies using Mitomycin C. The blood chemistry and hematological tests were normal (e.g., white blood count was 5.5, hematocrit was 33, and platelets were 229,000 and a normal differential). A total of 220 peripheral blood lymphocytes were routinely studied cytogenetically in F10 medium alone for 72 hours and with Mitomycin C (48 and 72 hour exposure using both 20 ng/ml and 50 ng/ml final concentrations). No increased chromosome breakage was found compared with cells analyzed from a control individual grown in the same culture conditions. Interestingly, of the total of 220 cells analyzed from both routine and Mitomycin C exposed cultures, 80 cells (36%) contained an extra number 18 chromosome. A repeat peripheral blood specimen was obtained 10 days later and cultured in F10 medium. Six of these 40 cells were also trisomy 18. No other chromosome abnormalities were observed. She underwent a bone marrow biopsy which showed a normal number of cells with normal maturation with no evidence of tumor and granuloma. The bony trabeculae was also unremarkable. Subsequently, her bone marrow was donated to her 26-year-old brother with leukemia but unfortunately he died following the transplant procedure.

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