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Stanozolol induced precocious puberty

Siddhanta Sattik[1], Sahana Pranab Kumar[2], Sengupta Nilanjan[3], Goswami Soumik[4], Baidya Arjun[5]

1 Senior Resident,2 Associate Professor,3 Professor & Head,4 Clinical Tutor,5 Assistant Professor
Department of Endocrinology, Nilratan Sircar Medical College, Kolkata, West Bengal, India
Corresponding Author: Pranab Kumar Sahana

Abstract: *Precocious puberty in males has multiple aetiologies.We report a case of a four and a half year old boy with an unremarkable medical and family history who presented to us with progressive increase in phallic length and appearance of pubic hairs without concomitant testicular enlargement or increase in height velocity following Stanozolol therapy for aplastic anemia. A meticulous clinical examination supplemented with all the necessary hormonal investigations including bone age revealed the possibility of Gonadotropin independent precocious puberty. After exclusion of all the treatable causes of Gonadotropin independent precocious puberty, a final diagnosis of Stanozolol induced precocious puberty was made and the child was kept under regular follow up. Precocious puberty following stanozolol administration is a rare aetiology which has hardly been reported worldwide.*

Keywords*: Aplastic anemia, dihydrotestosterone, precocious puberty, Stanozolol*

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I. Introduction

Puberty is a phase of transition from childhood to adulthood and involves the development of secondary sexual characteristics and attainment of reproductive capacity.[1]Precocious puberty denotes early pubertal development.[2]Though rare, it is one of the commonest endocrine challenges encountered in clinical practice among pediatric population. It is defined as the development of secondary sexual characteristics before the age of eight years or menarche before the age of nine years in girls and any sexual characteristics before the age of nine years in boys.[3] It is due to excessive production of sex steroids either due to activation of Hypothalamo Pituitary Gonadal(HPG) axis(Central Precocious Puberty or Gonadotropin dependent Precocious puberty) or due to non hypothalamic medicated increase in sex steroid production(peripheral precocious puberty or Gonadotropin independent precocious puberty or precocious pseudopuberty).[4]Though the former type is relatively more common, the latter variant is also encountered quite often in clinical practice. However, precocious puberty due to exogenous steroid administration is extremely rare and has hardly been reported in literature. We describe a four and a half year old boy suffering from aplastic anemia on Stanozolol who presented with precocious pseudopuberty.

II. Case presentation

A four and a half year old boy was referred to endocrine clinic for evaluation of precocious puberty. His mother complained of progressive increase in penile length and appearance of pubic hairs for the last three months. However, she negates any obvious increase of testicular size or acceleration in growth velocity. She admits that her son became muscular recently and that his voice has deepened over the last one month.He did not have any acne, oily skin, adult body odour, breast enlargement or discharge, headache, visual difficulties or seizures. There was no past history suggestive of any crisis, head injury, meningitis, meningoencephalitis or brain abscess. The boy was a product of an uncomplicated full term gestation without any remarkable perinatal events. He is the only child of his parents without any history of consanguineous marriage. His developmental milestones were normal and he received all vaccinations till date. He is a diagnosed case of Aplastic Anemia on regular hematological follow up. Besides receiving blood transfusion at regular intervals, he is also receiving Stanozolol at a dose of 20 mg daily in divided doses for the last six months. She denies history of any other chronic drug intake, exposure to radiation or use of exogenous creams or ointments. There was no history of similar illness in his parents.

Examination revealed he weighed 17 kgs (> 25 th percentile) with a weight SDS+0.44 and a weight age of 5 years. His height was 110cms (between 75- 97th percentile) with a height SDS +0.84 and height age of 5.5 years .His upper segment: lower segment(US:LS) ratio was 0.99 and arm span was 109 cms. His vital signs were normal. His penile length was 9 cms [Normal stretched penile length for age, 5.7±0.9 cms

(Mean±SD)].(Fig 1)He had bilaterally palpable and symmetrical scrotal testes with volume of 2 ml each(Prader's orchidometer)(Fig 2).Sexual Maturity rating(SMR) was G1P2.Axillary and facial hairs were absent. He also had increased muscle bulk and developed deepening of voice but there was no gynecomastia or goitre.There was no skin changes or bony abnormalities. Hematological examination revealed mild anemia but there was no hepatosplenomegaly or lymphadenopathy. Waldeyer's ring was normal. There was no petachia or purpura anywhere or sternal tenderness. Neurological examination including fundoscopy was normal. Other systemic examinations including abdominal examination were within normal limits.

Investigations revealed a complete blood count of 11.5 gm%, with a total leukocyte count of 4100/cu mm and adequate platelets on smear. His renal and liver function tests were normal. His thyroid function tests, potassium and 8 am serum cortisol levels were within normal limits. His bone age was 5 years (matched with Modified Greulich and Pyle Chart)(Fig 3).His basal Follicle stimulating hormone (FSH) and Luteinizing Hormone (LH) levels were 0.37 Miu/ml(N-1.79-8.78) and 0.11 Miu/ml(N-2.12-10.89) respectively. A GnRHa stimulation test with a GnRH agonist, Inj. Triptorelin (100 ug) subcutaneously was performed .The peak Follicle stimulating hormone(FSH) and Luteinizing hormone(LH) levels after thirty minutes of administration were 0.97 mIU/ml(N-1.79-8.78) and 1.62 mIU/ml(N-2.12-10.89) respectively. Thus, the dynamic test yielded a flat response. His serum total testosterone and dihydrotestosterone levels were 54.2 ng/dl (prepubertal N 10-30ng/dl) and 440 pg/ml (Prepubertal N <50 pg/ml) .Ultrasonography of abdomen including pelvis was unremarkable .His 17 OH progesterone was 1.1 nmol/L (Ref value<8), DHEA-S is 161.3ug/dl (Ref-125-619 ug/dl) and βHCG were within normal limits. His lipid profile and liver function tests were normal too.

