Sequential teratoma in pediatric patients: causation or coincidence?

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ABSTRACT

We describe the unusual case of a female patient with a history of two mature teratomas non-correlated in terms of location and occurrence. A 12-year-old girl presented at our consultation as a result of a growing tumor in the hypogastric region, with no further clinical signs. She had undergone surgery neonatally due to a mature cystic sacrococcygeal teratoma, which was fully removed. No clinical sequelae were noted and no additional treatment was required over a 10-year follow-up. Radiological examination showed a large 20 × 12 × 18 cm cystic mass extending from the pelvic region to the lower hemiabdomen, associated with two similar small formations adjacent to the right ovary. Tumor markers were negative, and a laparoscopic right salpingoophorectomy was carried out, with an excellent postoperative progression. Pathological examination revealed it was, again, a mature cystic teratoma. The genetic study ruled out causation in this respect.

KEY WORDS: Mature teratoma; Sacrococcygeal; Ovary; Metachronous.

TERATOMA DE APARICIÓN SECUENCIAL EN EDAD PEDIÁTRICA: ¿CASUALIDAD O CAUSALIDAD?

RESUMEN

Describimos el inusual caso de una paciente con antecedente de dos teratomas maduros no relacionados en cuanto a su localización y debut. Una niña de 12 años consultó por la aparición de una tumoración en la región hipogástrica de crecimiento progresivo sin otra clínica asociada. Había sido intervenida por un teratoma quístico maduro sacrococcígeo en el periodo neonatal con su extirpación completa y, ausencia secuelas clínicas y tratamiento adicional durante diez años de seguimiento posterior. Los exámenes radiológicos mostraron una gran masa quística de 20 × 12 × 18 cm que se extendía entre la región pélvica y el hemiabdomen inferior, acompañada por otras dos pequeñas formaciones similares adyacentes al ovario derecho. Los marcadores tumorales resultaron negativos y se llevó a cabo una salpingooforectomía derecha laparoscópica con una excelente evolución postoperatoria. El examen histopatológico, de nuevo, informó la lesión como teratoma quístico maduro. El estudio genético descartó una posible causalidad en este ámbito.

PALABRAS CLAVE: Teratoma maduro; Sacrococcígeo; Ovario; Metacrónico.

INTRODUCTION

As tumors developing from primordial totipotent cells, teratomas may host cells stemming from one of the three germinal layers or more[1]. Classified typology-wise as mature or immature, and location-wise as gonadal or extragonadal, they are one of the most frequent tumors in pediatric patients, with a certain prevalence in female ones (4:1). Among all variants found, sacrococcygeal teratomas (SCT) are the most frequent in the neonatal period, whereas mature ovarian teratomas (OT) represent up to 50% of all pediatric gynecological neoplasias[2].

In spite of the evidence already found in ancient texts, which demonstrates this type of tumors have existed for a very long time, it was not until 1659 that Doctor Johannes Scultetus published the first official case of OT. Subsequently, Rudolf Virchow first proposed the term "teratoma" to describe this type of lesions 200 years later[3,4]. From then on, scientific publications related to this type of tumor greatly increased, thanks to which it gradually became one of the most prolific subjects in the field of pediatric oncology. However, references to the potential metachronous occurrence of teratomas with an identical histology in various organs remain scarce[5-8]. Indeed, to our knowledge, no cases of metachronous mature ovarian teratoma following mature sacrococcygeal teratoma have been reported yet.

