

Hemifacial Microsomia in a Patient with Klinefelter Syndrome

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A patient with 47, XXY karyotype, *Klinefelter Syndrome*, and *hemifacial microsomia* (unilateral microtia and mandibular hypoplasia) is described. In view of the fact that this is the second reported patient with hemifacial microsomia and a *sex chromosomal abnormality*, the relationship of these two findings is discussed. Appropriate diagnostic work-up of the patient with hemifacial microsomia is reviewed.

Case Report

A male infant weighing seven pounds, four ounces, was born, following an uncomplicated pregnancy, to a 37-year-old GVI PIV Ab1 mother. Although a deformity of the left ear and hypoplasia of the left side of the face were noted at birth, the parents did not seek medical help. The infant was initially cared for by his mother and subsequently was adopted by a maternal aunt, who stated that his early growth and development were normal.

The patient was first seen at the University of Illinois Pediatric Clinic at the age of 11 years for evaluation of his ear deformity. Physical examination at that time revealed a well built, well nourished child with a small deformed left pinna, atresia of the auditory canal, facial asymmetry, hearing loss on the left, and bifid uvula. The penis was small, and the testes were palpated in the inguinal canals. The remainder of the physical examination was normal. The patient was referred

to the Center for Craniofacial Anomalies, Abraham Lincoln School of Medicine, University of Illinois, where the described craniofacial findings were further documented (Figures 1, 2) (Pruzansky, 1969).

The patient was admitted to the University of Illinois Hospital at the age of 12 years for reconstruction of the left ear and bilateral orchiopexy. Laboratory investigations including complete blood count, urinalysis, chest X-ray, blood urea nitrogen, serum creatinine, intravenous pyelogram and voiding cystourethrogram were all normal. Roentgenograms of the spine revealed a spina bifida occulta at L-5. Chromosome evaluation of peripheral blood lymphocytes demonstrated a 47 XXY karyotype in 92 cells analyzed. Testicular biopsy demonstrated a pattern of infantile testes consistent with cryptorchidism. The child was begun on intramuscular testosterone, 200 mg. every four weeks, at the age of 14 years.

The patient was last examined in October, 1976, at the age of 19 years. He was then 5 feet 9½ inches tall and weighed 143 pounds. The left silastic ear was in place. There was mild hypoplasia of the left side of the face similar in degree to that observed on initial examination. Gynecomastia was present. Axillary and pubic hair were present in a normal male distribution. The penis was small. The testes were easily palpable and soft but were less than normal in size. The remainder of the physical examination was normal.

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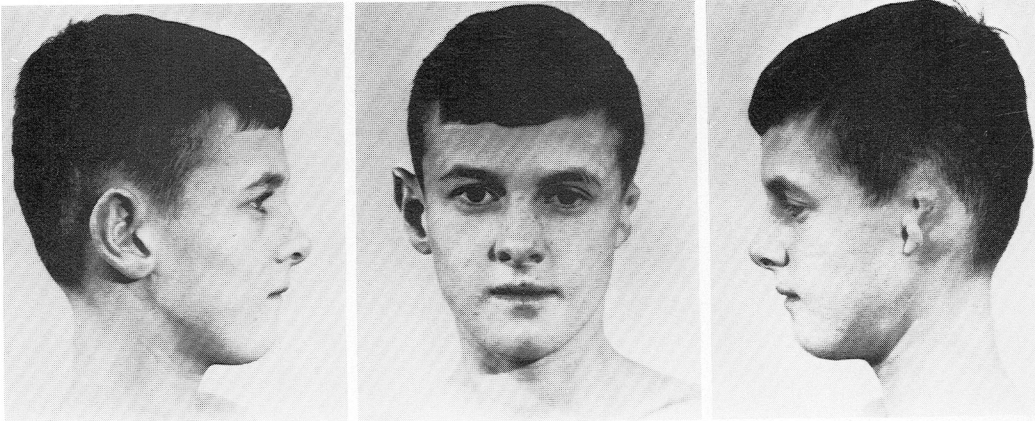


FIGURE 1. Hemifacial microsomia at age 11-8. Note left grade II microtia and minimal asymmetry of lower face.

