Cleft lip and palate is one of the most common human birth defects with an incidence of 1:600 in some racial populations. The purpose of this study was to characterize the phenotypic and molecular features of a novel mutant mouse model, *Twirler* (*Tw*), for studies of clefts of the lip and palate. *Tw* is a semi-dominant mutation that affects the development of the midfacial region. Due to the identification of microsatellite markers at the *Tw* locus on mouse chromosome 18, genotyping of *Tw* mice is possible at all stages of development. We characterized the phenotypic and molecular changes in *Tw* mutant mouse embryos at critical stages of midfacial development by morphological, histological, and molecular means. We showed that all *Tw/Tw* embryos presented with clefts of the palate and lip. Clefts of the lip in *Tw/Tw* were uni- or bilateral and complete or incomplete. The secondary palatal shelves in *Tw/Tw* were retarded both in vertical growth and elevation to a horizontal position, remaining short and unfused in newborn pups. In addition, we showed (by *in situ* hybridization) that the expression patterns of *msx1*, *bone morphogenetic protein-4* and *sonic hedgehog*, all shown previously to play critical roles in the development of the facial primordia, were altered in the midfacial region of homozygous *Tw* embryos. The results indicate that the *Tw* model is a useful system for analyzing the cellular and molecular processes involved in normal and abnormal formation of the midface region.