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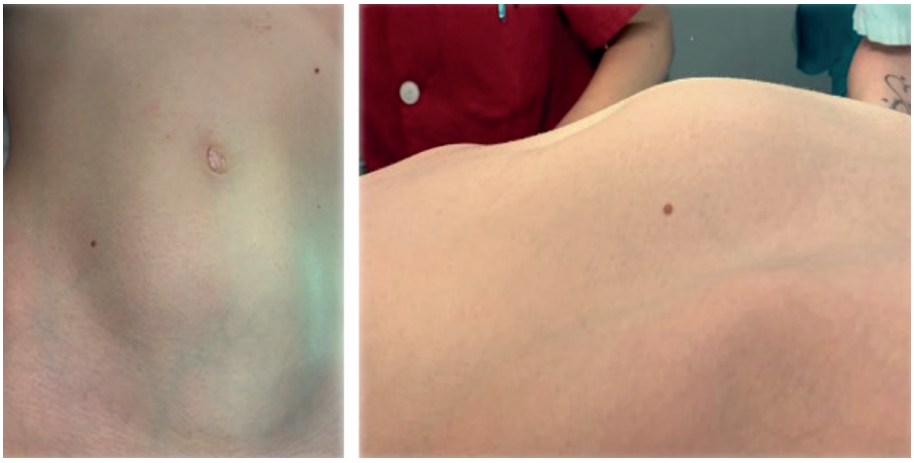

Figure 1. Physical exploration of the abdomen with a suspected large hypogastric mass.

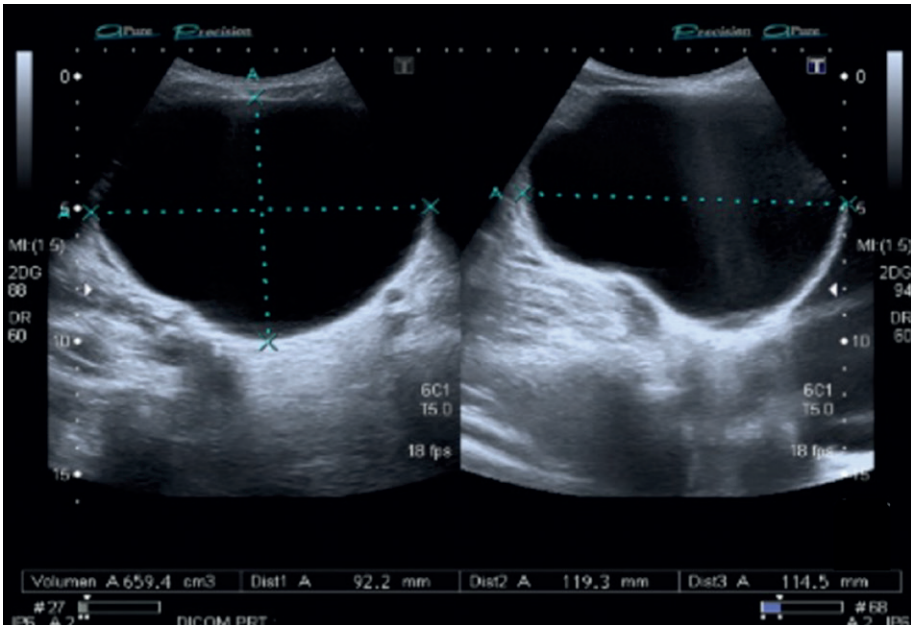

Figure 2. Ultrasound examination: large (92.2 × 119.3 × 114.5 mm) cystic lesion seemingly attached to the right adnexa.

We describe the unusual case of a female patient with a history of two mature teratomas non-correlated in terms of location and debut.

CLINICAL CASE

Female patient prenatally diagnosed with sacrococcygeal teratoma. She had undergone surgery at 24 hours of life, with the tumor being fully removed, no clinical sequelae, and progression being uneventful for 10 years of close follow-up. She presented to our consultation at 12 years of age as a result of a growing large abdominal mass in the hypogastric region, with no further clinical signs (Fig. 1). Radiological examinations – ultrasonography and MRI – showed a large 9 x 12 x 15 cm cystic mass at the pelvic region and the lower hemiabdomen. It was associated with two further similarly-looking small formations adjacent to the right ovary (Fig. 2).

The analytical study of tumor markers was negative. The case was presented at a cross-disciplinary session, and surgical removal was decided upon. Under laparoscopic approach, a great mass attached to the right ovary and tube was identified. Following content aspiration for study and ease of maneuverability purposes, a right salpingoophorectomy was conducted, with an excellent postoperative progression. Again, the pathological examination classified the surgical specimen as a mature cystic teratoma with a negative cytology.

