NEW MUTATION OF GENES GNAS IN A 2 YEAR OLD ONCOLOGICAL PATIENT

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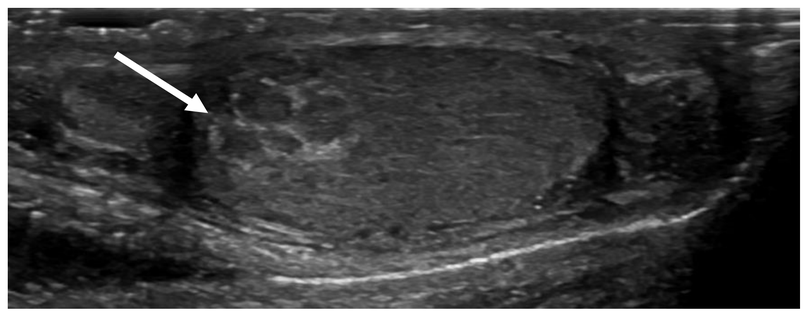
INTRODUCTION

Leydig cell tumors are rare (3% of testicular neoplasms). 80% of cases occurs in adult population, although a quarter is described in prepubertal patients older than four years. The clinic differs according to the patient's age. Activating mutations, acquired and limited to the tumor tissue, are described in exon 11 of the LH receptor gene. And in mixed Sertoli-Leydig tumors activating mutations of the Gs-alpha subunit of the stimulating G protein (GNAS) and in the DICER1 gene are described.

CASE DESCRIPTION

We show a 2-year-old boy with testicular asymmetry, increase in penis size and thickness, and increase in weight, height, and growth rate. On examination, he showed hyperpigmented coffee-milk macules with a metameric distribution on the back and right upper limb, right testicle 10 cc and left testicle 3cc, and penis 8 cm long and 7.5 cm thick. On complementary tests he showed testosterone 4.02 ng/ml, antimullerian hormone 22.96 ng/ml (both high), and AFP and stimulus test after GnRH negative. We observed, through ultrasound, heterogeneous lesion in the right testis compatible with Leydig cell neoplasia, which is confirmed in an anatomopathological study after tumorectomy with preservation of the testicle. In the tumor piece, a change of uncertain clinical significance c.180_185del (p.Met60_Arg61del) was detected in the GNAS gene. Bone gammagraphy normal. He received treatment with aromatase inhibitors and antiandrogens. After tumorectomy, testosterone were normal. Nowadays, close follow-up is maintained.



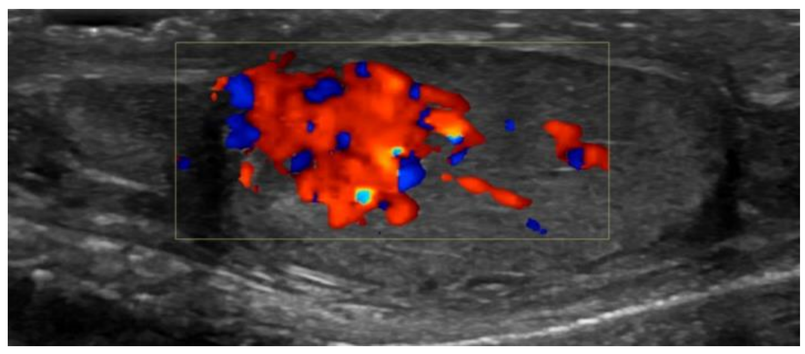
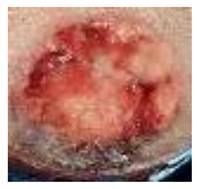
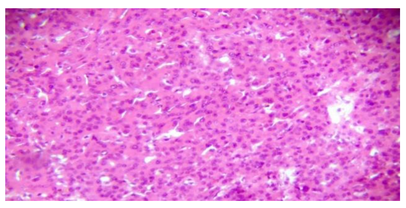


Fig. 1 Fig 2. intrathesticular lesion, 10 mm x 8 mm, of heterogeneous echogenicity, of hyperechogenic predominance with isoechogenic areas inside, with marked color doppler flow, compatible with non-germ cell neoplasia.



Tumor of brownish appearance and hard consistency delimited. Structure with irregular multilobed morphology of 1.5x1cm.



Leydig cell tumor with occasional seminiferous tubules with germinal atypia and focal nuclear pleomorphism. Size: 1.4 x 0.9 x 0.5 cm. Multinodular No necrosis or evidence of lymphovascular invasion. Well preserved edges although not completely defined
It is objected in a genetic study (deletion c.180_185del) that produces in-frame deletion of two amino acids (p.Met60_Arg61del). This change has not been described in the bibliography or in the databases consulted. Another change is also detected (c.396C> T), considered as a benign or probably benign variant taking into account the recommendations of the American College of Medical Genetics and Genomics.

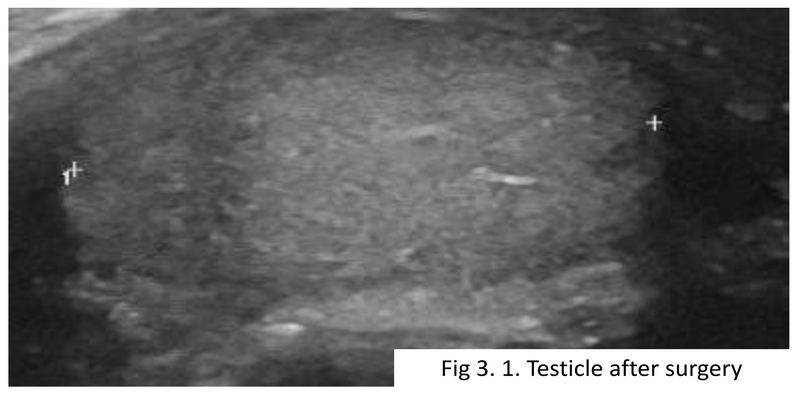


Fig 3. 1. Testicle after surgery

CONCLUSIONS

We show a Leydig tumor at an uncommon age, with a mutation in the tumor tissue not described in the GNAS gene in a non-mixed tumor. In childhood, the behavior is generally benign, especially in those with normal AFP levels at diagnosis. In these cases it is recommended conservative treatment, which decreases the risk of hypogonadism and subfertility. It is important close and prolonged follow-up, both because of the risk of recurrence, and the risk of central precocious puberty with changes on final size.

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