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CLINICAL CASE

Challenges in diagnosis of primary penile tumor of the endodermal sinus in infants

Desafíos diagnósticos del tumor peneano primario del seno endodérmico en lactantes

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What do we know about the subject matter of this study?

In pediatrics, germinal cell tumors represent a rare group of malignant neoplasms. Endodermal sinus tumors, also known as yolk sac tumors, are usually of gonadal origin, and their extragonadal presentation is exceptional, particularly in the penis.

What does this study contribute to what is already known?

We present a case of an extragonadal endodermal sinus tumor in an infant, highlighting the efficacy of surgical resection and chemotherapy, with a favorable prognosis. We emphasize the usefulness of alpha-fetoprotein as a marker for diagnosis and follow-up.

Abstract

Introduction: Germ cell tumors (GCTs) are an uncommon group of malignant neoplasms in the pediatric population. The endodermal sinus tumor, also known as yolk sac tumor, is the most frequent subtype of GCT and typically originates in the gonads. Extragonadal presentation is rare, particularly in the penis. **Objective:** To describe the case of a male infant with an extragonadal penile endodermal sinus tumor, emphasizing the diagnostic challenges and the role of alpha-fetoprotein (αFP) as a monitoring biomarker. **Clinical Case:** A previously healthy 18-month-old male infant presented with a one-month history of a left inguinoscrotal mass. Imaging revealed a tumor arising from the corpus cavernosum with inguinal extension. The initial αFP level was 4,396 ng/mL. Endodermal sinus tumor with pulmonary metastasis (stage IV) was confirmed. A macroscopically complete surgical resection was performed, preserving penile and testicular structures, followed by six cycles of chemotherapy with bleomycin, etoposide, and carboplatin. αFP levels decreased progressively (2,325 ng/mL at 2 days, 103 ng/mL at 4 weeks, 12.21 ng/mL at the end of treatment, and 6.9 ng/mL at 6 months). At

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12 months of follow-up, the patient remained disease-free, with normal psychomotor development and preserved urinary function. **Conclusions:** Extragonadal penile localization of endodermal sinus tumor is rare but has a favorable prognosis when treated with conservative management and chemotherapy. αFP is a useful marker for both diagnosis and follow-up.

Introduction

Germinal cell tumors (GCT) are a heterogeneous group of malignant neoplasms with highly variable histopathological characteristics. They originate from precursor cells of primordial germ cells and are classified as seminomatous and non-seminomatous tumors[1].

These tumors represent a rare group of malignant neoplasms in children. According to the National Childhood Cancer Registry of Chile, GCTs account for 4.9% of cancers in children under 15 years of age, with an incidence rate of 6.7 per million children in that age group[2]. This pattern is consistent with data from the US Surveillance, Epidemiology, and End Results Program, which shows a bimodal distribution, with peaks in incidence in children under 4 years of age and between 10 and 15 years of age[3].

Endodermal sinus tumors, also known as yolk sac tumors, are malignant neoplasms derived from germ cells and histologically may present microcystic, reticular, hepatoid, and endodermal patterns, although these have no proven clinical implications[4]. They usually appear in the gonads, and only 10 to 20% occur at extragonadal sites. Among these, the mediastinum is the most frequent location, followed by intracranial, sacrococcygeal, and retroperitoneal sites[5]. Endodermal sinus tumors are considered non-seminomatous, meaning that histologically they originate from differentiated germ cells[4,5].

High levels of alpha-fetoprotein (αFP) are present in more than 90% of patients with this type of tumor, so this biomarker is used to support the diagnosis and monitor response to both surgical and chemotherapeutic treatment[1]. It is important to note that in infants, αFP levels must be interpreted according to age, as they may be physiologically elevated in the first months of life[6,7].

Klinefelter syndrome (karyotype 47, XXY) has been associated with a significant increase in the risk of extragonadal germ cell tumors, especially mediastinal tumors, with a 50-fold higher risk compared to the general population[1]. In addition, associations with congenital defects and other chromosomal abnormalities, both syndromic and non-syndromic, have been described[6].

