A DISEASE WITH IMMUNE DEFICIENCY, SKIN
ABSCESSES, PANCYTOPENIA, ABNORMAL BONE
MARROW KARYOTYPE, AND INCREASED SISTER
CHROMATID EXCHANGES: AN AUTOSOMAL
RECESSIVE CHROMOSOME INSTABILITY SYNDROME?

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Summary A 19-year-old girl is described with microcephaly, short
stature, mental retardation, pigmentation of the skin, and recurrent skin
abscesses over the whole body. Her elder brother and sister both showed
growth and developmental retardation, microcephaly, and anemia. Both
died during childhood. Their parents were first cousins. Laboratory
studies of the proband revealed hyperchromic erythrocytes with an in-
creased HbF content, thrombocytopenia, an impaired mitogenic response
of the PHA-stimulated lymphocytes, and partial impairment of humoral
and cellular immunity. She developed pancytopenia in the terminal stage
of the disease. Cytogenetic studies of the bone marrow revealed 46,XX,
15p+,−18,+mar karyotype, increased chromosomal aberrations and
sister chromatid exchanges, in cultured lymphocytes and skin fibroblasts.
She died at age 20. Thus, the disorder in the patient was deduced as an
unclassified chromosomal breakage syndrome with an apparently auto-
somal recessive inheritance.

Key Words immune deficiency, pancytopenia, preleukemia, autosomal
recessive inheritance, chromosome instability syndrome

INTRODUCTION

The Bloom syndrome, Fanconi anemia and Luis-Bar syndrome are all auto-
somal recessive disorders with an increased tendency towards chromosomal aberrations in cells in vitro (German, 1969). There is a tendency towards malignancy and
immunological disturbances in all three disorders. Clinically and cyogenetically, these syndromes are clearly different from one another, but some unclassifiable cases have been reported in the literature (Marashio et al., 1986; Conley et al., 1986). The present paper deals with a patient with an unclassified chromosomal instability syndrome, with clinical and laboratory features corresponding to some of the Bloom syndrome, Fanconi anemia or Nijmegen syndrome (Weemaes et al., 1981), in addition to intractable skin abscesses, which has not been previously recorded in any of these syndromes.

CASE REPORT

The proband, a girl, was born as the third child of healthy parents who were first cousins, after a pregnancy of 38 weeks and birth weight of 3,200 g. Her elder brother had died of measles pneumonia at age 8 and elder sister of intracranial bleeding at age 7. While alive, both showed microcephaly, growth and developmental retardation, and anemia (brother's RBC, $660-1,660 \times 10^6$/mm$^3$) or pancytopenia (sister's RBC, $1,080 \times 10^6$/mm$^3$; nuclear cell count in bone marrow, $10,375$/mm$^3$). No other details are known of them. Polio vaccination of the proband at 1 year of age was tolerated without sequelae. She appeared healthy until age 6 years, when she developed pyelonephritis and then measles pneumonia. Her growth delay became apparent at around this age. From age 11 years, she suffered repeatedly from severe skin abscesses. At age 15 years, she was hospitalized for the treatment of skin abscesses, but no improvement was noted. When first examined by us at age 19, she measured 140.2 cm (−3.3 # S.D.), weighed 33.9 kg (−2.7 # S.D.) and head circumference 49.5 cm (−3 # S.D.). She had neither teleangiectatic erythema nor photosensitivity. Her skin was oily and dirty (Fig. 1). Staphylococcus epidermidis skin abscesses were seen all over the body, accompanied by numerous scars and irregularly pigmented areas. Her breast and pubic hair development was at the Tanner stage 2. Skeletal abnormalities were not observed. Her IQ was 46. A menarche was age 15. Since then, her menses has been irregular and amenorrhea continued for at least last 2 years.

Laboratory examination of the peripheral blood revealed: RBC, $3,640 \times 10^6$/mm$^3$; Hb, 13.2 g/dl; MCV, 110.4 μm$^3$; MCH, 36.1 pg; MCHC, 32.7%; HbF, 36.0%; WBC, $5,400$/mm$^3$ (band form 4%, segmented granulocytes 41%; lymphocytes, 17%; monocytes, 38%); platelets, $27 \times 10^9$/mm$^3$. The nuclear cell count in the bone marrow was $50 \times 10^9$/mm$^3$ and the M/E ratio The 2.4. megakaryocytes were small and decreased in number. Megaloblastic changes in the erythroblasts and abnormal cells of monocyte and granulocyte lineage (18%) were seen in bone marrow specimens. The colony-formation test was negative.

Normal serum levels included albumin, ferritin, electrolytes, transaminases, zinc, copper, vitamin B$_{12}$ and folic acid. The serum iron level was slightly reduced ($47 \mu g$/dl), whereas serum immunosuppressive acid protein (810 ng/ml) and lysozyme (18.5 μg/ml) were both elevated. Serum thyroid and growth hormone levels were