Case Report

Ovarian Cell Tumor in a Child with Neurofibromatosis Type 1

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Abstract

Juvenile granulosa cell ovarian tumor is a rare cause ofpseudo-precociouspuberty. We report a case of a 6-year-old female with neurofibromatosis type 1 (NF1), associated with pseudo-precocious puberty (PPP). A thorough workup revealed a large multi-cystic right ovarian mass, which turned out to be a juvenile granulosa cell tumor (JGCT). This report documented a rare case of PPP caused by JGCT in a child with NF1. Verbal consent was taken from the family.

Keywords: Granulosa cell, juvenile, neurofibromatosis, ovarian tumor, precociouspuberty

Résumé

La tumeur ovarienne juvénile à cellules de la granulosa est une cause rare de puberté pseudo-précoce. Nous rapportons le cas d'une fillette de 6 ans atteinte de neurofibromatose de type 1 (NF1), associée à une puberté pseudo-précoce (PPP). Un bilan approfondi a révélé une grande masse ovarienne droite multikystique, qui s'est avérée être une tumeur juvénile des cellules de la granulosa (JGCT). Ce rapport a documenté un cas rare de PPP causé par JGCT chez un enfant atteint de NF1. Le consentement verbal a été recueilli auprès de la famille..

Mots-clés: Cellule de la granulosa, juvénile, neurofibromatose, tumeur ovarienne, puberté précoce

Introduction

Precocious puberty refers to secondary sexual development, which occurs earlier than the normal onset of puberty in males and females.[1] It was classified into two types: pseudo-precocious puberty (PPP) and central precocious puberty (CPP). Neurofibromatosis type 1 (NF1) is a frequent autosomal dominant neurocutaneous disease due to defects in the NF1 tumor suppressor gene located at chromosome 17q11.2. Occasionally, NF1 induces CPP in the presence of central nervous system tumors.[2]

Granulosa cell tumor (GCT) is a rare form of sex cord-stromal tumors, which occurs in about 2%–5% of ovarian neoplasms, and consists of Juvenile granulosa cell tumor (JGCT) and adult GCT. In prepubertal girls and young women, JGCT is predominantly present, accounting for 97% of the patients during their first three decades of life. GCTs are estrogen-producing tumors of varying appearance depending on the age of the patient. Prepubertal girls typically have PPP with secondary sexual characteristics, vaginal bleeding, breast enlargement, and advanced bone age. Postpubertal girls typically experience intermittent abdominal pain and irregular uterine bleeding.[3-5] Here, we report a rare case of a 6-year-old child with NF1 and unexpected PPP caused by GCT of the ovary.

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Case Report

A 6-year-old female with NF1 had a 3-week history of bilateral breast enlargement followed by vaginal bleeding 2 days before presentation. The vaginal bleeding was associated with abdominal pain and distention. There was no history of change in body odor, pubic or axillary hair growth, acne, or increase in height. There was no headache, visual impairment, emesis, seizures, or symptoms suggestive of high intracranial pressure. There was no evidence of sexual abuse, trauma, abnormal bleeding from any other orifices, or any medication intake. There was a history of neurofibromatosis in the family [Figure 1].

She was alert, active with normal vital signs. Her growth parameters revealed a height of 111 cm, a weight of 18.5 kg, both on the 25th percentile. Skin examination revealed more than six café-au-lait macules, with axillary freckling [Figure 2]. Ophthalmology examination was significant for Myopic Astigmatism, with clear corneas, iris, and lens bilaterally. We did not detect any lich nodules or oculomotor difficulties. Tanner staging of the breast revealed Tanner stage 2, with no pubic or axillary hair. The abdomen was distended with a large hard nontender mass measuring 7 cm × 7 cm located in the right lower quadrant [Figure 3]. Bone age assessment of left hand using Greulich and Pyle method was corresponding to chronological age. Abdominal and pelvic computed tomography scan with contrast was suggestive of right-sided ovarian tumor [Figure 4]. A complete blood count, electrolytes, liver function test, coagulation profile, and thyroid function tests were within normal values. Her hormonal investigations for precocious puberty were indicative of PPP [Table 1], with a high Inhibin B level suggestive of GCT.

The patient underwent surgical removal of the right ovary, including a large solid multicystic mass weighing 150 g, size 9 cm × 6.5 cm × 5 cm.

Histopathology examination of the right ovary/ovarian cyst shows predominant features of JGCT type. Microscopic evaluation revealed a follicular pattern, which was variable in size and shape, and filled with eosinophilic fluid. Cytology showed no malignant cells.

Table 1: Hormonal investigations confirming pseudo-precocious puberty

Laboratory test	Result	Reference range
LH (mIU/L)	0.04	1.9-12.5
FSH (IU/L)	2.17	2.5-10.2
Serum estradiol (Pmol/L)	152.72	26-125
β-hCG (mIU/mL)	<0.1	0-5
Inhibin B (pg/ml)	>1300	0-18
α-FP (ng/ml)	0.57	0-8.7
CEA (ng/ml)	0.95	0-5

LH=The luteinizing hormone, FSH=Follicle stimulating hormone, β-hCG=Beta human chorionic gonadotropin, α-FP=Alpha fetoprotein, CEA=Carcino-embryonic antigen