Treatment consists of complete macroscopic surgical resection of the lesion combined with chemotherapy. A regimen based on bleomycin, etoposide, and platinum derivatives is the standard in children, usually with an adequate response to treatment[8]. The prognosis is variable, depending mainly on early detection, tumor biology, clinical stage, and early initiation of treatment. Survival in gonadal endodermal sinus tumors can exceed 90% even with metastasis[8-10], while in extragonadal locations such as the mediastinum, it is significantly lower[11].

The objective of this work is to describe the case of an infant with an extragonadal penile endodermal sinus tumor, highlighting the diagnostic challenges and the value of αFP as a follow-up marker.

Clinical Case

An 18-month-old male infant born via uncomplicated vaginal delivery, with no history of acute infectious conditions, no oncologic family history, chromosomal abnormalities, or genetic disorders, presented with a one-month history of a rapidly growing mass in the left inguinal region, not associated with inflammatory changes or constitutional symptoms.

On physical examination, the patient presented adequate nutritional status, with no phenotypic abnormalities suggestive of a syndromic diagnosis. A mass of approximately 10 cm in diameter was observed in the left inguinal region, with a hard consistency, displacing the penis and crossing the midline. It was non-tender, without erythema or other inflammatory signs, and there were no inguinal lymphadenopathies or abdominal masses.

The results of hematological, biochemical, and microbiological studies were within normal ranges for age; tumor markers with elevated αFP at 4396 ng/mL [normal value 0-20 ng/mL (6 months to adult)], but carcinoembryonic antigen and β-HCG were negative.

Testicular ultrasound showed a diffuse enlargement of the left testicle, with heterogeneous echogenicity and increased vasculature. In addition, a mass was observed displacing the contralateral testicle and the root of the penis, extending into the ipsilateral inguinal canal. The CT scan showed a mass with similar characteristics in the same location, measuring 3.7x3.6 cm, heterogeneous, oval, well-defined, with thick walls and

diffuse enhancement. However, MRI showed that the lesion originated from the left contour of the mid-portion of the corpus spongiosum, extending into the left inguinal canal, in contact with the vas deferens and adjacent pampiniform vessels, with infiltration of the penile urethra and extrinsic compression of the corpora cavernosa. There was no evidence of testicular or prostatic involvement and no retroperitoneal lymphadenopathy (Figure 1).

A biopsy of the lesion was performed during an initial surgical procedure, which showed an immunophenotypic study with no evidence of hematolymphoid infiltration. Histopathology showed large cells with vesicular nuclei and foamy cytoplasm, high mitotic activity, and a heterogeneous infiltrative pattern, forming papillary, microcystic, and reticular areas with cell cords and myxoid regions. Areas of necrosis, as well as foci of vascular and perineural invasion, were also observed, consistent with a diagnosis of pure endodermal sinus tumor with vascular and perineural invasion (Figure 2).

During the second surgical procedure, the tumor was identified, which originates from the left corpus cavernosum (Video 1), where a complete macroscopic surgical resection was achieved. The anatomical findings were subsequently confirmed by histopathology and pathological anatomy studies. This course evidenced a discrepancy between the imaging studies and the definitive surgical findings, attributable to the complex anatomy of the penile/inguinal region and the proximity of the involved structures.

Definitive pathology with immunohistochemical staining showed characteristic positivity of the tumor cells for Glypican 3 and αFP markers, consistent with a pure endodermal sinus tumor with involved resection margins. A nodule within the left corpus cavernosum had a tumor in contact with the resection margins. CD117 marker was positive, which is usually negative, but its positivity may be attributed to solid components in endodermal sinus tumors. OCT3-4, CD20, HGC, and D2 40 were negative, ruling out a seminomatous component (Figure 3).

