the child arrives home. This tragic case illustrates the importance of providing a safe venue for the dental patient. This case also points out how adverse events can occur despite the best intentions of those providing care. If the health care industry regarded dental procedures as having a recognized need for anesthesiology services, just like other medical procedures, such tragic outcomes might be avoided. Unfortunately, insurance companies and HMOs do not consider dental procedures important enough to pay for anesthesiology services, thus forcing the dentist to be both the anesthesiologist and the dentist at the same time. This case and a number of others point out the need for improved dental anesthesiology care.3

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Premature thelarche in girls after growth hormone therapy

To the Editor:

The increased availability and the broadened indications for growth hormone (GH) therapy have markedly in-
creased the number of children who are being treated. Prepubertal gynecomastia has been reported in boys receiving GH therapy, but premature thelarche in girls after GH therapy has not been reported.1,2 When breast development in girls with GH deficiency indicates onset of puberty and height is inappropriate, suppression of puberty with gonadotropin-releasing hormone (GnRH) analogs may be considered to improve final height.3 From 1995 to 1999, we treated 159 Brazilian children with recombinant GH (76 boys and 83 girls, including 30 with Turner’s syndrome). Four prepubertal girls, 2 with GH deficiency and 2 with Turner’s syndrome [karyotypes 45,X/46,X,r(X) and 45,X/46,X,i(Xq)] had bilateral breast development (Tanner stage II to III) during GH therapy (0.1-0.15 U/kg/d, given subcutaneously, 7 days a week). At the time of thelarche, their chronological ages were 5.6, 7.8, 7.7, and 7.3 years; bone ages were not increased at 5.7, 4.8, 5.8, and 6.8 years; and duration of GH therapy was 26, 60, 7, and 2 months, respectively. The patients with GH deficiency had prepubertal levels of estradiol (<6.8 pg/mL), luteinizing hormone (<0.6 U/L), follicle-stimulating hormone (<1.2 U/L), and a prepubertal gonadotropin response to GnRH (peak levels of luteinizing hormone, 3.1 and <0.6 U/L; and follicle-stimulating hormone, 10 and 3.6 U/L, respectively). The patients with Turner’s syndrome also had unmeasurable estradiol levels (<6.8 pg/mL) with gonadotropin levels compatible with Turner’s syndrome. During GH therapy insulin-like growth factor (IGF)-I and IGF binding protein-3 measurements were less than +2 SDs above the normal mean for sex and age. Despite continued GH treatment, breast development disappeared after 15, 4, 3, and 10 months, respectively, in all patients, but recurred after another 4 months in the first patient with GH deficiency. The mechanism for development of thelarche in prepubertal girls during GH therapy, as well as that of gynecomastia in boys, is not established. Prepubertal basal and GnRH-stimulated gonadotropins exclude activation of the pituitary-gonadal axis, and therefore suppression with GnRH analogs is not indicated. Low estradiol levels and dysgenetic ovaries in patients with Turner’s syndrome make an ovarian estrogen source unlikely. Cohn et al4 reported gynecomastia in elderly men receiving GH therapy, which correlated with increased IGF-I levels. GH receptors have been identified in human breast tissue, and GH could be acting on these receptors, on other lactogenic receptors, or indirectly through IGF-I. Appearance of breast tissue in GH-deficient boys during early GH therapy has been attributed to a “re-feeding” mechanism.1,2 Prepubertal gonadotropin and estrogen levels, lack of bone age advancement, and disappearance or stabilization of breast development in most patients indicates the benign nature of this condition, which could be misdiagnosed as activation of the pituitary-gonadal axis.

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