Position of the Human X Inactivation Center on Xq

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Summary. In three women with a 46,XXq- chromosome constitution, the length of the deletion was expressed as the ratio of the remaining part of Xq to Xp \( \frac{c}{a+b} \). In one of them (KH) this ratio was 0.33, in another (GE) 0.59, and in the third (AP) the ratio fell between these values. The break in KH is more or less on the border of the Q-dark proximal region. A comparison with relevant X-autosomal translocations indicates that the X inactivation center lies near, but not at the border of, the Q-dark and the adjoining bright region (c and d).

Introduction

Therman et al. (1974) proposed the hypothesis that the human X chromosome has an inactivation center situated in the proximal Q-dark region on Xq. A chromosome lacking this segment would be unable to form a Barr body, thus leading to the presence of more than one active X chromosome in the cell, a presumably inviable condition. By comparing three Xq- chromosomes with relatively long deletions with unbalanced X-autosomal translocation chromosomes, we have attempted to limit further the region in which the inactivation center must be localized.

Materials and Methods

Lymphocyte cultures were performed according to a modification of the usual Moorhead technique. The chromosomes were studied with the aid of QFQ and GTG banding. The late-
replicating X chromosome was determined in KH and GE by means of autoradiography. Barr bodies were analyzed in buccal smears stained with acid fuchsin. Measurements of the chromosome segments were done on photomicrographs of Q-banded cells.

**Case Reports**

KH06251 was seen at the age of 20 because of primary amenorrhea. She was 165 cm tall, weighed 68.0 kg, and had pubic and axillary hair. Of the symptoms characteristic of Turner's syndrome, she displayed fourth short metacarpals and cubitus valgus. On laparoscopy she was found to have streak gonads. She also showed slight but definite clitoromegaly. Low hair line, shield chest, and webbed neck were absent. The patient was color-blind.

GE071658 was first seen at the age of 15 years 7 months for evaluation of lack of secondary sexual characteristics and short stature. She had always been shorter than her peers. She was in the seventh grade making C's and D's, having had to repeat several grades. She had had no unusual childhood illnesses and was generally healthy.

Her mother was 21 and her father, 33 at the time of her birth. Birth weight was 3030 g, birth length 45 cm. She was the third of five children; there were no abortions or twins. She had one older and two younger sisters, all of whom had normal secondary sexual development.

When first seen, GE was 137.5 cm tall and weighed 50 kg. Her blood pressure was 120/70. On physical examination she was noted to have a short neck, low posterior hair line, high-arched palate, micrognathia, lymphedema of the dorsa of hands and fingers, and deep-set hyperconvexed nails, and cubitus valgus. She did not have a webbed neck, shield chest, elevated number of pigmented nevi, short IV metacarpal, hearing anomaly, auricle anomaly, cardiovascular anomaly, or hypertension. There was no breast development and evaluation of the heart and lungs was negative. The pelvic examination revealed normal though infantile external genitalia with scant pubic hair, a normal vagina with lack of estrogen stimulation, and a small cervix and uterus. The adnexae were not palpable. The bone age was retarded by over 2 years, and skull X-ray and chest X-ray were normal. Neither an evaluation of the urinary tract nor a check for other anomalies was done.

The results of laboratory studies, including a CBC and blood chemistries, were normal. Fasting blood sugars and standard glucose tolerance tests were normal. Thyroid evaluation was normal, as were the results of urinary 17 ketosteroid determinations. Serum LH and FSH were 61 and 422 mIU/ml, respectively, both elevated for a premenopausal female. Following her evaluation, she was placed on cyclic hormonal therapy, which induced breast development and withdrawal bleeding. She was followed by her referring physician and was not seen again by GES until she was 20 years of age. At that time she was 146 cm tall, and weighed 73 kg. She was normotensive, had obvious breast development, and was working as a baby sitter.

AP210239, who is a laboratory nurse, was seen at the age of 33 because of primary amenorrhea. Unfortunately only one blood sample and a buccal smear were obtained from her. Her height was 160 cm, her weight 53 kg. Results of urography were normal, as were those of skull X-ray studies. The fundi were normal. The breasts were well developed and pubic and axillary hair were normal. The external genitalia were hypoplastic, the uterus of smallish normal size. The ovaries could not be palpated. She had been receiving estrogen-progesteron substitution therapy since the age of 16. It is not known whether the fairly normal development of the secondary sex characteristics and the genitalia was spontaneous or a response to the hormone treatment. Apart from primary amenorrhea, symptoms characteristic of Turner's syndrome, including short or webbed neck, elevated number of pigmented nevi, shield chest, short IV metacarpal or cubitus valgus, were absent in this patient.

**Cytological Observations**

All three patients had the chromosome constitution 46,XXq– and their lymphocytes did not display any significant mosaicism (Table 1). Buccal smears of KH taken on three occasions showed small Barr bodies ranging in frequency from 4%