Staging studies with preoperative chest CT scan show a solid nodule measuring 0.7x0.6 cm, with spiculated margins, located in the apical segment of the right lower lung lobe. A whole-body bone scan, initially requested due to right hip pain in the postoperative period, showed no signs of metastasis. Karyotype 46, XY. The patient was classified as clinical stage IV, standard risk, according to the GCT-GALOP-2017 protocol (12). Chemotherapy was initiated for extracranial germ cell tumors using the BEJ protocol (bleomycin, etoposide, and carboplatin).

During the clinical course, the patient developed a urinary tract infection with isolation of susceptible *Pseudomonas aeruginosa* in the context of a febrile neutropenia episode, with no further complications. Postoperative αFP decreased to 2325 ng/mL at two days

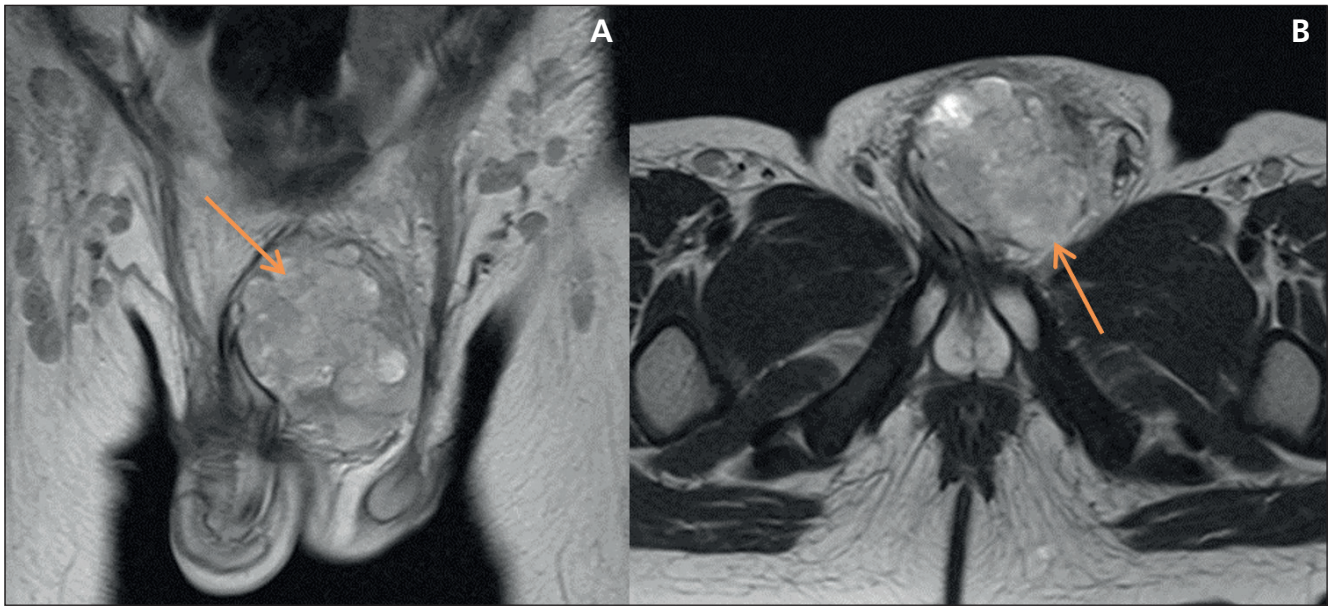

Figure 1. Pelvic Magnetic Resonance Imaging. A and B: Axial and coronal T2-weighted sequences of the inguinal and perineal regions demonstrate a well-defined, moderately hyperintense, and heterogeneous solid mass within the left inguinal region. The lesion exerts an extrinsic mass effect on both the corpus cavernosum and corpus spongiosum, without evidence of disruption of the surrounding tunica albuginea. The left inguinal structures are mildly displaced laterally, with no evidence of tumor infiltration. Bilateral inguinal lymph nodes are noted, likely benign based on size, morphology, and signal characteristics.