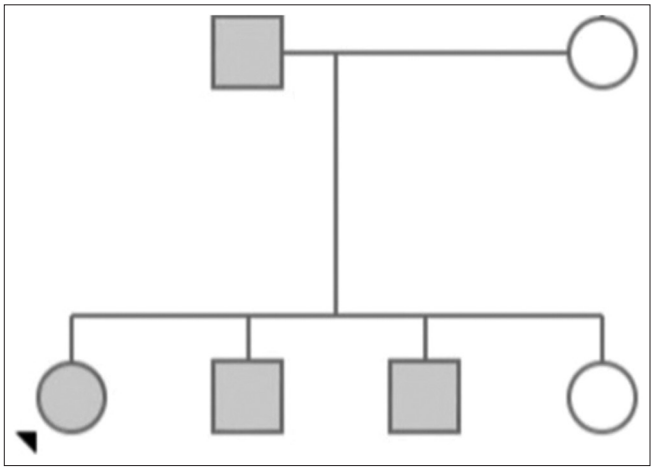

Figure 1: Family pedigree indicating autosomal dominant penetrance of NF1

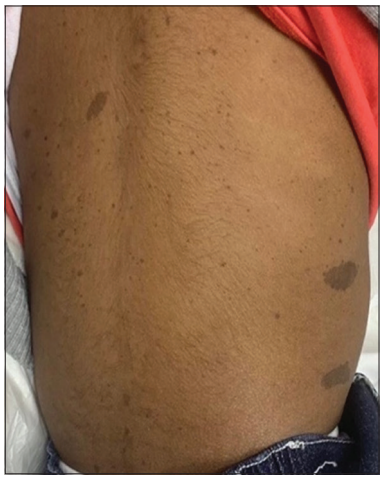

Figure 2: Multiple café au lait macules with well-demarcated, smooth borders and homogenous appearance, ranging from 20–60 mm in diameter

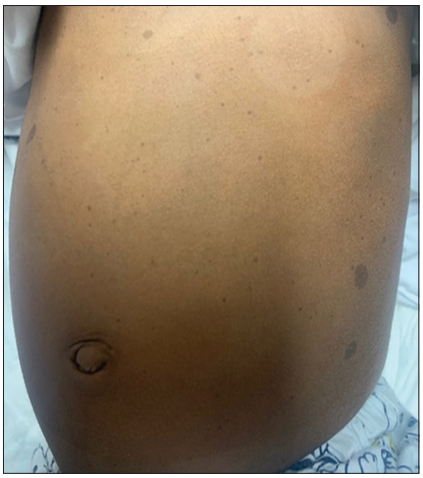

Figure 3: Asymmetrical distended abdomen with a right-sided palpable mass

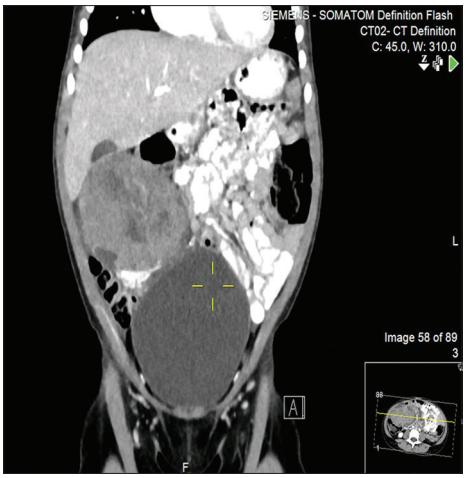

Figure 4: Abdominal and pelvic computed tomography scan with contrast showing a well-defined Heterogenous solid right ovarian mass measuring 7.8 cm × 7.4 cm × 6.2 cm associated with stretching of the uterus superiorly and thickened endometrium

Discussion

Pseudoprecocious puberty has a wide differential diagnosis. In females, it includes ovarian or adrenal tumors, ovarian cysts, genetic syndromes such McCune Albright syndrome (MAS), exogenous sex steroids, and congenital adrenal hyperplasia.[1,6] Sex cord-stromal cell tumors and germ cell tumors are associated with endocrine manifestations. Ovarian sexcord-stromal tumors account for various types of rare tumors, including JGCT. JGCT was estimated to occur in about 67% of pediatric sex cord-stromal tumors with a prevalence rate of 5%–12% of all ovarian neoplasm in childhood. Inhibin B was observed to be secreted in JGCT, and therefore, it is used as tumor marker; its elevation is pathognomonic.[5,6] Our patient in this case report had markedly elevated inhibin B level.

The patient presented with café–au–lait-macules and isosexual PPP. The differential diagnosis includes MAS and NF1. MAS is a rare condition that is characterized by fibrous dysplasia, PPP, and café au lait macules. The caféaulait macules in MAS are classically defined as hyperpigmented, unilaterally distributed on the same side of bone lesions, with irregular borders (Coast of Maine). These lesions usually follow the lines of Blaschko and do not cross the midline. In contrast, the caféaulait macules in NF1 are characterized by uniform, smooth, and regular boarders (coast of California).[7,8] Our case demonstrated the typical café–au–lait macules seen in NF1.

NF1 is a common disorder with several manifestations, including café–au–lait macules, Lisch nodules (iris hamartomas), axillary and inguinal freckling, and neurofibromas. NF1 can cause nervous system tumors, commonly optic pathway gliomas. Lesions occurring near to or involving the hypothalamus can result in CPP. NF1 diagnosis is made clinically using the National Institute of Health (NIH) of the USA diagnostic criteria and the presence of 2 or more of the criteria is sufficient to establish the diagnosis.[2,9,10]

Our case met the NIH criteria for the diagnosis of NF1. She had isosexual pseudoprecocious puberty based on the advancement of pubertal status, biochemical evidence, and the presence of GCT on histopathology examination, which is not the usual presentation of patients with NF1. The patient, had both thelarche and menarche with no adrenarche, which is expected in PPP. Finally, on literature review, we did not observe any case report of JGCT associated with NF1.

Conclusion

Ovarian JGCT is a rare cause of PPP. Although CPP is a common cause in NF1, a high index of suspicion plays an important role in the early diagnosis and treatment for this condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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