detected in the fragment encoding part of the fourth, the entire fifth and sixth helices (nucleotides 1471–1804). However, sequence analysis of the amplification product, derived from the fragment encoding part of the first and the entire second transmembrane helix of the *LHR* gene (nucleotides 1072–1288), revealed a heterozygous transition T1193C (Fig. 2A). The same mutation was detected in the patient's mother (Fig. 2B) and her brother (Fig. 2C). Sequence analysis of the same fragment in the patient's grandmother (Fig. 2D) did not reveal any abnormalities. Although it was impossible to diagnose the patient's father, this mutation was not found in the father's parents or in his sister.

The T1193C transition in exon 11 of the *LHR* gene has previously been described [12–14] in both sporadic and familial forms of testotoxicosis. However, only in one case was this mutation maternally inherited [14] and our case was the second reported familial form of testotoxicosis.

Kraaij *et al.* [12] and Yano *et al.* [13] investigated the effects of this mutation on the receptor function. In the cells transfected with recombinant plasmid harboring the mutated receptor, they independently showed an increase in the basal cAMP production, compared to the same cells transfected with recombinant plasmid containing the normal receptor.

We suggest that the heterozygous T1193C transition in exon 11, which caused substitution of Met^{398} for Thr in the second transmembrane helix, is responsible for the symptoms of the disease. It remains to be determined how the Met^{398} activates LHR.

The mutation described herein was maternally inherited, and was probably transmitted to mother by her father, who did not exhibit symptoms of precocious puberty, or else these symptoms were overlooked in childhood. The same mutation was also found in his son who did not exhibit any abnormalities of sexual maturation. Interestingly, Yano *et al.* [13] and Evans *et al.* [14] independently described the same mutation in male individuals asymptomatic for MPP. At present, no reasonable explanation can be offered why the same mutation causes MPP in one individual and does not affect sexual maturation in the other, unless we assume that

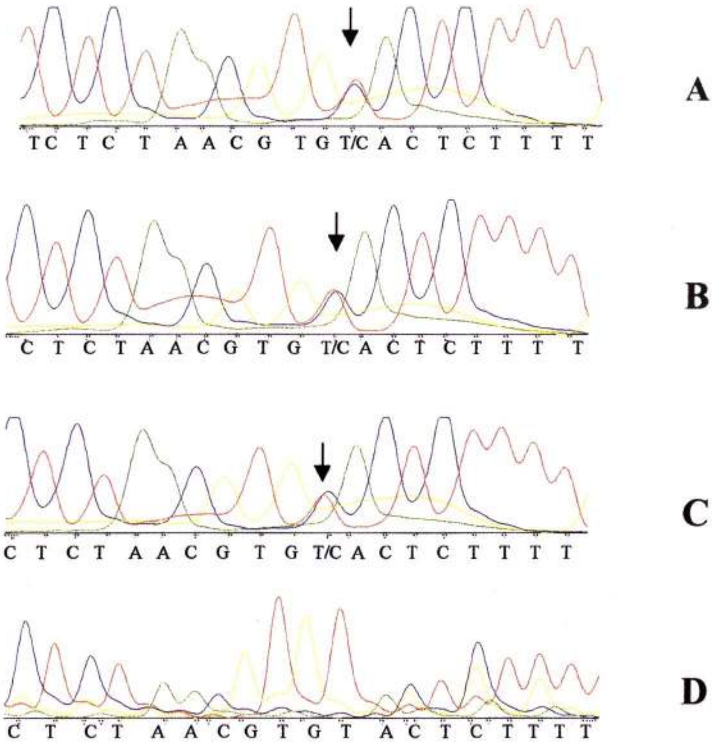

Fig. 2. Sequence analysis of the DNA fragment of exon 11 of the LHR gene, encoding the transmembrane helix. A—patient, B—his mother, C—her brother, D—grandmother. The T1193C transition is marked by arrow.