Given the particular sequentiality of the case, a thorough genetic study was carried out to search for potential mutations or other abnormalities in both tumors, which allowed causation to be ruled out. After two years of follow-up, the patient remains completely asymptomatic and

remains under follow-up by a cross-disciplinary medical/surgical team.

DISCUSSION

Even though they may occur anywhere in the body and at any given period of life, teratomas are typically isolated lesions[1,9]. However, bilaterality in paired organs may account for up to 12% of cases in ovarian teratomas, and up to 2-3% of cases in testicular teratomas[9,10]. Nowadays, long-term patient surveillance is preferred as a result of this, and also in light of the increase in cases associated with metachronous contralateral mature ovarian teratomas in patients with a history of unilateral mature ovarian teratoma, which may cause hormonal and reproductive complications. Similar data has been published regarding testicular teratomas. The risk of developing a metachronous tumor like this is estimated between 2.5% and 23%, with most of them being diagnosed in the first 5 years following diagnosis of the first tumor. However, it should be noted that, in two publications at least, the second tumor emerged up to 14 years following the occurrence of the first[2,11-13].

Our patient developed ovarian teratoma 12 years following sacrococcygeal teratoma surgery, which was carried out neonatally, with an identical histology of mature cystic teratoma. The occurrence of metachronous teratomas with a shared histology in different organs is very rare. Okino et al. presented the case of a mature diaphragmatic teratoma 33 years following mature ovarian teratoma[6]. Lovett et al. described a mature parietal teratoma 8 months after mature testicular teratoma[5]. Zhelnin et al. and Fenkel et al. treated two cases where immature intraocular teratoma occurred 1-2 months following immature sacrococcygeal teratoma[8]. However, no studies describing the emergence of metachronous teratoma following mature SCT had been published yet.

In light of the above, it remains to be clarified whether both tumors are directly related or if they emerged as a result of independent development events. Similarly to other authors, we also believe the second tumor is not a metastasis of the first, since they occurred many years apart and the original histology was clearly benign, without immature elements or malignancy foci. The fact tumor markers were normal during the whole follow-up period also makes it an unlikely possibility.

Under another perspective, one should wonder whether the metachronous occurrence of these tumors could be of a genetic nature. Deletions in chromosomes 1 and 6 have been reported in children, whereas disorders in chromosome 12 and expression of the N-myc gene have been described in adults. However, this always occurred in the presence of immature teratomas, and never with mature ones[14]. Familial cases have also been reported, and Rayburn and Barr even described OT in a pregnant woman concomitant with SCT in her fetus[15,16]. The heterogeneity of results has led to a lack of understanding and medical usefulness of genetics in teratomas. Consequently, the possibility of these two tumors occurring as a result of genetic predisposition cannot be either taken for granted or ruled out.

Nevertheless, the metachronous multi-centric development of these tumors could originate during embryonic development, when totipotent germ cells – which are the origin of teratomas – migrate from the yolk sac to the primitive gonads between the fourth and the fifth gestational week. In this migration process, they may be subject to any given alteration which could potentially lead to teratomas of an identical histology anywhere in the body, from the brain to the coccygeal region[17]. This could explain the occurrence of synchronous teratomas with an identical histology in different organs, such as the instances described in the literature, and also the case reported in this article[18,19].

According to the literature reviewed, it is impossible to determine whether both tumors have a shared origin, they are two fully independent neoplasias, or there is a link between them still to be determined. Therefore, oncological groups should be fully aware of the importance of collecting and publishing all the data available related to potential new cases. This way, a consensual explanation regarding the origin of these lesions could be reached, and we could know which patients or cases have a higher risk of developing a new tumor.

In conclusion, the sequential development of second neoplasias of an identical nature in the same patient is possible, which makes it necessary to remain highly suspicious. Patients with a history of neonatal teratoma require a long-term follow-up and studies analyzing the impact of such surveillance in order to determine whether its benefits are greater than its drawbacks in terms of increased cost and patient and family anxiety. Genetic examination stands as a useful tool to rule out causation in this field.

