

Case Report:

Macroorchidism as presenting feature of Fragile X Syndrome

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ABSTRACT

Fragile X syndrome (FXS) is the most common cause of inherited intellectual disability.¹ We report the case of a 6-year-old boy who presented with the complaints of excessive cry and increased testicular volume, during the preceding six months. Physical examination revealed elongated faces, protruding cupped ears and macroorchidism (testicular volume 6-8 mL), anxiety, hyperactivity and attention deficit, clinically suggestive of FXS.

Key words : *Fragile X syndrome, Macroorchidism*

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INTRODUCTION

Macroorchidism is a rare condition in children and is usually associated with fragile X syndrome (FXS).¹ Other possible aetiological causes of macroorchidism include long-standing primary hypothyroidism, adrenal remnants in congenital adrenal hyperplasia, follicle stimulating hormone (FSH) secreting pituitary macroadenomas, local tumours, lymphomas, and aromatase deficiency.² Bilateral macroorchidism can be a normal variant in adult men.² We report the rare occurrence of FXS in a 6-year-old boy who presented with a testicular volume of 6-8 mL.

CASE REPORT

A 6-year-old boy presented to our outpatient service with the complaints of excessive cry and increase in testicular volume during the preceding 6 months. There was a history suggestive of delayed occurrence of developmental parameters for his age; the child was still not able to sit without support. There was a history of seizures in infancy and the child was mentally retarded. Clinical examination revealed his length to be 112 cm. He had an elongated face with large, protruding and cupped ears (Figure 1) and flat feet. He also had large testes (6-8 mL) for his age suggestive of macroorchidism (Figure 2). Head circumfer-

ence was 47.5 cm which was less than 2 standard deviations for his age. He also had low muscle tone and laxity of joint movements.



Figure 1: Clinical photograph showing elongated face, cupped ears, dysmorphic features, of Fragile X-Syndrome

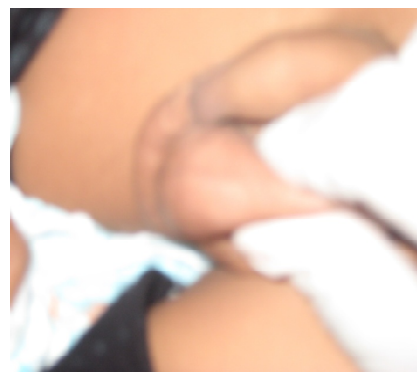


Figure 2: Clinical photograph of the same patient showing macroorchidism with a testicular volume of 6-8 mL

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Speech was cluttered and nervous. Behavioral assessment showed evidence of attention deficit with presence of irritability, panic attacks and shyness. Magnetic resonance imaging (MRI) of the brain was suggestive of normal pituitary fossa and mildly thickened cerebral cortex with flat gyri and deep sulci. Laboratory investigations revealed a serum calcium of 9.1 mg/dL, serum thyroid stimulating hormone was 0.32 mIU/L, serum testosterone 0.03 ng/mL, luteinizing hormone 0.33 mIU/L and follicle stimulating hormone was 0.42 mIU/L.

DISCUSSION

FXS is the most common cause of inherited intellectual disability.¹ A typical personality is characterized by anxiety, hyperactivity, attention deficit and, in most severe cases, autism.³ Anxiety symptoms and poor communication skills may lead to behavioural difficulties.¹ Social anxiety is one of the most common features associated with FXS with excessive shyness and panic attacks being evident in 75% and 50% patients respectively.⁴ These were evident in the boy evaluated in the present study. This phenotype, which tends to become more marked with age, depends on the presence of congenital muscular hypotonia accompanied by joint laxity.¹ Delayed speech is very common and mental retardation seems to increase with age as observed in this case. Seizures may be observed during infancy and a characteristic electroencephalogram (EEG) pattern has also been reported.⁵ Many males develop enlarged testicles, a condition called macro orchidism. In this condition, the testicles may grow to twice their normal size. This condition is not due to hormonal imbalance and does not affect sexual development. Macroorchidism in *Fmr1* knockout male mice is found to be caused by an increased rate of Sertoli cell proliferation. This increase does not appear to be the result of a major change in FSH signal transduction in *Fmr1* knockout mice.⁶ MRI of the brain shows overall volume

conservation of tissue, diminished white-to-gray matter ratio, relatively enlarged caudate nucleus and hippocampus, and slightly decreased cerebellar vermis with enlarged fourth ventricle.^{7,8} We observed increased gray matter area and decreased white to gray matter ratio. FXS is found in all races and the name of the syndrome comes from its location on the X-chromosome; the bottom of the chromosome appears to be broken or fragile when examined under a microscope. FXS was first identified in 1969 and in 1991 the *FMR1* gene which is altered in patients with FXS was discovered. As on date, there is no cure for FXS at this time.

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