Hypertension during GNRH analogues therapy in a 10-year-old girl

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BACKGROUND

Conventionally, precocious puberty has been defined as onset of breast stage II development before the age of 8 years in girls and genital stage 2 development before 9 years in boys[1]. Precocious puberty represents increased sex hormone production by the gonads either independently [gonadotropin-independent precocious puberty (GIPP)] or under the effect of gonadotropins (gonadotropin-dependent precocious puberty)[2]. The aims of management include treatment of the underlying cause, attainment of target height and amelioration of psychological distress. GnRH analogs have been developed by chemical modification of the GnRH molecule to ensure prolonged receptor occupancy culminating in prolonged duration of action. Continuous as against pulsatile GnRH exposure desensitizes the pituitary, resulting in reduced gonadotropin production and reversal of pubertal changes[3]. GnRH analog treatment has been found to be safe in a large number of subjects[3] The treatment is associated with decrease in growth velocity and treatment may theoretically cause decreased bone mineral density due to decreased estradiol levels. Chronic toxicity studies have shown that repeated administration does not induce changes to organs and systems other than reproductive system. Animal studies have not revealed teratogenic effects[4]. There is no increased risk of polycystic ovarian disease, obesity and compromised reproductive potential.

OBJECTIVE

Description of a case of arterial hypertension secondary to chronic therapy with GNRH analogous.

CASE REPORT

A 10-year-old girl born at 41st week and spontaneous birth, in therapy with analogous GnRH for idiopathic central puberty. At 4 years bilateral thelarche, performed first and second level investigations and recives diagnosis of early idiopathic central puberty. Since then, therapy with triptorelin 3.75 mg i.m every 21 days was administrated. Regular checks, good compliance, and response to therapy. At 10 years old recurring episodes of headache and vertigo. Clinical examination was negative.

Height 1.5 SDS, weight -0.3 SDS, Tanner stage was P2 B1. Blood pressure (BP) was 124/90 mmHg (95-99th centile for systolic and >99th centile for diastolic). Pressure values were confirmed in several ambulatory and home assessment and were suggestive of stage I hypertension. Ambulatory BP monitoring revealed: mean 24 h systolic/diastolic BP 116/79 mmHg, mean day time and night time systolic/diastolic BP 118/80 and 110/73 respectively, nocturnal dipping 8,7%, and diastolic BP load 39,9%, confirming a stage I hypertension. Electrocardiography and echocardiography were normal. Renovascular and renal parenchymal diseases and endocrine causes of hypertension were excluded. Considering the girl symptomatology, anti-hypertensive therapy was started (Enalapril 0,15 mg/kg/die). No improvement of BP values were observed and GnRH-analog therapy was discontinued. Later the girl showed normalisation of BP values, and Enalapril was stopped. To date BP values persists on normal range for sex, age and height.

COMMENTS

Triptorelin is a GnRH agonist used for treatment of central precocious puberty because it suppresses pituitary gonadotropin secretion when administered continuously. Tolerance to GnRH agonist is usually good, although adverse effects such as headaches, rash, gastrointestinal compliants were observed.
In the last years few case reports were published, suggesting a link between GnRH agonist treatment and hypertension. If we consider that: I) the patient had a normotensive condition at the beginning of therapy, II) blood pressure returned to normal values after discontinuation of triptorelin and, III) normal BP values were maintained even after antihypertensive drugs withdrawal, we suggest that hypoestrogenism induced by GnRH agonist treatment might have played a role in the development of high BP

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