Abstract
Anophthalmia with anomalies of hands and feet is a distinct syndrome which inheritance is most likely to be autosomal, recessive. A total of 18 families have been reported, male/female ratio was 1:3 and consanguinity was noted in 90% of the families. The most common clinical abnormalities were anophthalmia and foot malformations, which occurred in 90% of patients. Eyelids, eyebrows, eyelashes, and orbits were normal except for some shortness of the palpebral fissures and smallness of the bony orbits. The most common and distinctive foot abnormality was the presence of only four toes bilaterally. A wide gap between the 1st and 2nd toes has also been noted in most cases. Joint laxity, club foot, valgus deformity, hypoplastic fibula, bowed tibia, and hip dislocation were observed in some cases in addition to the other findings. Both hands were affected in 75% of the cases. Basal synostosis of the 4th and 5th metacarpals was the most distinctive abnormality. Camptodactyly affecting the 2nd through 5th fingers was noted in several cases. Postnatal growth delay was noted in half of the patients. Severe mental retardation was also present in half of reported cases.

Keywords
Anophthalmia, hands and feet anomalies, autosomal recessive inheritance, Ophthalmo-acromelic syndrome type Waardenburg

Disease name and synonyms
Ophthalmo acromelic syndrome
Waardenburg Anophthalmia Syndrome (OMIM 206920)

History
Anophthalmia with anomalies of hands and feet as a distinct syndrome was first described by Waardenburg in 1935 (12). Since then a total of 18 families (31 patients from 9 simplex and 8 multiplex families) have been reported (1-12). Six families were from Turkey (2, 8-10-13) suggesting a founder effect. Five families originated from Arabic countries (1, 3, 4, 11), two from Italy (5) and two from continental America (7).

Inheritance
Inheritance is most likely autosomal recessive because there was no example of vertical transmission, male/female ratio was 1.3 and consanguinity was observed in 90% of the families (2,10). Karyotypes were normal in 13 cases.

Clinical description
The most common clinical abnormalities were anophthalmia and foot malformations, which occurred in 90% of patients (2,10). Eyelids,
eyebrows, eyelashes, and orbits were normal except for some shortness of the palpebral fissures and smallness of the bony orbits. Among the four patients without anophthalmia, two had only limb findings and were sibs of the index cases (11, 12). The third had bilateral severe microphthalmia instead of anophthalmia (3), and the fourth had only unilateral mild microphthalmia and limb findings (1).

**Foot abnormalities**
The most common and distinctive foot abnormality was the presence of only four toes bilaterally. A wide gap between the 1st and 2nd toes has also been noted in most cases. Joint laxity, club foot, valgus deformity, hypoplastics fibula, bowed tibia, and hip dislocation were observed in some cases in addition to the other findings (3,7,9).

**Hand abnormalities**
Both hands were affected in 75% of the cases (2,10). Basal synostosis of the 4th and 5th metacarpals was the most distinctive abnormality. Camptodactyly affecting the 2nd through 5th fingers was observed in several cases.

**Facial characteristics**
Most patients had a distinctive facial appearance with prominent forehead, flat maxillary regions, a flat nasal bridge, and flared nostrils. Low-set, posteriorly angulated, over-developed ears with thick lobules were noted in some patients (5,7). Retragnathia, high palate, large incisor teeth, rugated tongue, long philtrum, and thin lips were described in some patients (1,5,7, 9).

**Other abnormalities**
Postnatal growth delay was noted in half of the patients. Severe mental retardation was also present in half of 18 fully reported cases (3,5,9,12).
The only internal abnormality reported was the interruption of the inferior vena cava with azygos continuation (10).

**Prenatal Diagnosis**
Prenatal diagnosis basis in ultrasonography is feasible. Up to now, only one case of Ophthalmo-acromelic syndrome was diagnosed, it was in Turkish family (14).

**References**