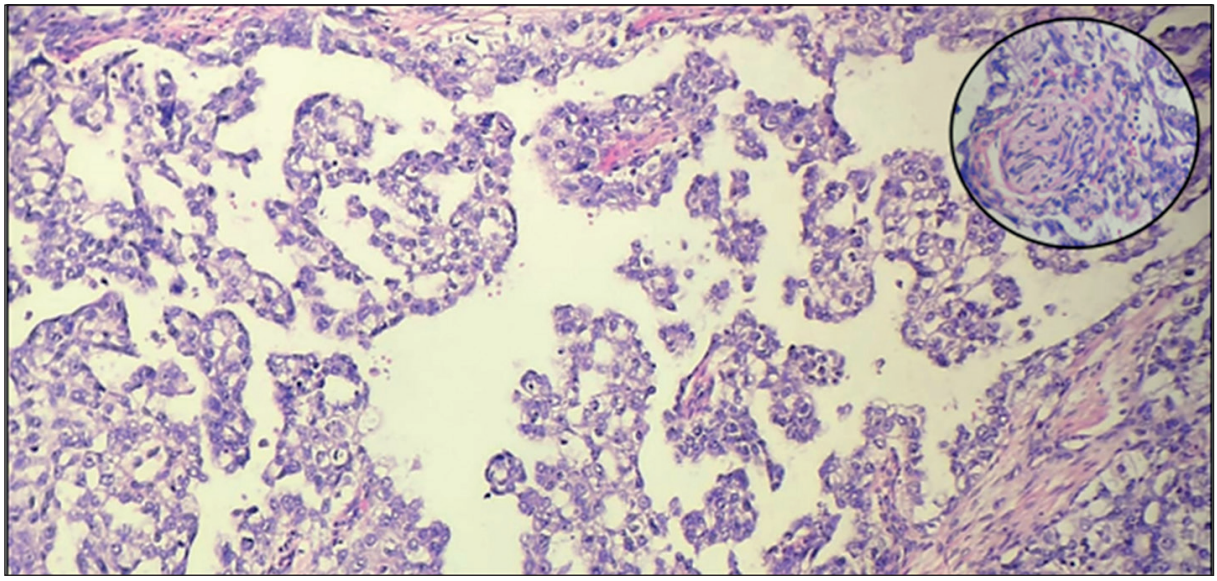

Figure 2. Lesion Biopsy. C: Yolk sac tumor. H&E stain. Microcystic and pseudoglandular structures with occasional fibrovascular cores. Note the perineural invasion highlighted in the circle, identified in a separate field.

and to 103 ng/mL at 4 weeks (Table 1). He completed 6 cycles of chemotherapy, with αFP reported at 12.21 ng/mL. End-of-treatment abdominal and pelvic MRI showed residual scar-like tissue located along the left lateral margin of the base of the penis and the ipsilateral inguinal region, with no evidence of viable tumor tissue and no adjacent or distant lymph node involvement.

Three months after completing treatment, αFP was measured at 9.8 ng/mL. Six months later, αFP was 6.9 ng/mL, and chest, abdomen, and pelvic CT scans showed resolution of the pulmonary nodule, with no recurrent or suspicious metastatic lesions in the abdomen or pelvis. At the one-year clinical evaluation, the patient remained free of clinical signs of recurrence, with adequate psychomotor development and normal urination.

Video 1. Macroscopic Resection of the Lesion. Surgical description showing a tumor arising from the left corpus cavernosum, with a hard, stone-like consistency. Within the corpus cavernosum, from which the lesion originates, a solid nodule is identified and successfully resected. No involvement of the testes is noted.

Note: To scan the video codes, point your smartphone camera at the image and open the displayed link. In some cases, you may need to install a QR code reader application.

Discussion

We present the case of an infant with an extragonadal endodermal sinus tumor in the penile/inguinal region with pulmonary metastatic involvement, but without pelvic or retroperitoneal disease, in whom complete surgical resection was achieved without damage to adjacent structures and with an adequate response to treatment.

