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Precocious Pseudo-Puberty in a 7-Year-Old Girl Due to Malignant Mixed Ovarian Germ Cell Tumor

Nicola Improda[1,2,*], Francesco Rosanio[1,*], Lucia De Martino[3], Stefania Picariello[3], Enza Mozzillo[1], Adriana Franzese[1], Lucia Quaglietta[3]

[1]Department of Translational and Medical Sciences, Section of Pediatrics, University Federico II, Naples, Italy
[2]Department of Pediatric Emergency, Santobono-Pausilipon Children's Hospital, Naples, Italy
[3]Department of Pediatric Oncology, Neurooncology Unit, Santobono-Pausilipon Children's Hospital, Naples, Italy
*These authors equally contributed to this work.

Precocious pseudo-puberty (PPP) is sexual maturation in the absence of activation of the gonadal axis. Although the most common etiology in girls is ovarian cyst, other rare causes include chronic primary hypothyroidism, McCune–Albright syndrome, and adrenal and gonadal tumors.[1] Diagnostic clues of PPP are elevated estrogens and suppressed or pre-pubertal basal and gonadotrophin-releasing hormone (GnRH)-stimulated gonadotropins.[1]

A 7-year-old girl presented with vaginal spotting and rapid pubertal progression (from Tanner stage B2 to B3 in only 3 months and pubic hair PH3). She had a pelvic mass detected at ultrasound, with elevated estradiol (111 pg/mL) and lactate dehydrogenase (LDH) (921 U/L, nv 22450), suppressed follicle-stimulating hormone (FSH) and very high beta-human chorionic gonadotropin (hCG) concentrations (31 373 mIU/mL, nv < 5) (Table 1). Computed tomography (CT) confirmed a large inhomogeneous mass (10 × 8 × 8.5 cm) with irregular profile connected through a peduncle to the left ovary, extending from the lower pole of kidney to the bladder dome and infiltrating the iliopsoas muscle and the abdominal wall (Figure 1). The Tc99 whole-body scintigraphy was negative.

After surgical removal and microscopic examination of the mass and peritoneal fluid, a stage 2 mixed germ cell ovarian tumor (MGCOT) was diagnosed. Hormone profile and tumor markers were normalized and chemotherapy was started (bleomycin, etoposide, and cisplatin every 3 weeks for 4 cycles). Three months after chemotherapy, cell content in the peritoneal fluid was negative for malignancy. Twelve months after surgery, growth velocity appeared to decrease (3 cm/1 year), and pubic hair and breast were not increased. Moreover, the hormone profile was normalized and tumor markers were all negative (Table 1). She had normal pubertal development, reaching menarche at 11.5 years.

Table 1. Laboratory Data of the Patient at Diagnosis and 1 year After Surgery

	Baseline	1 Year After Surgery	Normal Value
LDH	**921**	**263**	**227–450 U/L**
FSH	**<0.10**	**4.3**	**5–30 mU/mL**
LH	**18.6**	**0.4**	**5–60 mU/mL**
Prolactin	8.9	5.3	**5–25 ng/mL**
Estradiol	111	48	**20–240 pg/mL**
Testosterone	<20.0	<20.0	**20–120 pg/mL**
Beta-HCG	**31 373**	<1.00	**<5 mIU/mL**
AFP	0.8	0.6	**0–15 ng/mL**
CEA	0.7	-	**0–4 ng/mL**
CA 19-9	3.1	-	**0–37 U/mL**

LH, luteinizing hormone; AFP, alpha-fetoprotein; CEA, carcinoembryonic antigen; CA, carbohydrate antigen.
All numbers outside the reference range are highlighted in bold.

Corresponding author:
Nicola Improda
✉nicolaimproda@gmail.com
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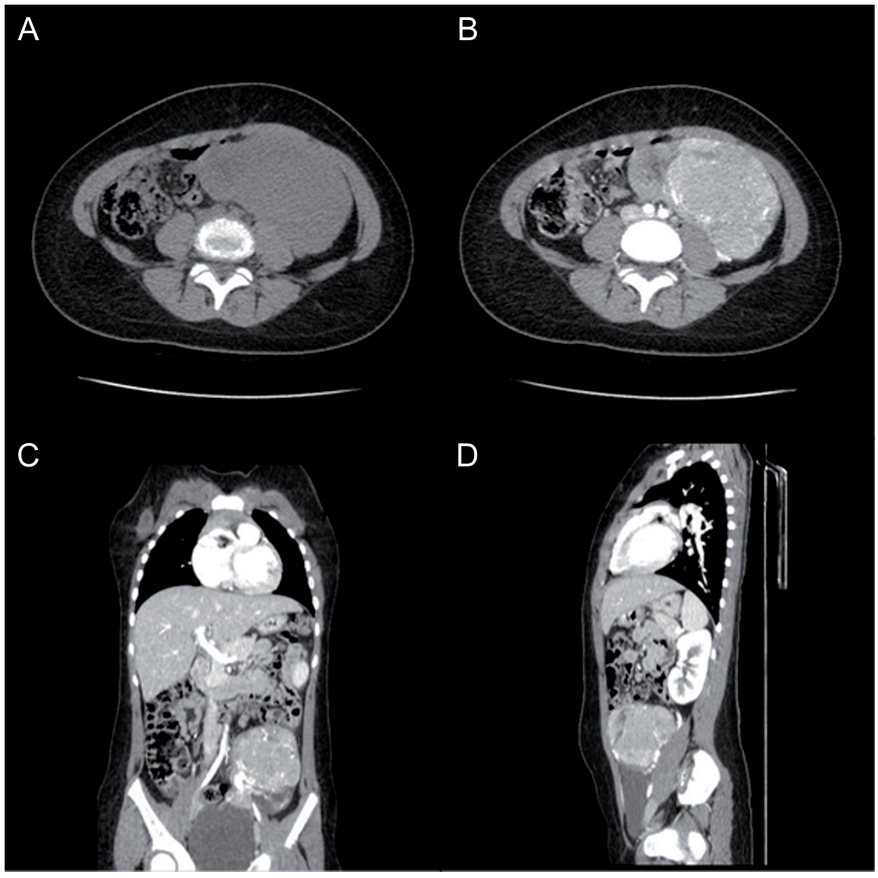

Figure 1. Abdominal computed tomography images in the basal scan (A), arterial scan (B), coronal scan (C), and sagittal scan (D), demonstrating a large inhomogeneous vascularized (B) mass (star) connected through a peduncle to the left ovary (C, arrow), infiltrating the iliopsoas muscle (D, right arrow) and the abdominal wall (D, left arrow).

Germ cell tumors represent 60%-80% of all ovarian tumors, and [2] only 2%-3% are malignant (MOGCTs), including dysgerminomas (most common) and non-dysgerminomas, which rarely (5.3%) comprise MGCOT.[3] Mixed germ cell ovarian tumors have a peak incidence between 16 and 20 years of age, while they are exceptional in the first decade of life.[4-7] Although typical symptoms are abdominal pain and fever, they may rarely cause PPP. The principal tumor markers produced by MOGCTs are alfa fetoprotein, beta-hCG.[3,4] However, in our case, only beta-hCG was detectable.

As also shown in our case, despite aggressive behavior, these tumors are curable if diagnosed early.[8] In girls with rapidly evolving pubertal signs, ultrasound findings along with positive tumor markers may orient toward rare and/or malignant causes of PPP, allowing timely and more effective cancer treatment.

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