4-YEAR-OLD FEMALE PATIENT WITH MIXED GERM CELL TUMOR AND UNTERLYING COWDEN SYNDROME

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COWDEN SYNDROME

Cowden syndrome (CS) is a cancer-predisposition syndrome. It is a syndrome of the *PTEN* harmatoma tumor syndromes, which are caused by mutations in the tumor suppressor gene *PTEN*. The clinical hallmarks of CS are macrocephaly and mucocutaneous symptoms. Several tumor types have been described, mostly tumors of the breast, thyroid and endometrium. The age of onset is extremely variable[1,2].

OVARIAN TUMORS

So far, there are only two publications reporting ovarian tumors in childhood in the context of *PTEN* harmatoma tumor syndromes:

- a granulosa cell tumor in a 16-year old girl[2] and
- a bilateral dysgerminoma in a 7-year old girl[3].

CASE REPORT

1 4-year old girl

The patient presented for hyper-androgenemia with slight clitoral hypertrophy, premature thelarche, pubarche and accelerated growth with increased bone age. The initial testosterone level was 1.58ng/ml, the estradiol level was 18pg/ml.

2 Laboratory findings

Date	Testosterone ng/ml	Androstendione ng/ml	17ß-Estradiol pg/ml
First consultation	1.58	1.24	18
2 months later	1.08	0.81	11
8 months later	0.63	0.35	15
9 months later	0.03	<0.24	<5
12 months later	0.03	<0.24	<5

3 Diagnostic findings

MRI of the pelvis: solid mass in the left adnexal area (4,5x3,8x2,9cm)

Other causes of precocious puberty or adrenal androgen excess were excluded.

4 Surgery

Resection in toto of the tumor took place 10 months after the first consultation. The testosterone, andro-stendione and estradiol levels fell continuously. Prepubertal levels were reached before the surgery took place.

5 Histology

Histologic examination revealed a mixed germ cell tumor with dysgerminoma and mature teratoma components, as well as structures suspicious for hemangioma component.

6 Genetics

The presence of other clinical abnormalities such as lipomas, keratosis pilaris and macrocephaly led to the suspicion of CS, which could be confirmed genetically.

c.406T>C, heterozygous missense mutation of the *PTEN* gene

7 Follow-up

The oncological follow-up was adapted according to the genetic diagnosis of CS.

CONCLUSION

Ovarian tumors due to Cowden syndrome are extremely rare in childhood.

In this case **the activity of the tumor changed from endocrine-active to endocrine-inactive** before the surgery was performed.

Diagnositic process and treatement were delayed due to the extensive impact of the COVID-19 pandemic.

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