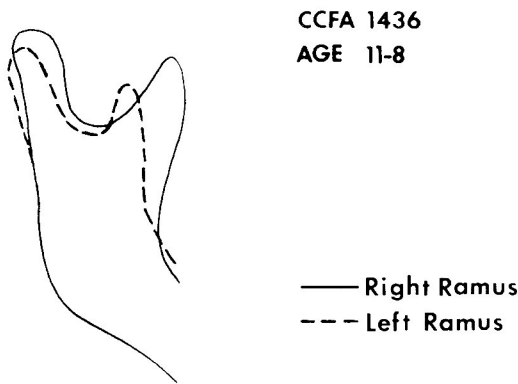


FIGURE 2. To validate the diagnosis, superimposed tracings of the right and left mandibular rami from oriented 45° oblique cephalometric radiographs were made. On the basis of morphology and comparison with the non-affected side, this was rated as a grade I mandibular deformity (Pruzansky, 1969).

Family History

Review of the family history revealed that the paternal grandfather had complete absence of one ear. Both parents and four siblings were normal. There was no other family history of birth defects.

Discussion

Hemifacial microsomia (HFM), a syndrome known by many names and with a wide spectrum of phenotypic variations, generally includes unilateral microtia with malformations of the middle ear, macrostomia, and malformation of the mandibular condyle and ramus. Most cases reported to date have

been sporadic. A recent report from our Center on a large series of cases, however, indicated a high frequency of positive family histories, suggestive of multifactorial inheritance (Kaye, et al., 1979).

The pathogenesis of HFM remains unclear. However, Poswillo's animal experiments (Poswillo, 1973) gave credence to the hypothesis of focal necrosis resulting from hemorrhage in the embryonic circulation. He was able to show destruction of differentiating tissues by an expanding hematoma. The severity of the ensuing malformation syndrome was related to the severity of local destruction.

Kushnick and Colondrillo (1975) reported on an infant with the unique association of the phenotype of HFM and the karyotype of a sex chromosomal abnormality (49, XXXXY). The authors concluded that the association of the chromosomal abnormality and the syndrome of HFM might be fortuitous in their case. The unexpected cytogenetic results in that instance, however, would support the view that chromosome studies should be performed in patients with multiple physical abnormalities, despite the physician's clinical impression of a non-chromosomal condition.

While the present authors are not prepared to support a recommendation for routine cytogenetic studies on all patients with HFM, the justification for doing so in this instance was the presence of an abnormality of the external genitalia which has been associated with abnormalities of the sex chromosomes. A

buccal smear was sex chromatin positive, after which complete chromosomal evaluations were obtained. These revealed the 47, XXY karyotype. The finding of this second patient with a sex chromosome abnormality in association with HFM does not, of course, disprove the hypothesis that the chromosomal abnormality is etiologically unrelated to the malformation syndrome. The concurrence of sex chromosome anomalies and HFM in two reported cases raises the suspicion, however, that the association may have been missed in other instances. It may be prudent, then, to screen such patients by buccal smear, an innocuous and relatively inexpensive test, in order to clarify the role of sex chromosomal abnormalities in the etiology of this clinical entity.

We share the caution expressed by Gorlin, et al. (1976) that terms such as hemifacial microsomia, first arch syndrome, and first and second arch syndrome may impart the erroneous impression that involvement is limited to facial structures when, in fact, other systems are often involved (Rollnick, et al., submitted for publication). In our view, the physician's responsibility is to examine each patient carefully for the presence of other malformations. When they are found, depending on their constellation, appropriate laboratory studies become mandatory to elucidate etiologic factors.

The term hemifacial microsomia (HFM) was given wide currency by Gorlin and Pindborg (1964) when applied to patients with unilateral (a) microtia, (b) macrostomia, and (c) underdevelopment of the condyle and ramus of the mandible. The etiology of HFM is unclear, although pedigrees illustrating both dominant and recessive inheritance have been published. We now report the second patient in whom a sex chromosomal abnormality has been detected in association with the clinical findings of HFM.

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