After hematological consultation, it was unanimously decided to continue the child on tablets Stanozolol in view of his aplastic anemia despite the development of sexual precocity. In fact, the patient had a sense of well being with decreased necessity of blood and blood component transfusions and decreased incidence of infections. At follow up visit after six months, there was no further increase in his penile length or pubic hairs. It was decided to follow up the child at regular intervals with periodic lipid profile and liver function tests in addition to the pertinent hormonal investigations.

III. Discussion

Stanozolol is the most commonly used anabolic steroids worldwide .It is a synthetic anabolic steroid derived from the hormone, Dihydrotestosterone (DHT) with two structural alterations- the first modification is addition of a Pyrazol group at A ring in place of 3-Keto and the second change is addition of a methyl group at C17 position which puts it into 17 alpha(C17aa) alkylated category.[5,7]Due to these structural alterations, the androgenicity of Stanozolol decreases markedly while its anabolic activity increases dramatically which has therapeutic implications. The anabolic rating of Stanozolol is 320 while the androgenic rating is 20 only.[5] Stanozolol has been used therapeutically in a swarm of conditions both in animals and human beings. In man, it has been successfully used in treating anemia (like our index patient)and hereditary angioedema.[6]During exogenous administration of Stanozolol, endogenous testosterone release is inhibited through feedback inhibition of pituitary luteinizing hormone (LH).[7]Large doses of exogenous anabolic steroids may suppress spermatogenesis by inhibiting pituitary follicle stimulating hormone (FSH).In females its use has resulted in virilization in the form of progressive deepening of voice, hirsutism, acne, clitoromegaly,breast atrophy and menstrual irregularities. Discontinuation of stanozolol during early stage of virilization may prevent irreversible virilization.[8]However, the incidence of precocious puberty in males after Stanozolol administration has hardly been reported in literature worldwide.

Our patient being a diagnosed case of aplastic anemia was put on tablet Stanozolol as it will increase red cell count resulting in increased oxygen carrying capacity in blood thereby enhanced muscle endurance. In our patient, after its use for a few months, there has been an increase in the penile length and appearance of pubic hairs without concomitant increase in testicular size. He also had increased muscle bulk and deepening of voice. However, there was neither any increase in height nor any increase in testicular size bilaterally. These findings are accounted for the dihydrotestosterone, the levels of which increases markedly after administration of Stanozolol. The biochemical reports corroborate our clinical diagnosis with a prepubertal Gonadotropin levels, a marginal rise in serum testosterone and a markedly high dihydrotestosterone levels. As Stanozolol is a non aromatisable steroid, there was no gynecomastia or any substantial advancement of bone age.

Hence, a diagnosis of Gonadotropin independent precocious puberty or Precocious pseudo puberty was made and the likely cause was exogenous steroid in the form of Stanozolol which was used as a primary treatment of aplastic anemia.

Learning Points/Take Home Messages

1. A child with precocious puberty may be stressed mentally due to the earlier onset of physical and hormonal changes; hence the health care team must deal the situation with utmost care and affection

2. Precocious puberty makes the child susceptible to adult sexual interest and sexual abuse; hence its social implications must be discussed with his parents
3. The cause of precocious puberty must be identified by a meticulous clinical examination supplemented by all the necessary investigations. It should be stamped as a case of iatrogenic precocious puberty only after all the other possible causes have been excluded.
4. Stanozolol, a commonly used exogenous steroid therapeutically may cause precocious puberty. Hence, the risk benefit ratio must be evaluated in each clinical situation not only during initiation but also during continuation of therapy

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FIGURES

Fig 1: Genitalia of the Boy showing increased penile length with pubic hairs

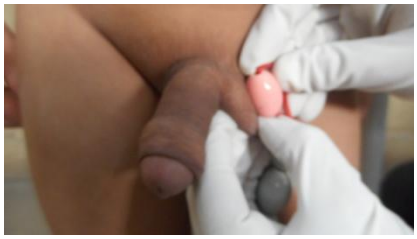

Fig 2: Testicular volume of 2 ml

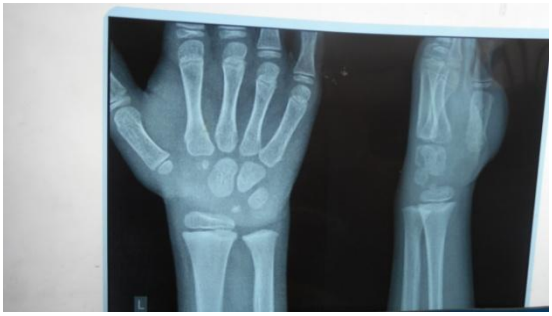

Fig 3: Bone Age of 5 years (matched with Modified Greulich Pyle chart)

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