AROMATASE INHIBITOR TREATMENT IN PATIENT WITH BETA-HUMAN CHORIONIC GONADOTROPHIN SECRETING TUMOR AND GONADOTROPIN-INDEPENDENT PRECOCIOUS PUBERTY.

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Introduction

CNS tumors may cause precocious puberty (PP): in most cases gonadotropin-dependent PP, but in boys ß-HCG-secreting tumors may cause gonadotropin-independent (GIPP) with extremely high testosterone secretion due to Leidig cell stimulation by ß-HCG. Rapid bone maturation in such cases can lead to growth plate closure and poor final height prognosis. Aromatase inhibitor (AI) are administered in children with McCune-Olbright disease, familial male-limited PP, and idiopathic short stature, but there is no data in children with ß-HCG-secreting tumors.

Clinical case

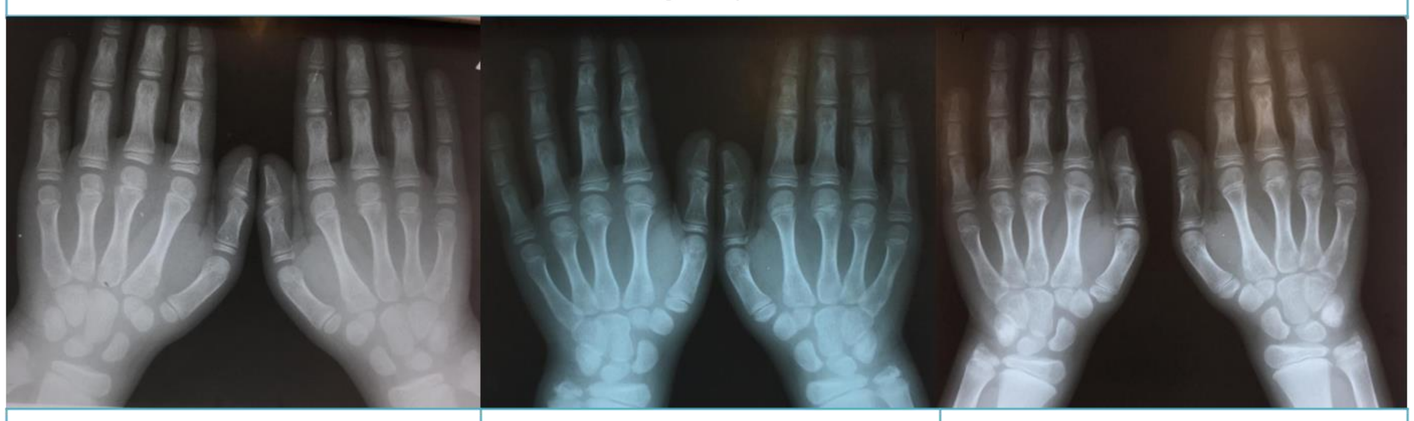
6-year boy presented with signs of PP (axillar and pubic hair growth, penis enlargement, voice deepening and acne). His sexual development was at Tanner stage IV, and his testes were about 3 ml. His height was 134.2 (+2.63 SDS), weight 36.7 kg (+2.03 SDS BMI) and his bone age was 9 years. Examination revealed high testosterone 55.5 nmol/L (N<0.5), estradiol 440 pmol/L (N<69) and ß-HCG 1,849.9 IU/l (N < 2.0) levels, but – LH and FSH <0.1 IU/l. A brain MRI showed pineal gland tumor 38x38x32 mm. The patient was referred to treatment with carboplatin, etoposide and ifosfamide according to the SIOP CNS GCT II trial.

Results

After 1st chemo block (38 days after primary investigation) ß-HCG level dropped to 106.8 mU/l, but testosterone was still elevated (51.8 nmol/L) and estradiol too (709 pmol/L), bone age progressed from 9 to 13 years. Due to rapid bone age progression, AI therapy (Exemestane 25 mg daily) was started. After 4 week treatment estradiol and testosterone level dropped to 78 pmol/L and 0.0 nmol/L, respectively. After 3th chemo block (70 days after primary investigation) ß-HCG dropped to 1.2 IU/l, testosterone to 0 nmol/L, and estradiol to 49 pmol/L. Bone age was still 13.5 years. There were no adverse events during AI treatment.

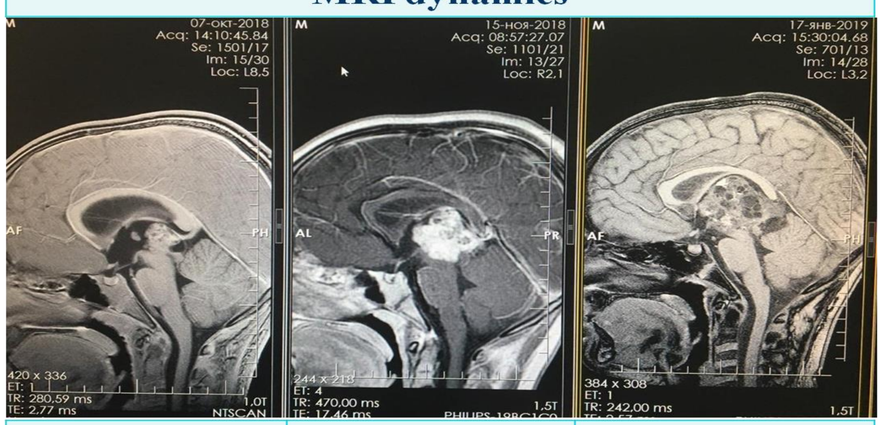
Laboratory data					
	ß-HCG, IU/l	Testosterone, nmol/L	Estradiol, pmol/L	LH, IU/l	FSH, IU/l
Nov	1049,94	55,55	440,52	0,04	0,04
Dec	106,81	51,85	709	0,03	0,00
Jan	1,2	0,00	78,0	-	0,11
Feb	<1,2	0,00	49,0	0,02	0,43
Mar	-	0,00	24	0,82	0,18
Apr	-	0,00	11,0	0,21	0,74
May	-	0,03	11,0	0,85	2,88
Jun	-	0,00	28	0,60	1,35
RI	0,0-5,0	m: 12,1-38,3	m: <282,6	m:0,8-8,4	m:1,0-8,0

Bone age dynamics



November	December	January-June
Bone age 9 years	Bone age 13 years	Bone age 14 years

MRI dynamics



Oct 2018	Nov 2018	Jan 2019
22*19,5*18 mm	37,6*37,6*32 mm	44,3*51*36 mm

Conclusions

To our knowledge, it is the first case of AI administration in patients with GIPP due to ß-HCG-secreting tumors. In this clinical case treatment was effective and safe.

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