REFERENCES

1. Lakhoo K. Neonatal teratomas. Early Hum Dev. 2010; 86: 643-7.
2. Szymon O, Bogusz B, Taczanowska-Niemczuk A, Ma´slanka M, Górecki W. Ovarian sparing surgery in mature ovarian teratomas in children: A 20-year Single-Center Experience. Eur J Pediatr Surg. 2021; 31: 2-7.
3. Pantoja E, Noy MA, Axtmayer RW, Colon FE, Pelegrina I. Ovarian dermoids and their complications. Comprehensive historical review. Obstet Gynecol Surv. 1975; 30: 1-20.
4. Peterson F. Malignant degeneration of benign cystic teratomas of the overy; a collective review of the literature. Obstet Gynecol Surv. 1957; 12: 793-830.
5. Lovett RW, Councilman W. A case of double teratoma. J Exp Med. 1897; 2: 427-38.

6. Okino H, Koga Y, Tsuneyoshi M, Takeda S. Metachronous mature cystic teratomas in the left ovary and bilateral diaphragm: Report of a case. Surg Today. 2006; 36: 1012-4.
7. Hirano T, Kumabe T, Murakami K, Watanabe M, Shirane R, Yoshimoto T. Metachronous neurohypophysial immature teratoma occurring 10 years after total resection of pineal mature teratoma. Child's Nerv Syst. 2001; 17: 286-9.
8. Zhelnin KE, Gebhard GM, Mirsky DM, Oliver SCN, Lovell MA, Galambos C, et al. Pediatric intraocular immature teratoma associated with sacrococcygeal teratoma: Case report and review of the literature. Pediatr Dev Pathol. 2017; 20: 240-4.
9. Ahmed A, Lotfollahzadeh S. Cystic teratoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
10. López PC, Navarro HP, Tobarra MA, Ruiz JM, Romero GL, María J, et al. Tumor testicular bilateral sincrónico de distinta histología. Arch Esp Urol. 2008; 6: 741-4.
11. Delehaye F, Sarnacki S, Orbach D, Cheikhelard A, Rouger J, Parienti JJ, et al. Lessons from a large nationwide cohort of 350 children with ovarian mature teratoma: A study in favor of ovarian-sparing surgery. Pediatr Blood Cancer. 2022; 69: e29421.
12. Arthur F, Hennessey I, Pizer B, Losty PD. Surgical management and outcomes of paediatric ovarian tumours—a 25-year UK single centre experience. Pediatr Surg Int. 2021; 37: 1355-9.
13. Kiely D, Lewis C, Gray J, Hall N. Prevalence of metachronous contralateral mature ovarian teratoma: A systematic review. Pediatr Blood Cancer. 2021; 68: e29237.
14. Harms D, Zahn S, Göbel U, Schneider DT. Pathology and molecular biology of teratomas in childhood and adolescence. Klin Padiatr. 2006; 218: 296-302.
15. Nezhat C, Kotikela S, Mann A, Hajhosseini B, Veeraswamy A, Lewis M. Familial cystic teratomas: four case reports and review of the literature. J Minim Invasive Gynecol. 2010; 17: 782-6.
16. Rayburn WF, Barr M. Teratomas: Concordance in mother and fetus. Am J Obstet Gynecol. 1982; 144: 110-2.
17. Isaacs H. Perinatal (fetal and neonatal) germ cell tumors. J Pediatr Surg. 2004; 39: 1003-13.
18. Chaudhary N, Malik KPS, Gupta A, Rai AK, Gupta P, Khanna G. Synchronous cystic teratomas of the craniofacial region. J Laryngol Otol. 2003; 117: 824-6.
19. Tauro LF, Shetty P, Kamath A, Shetty A. Double whammy - Mediastinal and ovarian teratoma: A rare clinical co-existence. J Thorac Dis. 2012; 4: 434-6.