Germ cell tumors represent a rare group of malignant neoplasms in children. They have a bimodal distribution, with peaks of incidence in children under 4 years of age and between 10 and 15 years of age. Although gonadal presentation is the most common, between 10% and 20% of germ cell tumors originate in extragonadal locations[2,3]. This presentation results from aberrant migration of primordial germ cells during embryogenesis, which explains their preferential location along the midline, including the mediastinum, retroperitoneum, sacrococcygeal region, and intracranial sites[4,5].

Extragonadal presentation in the penis, as in the case described, is exceptional and represents a diagnostic and therapeutic challenge. Few cases have been

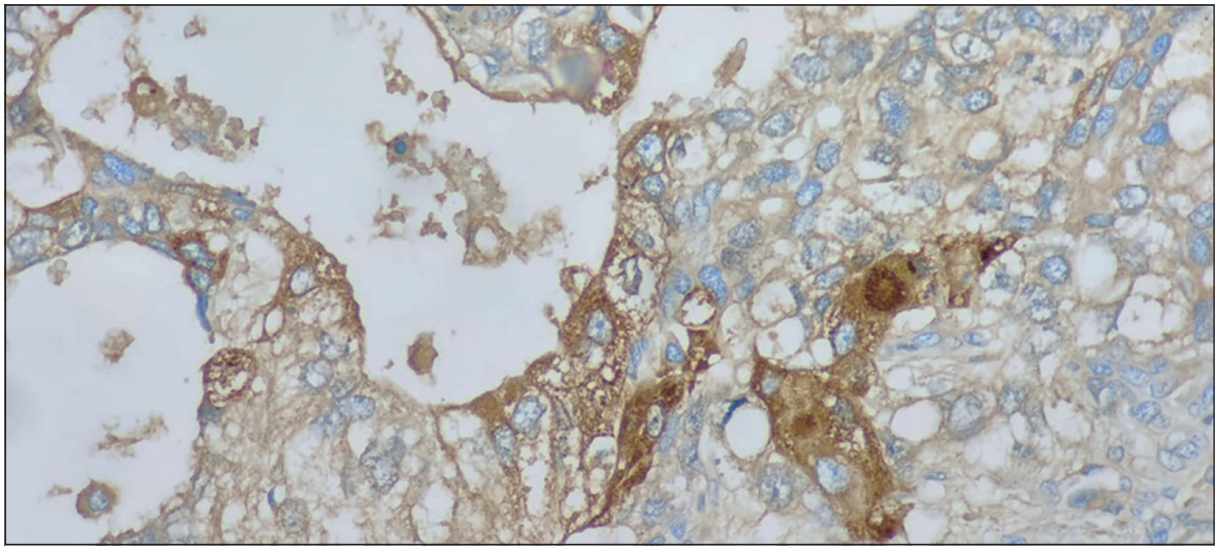

Figure 3. Immunohistochemistry. E: Immunohistochemical stains demonstrate characteristic positivity of the tumor cells for Glypican-3 and Alpha-fetoprotein. Additional studies with D2-40, CD30, and hCG immunomarkers were negative, supporting the diagnosis of a pure yolk sac tumor.

Table 1. Alpha-fetoprotein (αFP) Evolution

Time Point	αFP (ng/mL)	Interpretation
Diagnosis	4396	Marked elevation
2 days post-surgery	2325	Initial decline
4 weeks post-surgery	103	Favorable response
End of chemotherapy	12.21	Near normalization
3-month follow-up	9.8	Normalization
6-month follow-up	6.9	Sustained normal level

Normal range: 0–20 ng/mL (6 months to adult)

reported, some with associations with genetic pathologies such as achondroplasia (Karan et al)[13], who ultimately report that the relationship could be incidental, or cases such as that of Alurkar et al, reported in 1991[14], who presented the first case of this presentation, very similar in terms of its clinical course and increased αFP levels, to which they used the same chemotherapeutic protocol without surgical management, and with a good response of tumor regression, however, they present the limitation of maximum follow-up at 6 months.

In endodermal sinus tumors, elevated αFP levels are present in 90% of cases in males and 95% in females, making it a highly sensitive marker for diagnosis and useful for follow-up, as evidenced in our case. However, it may be elevated in the first months of life, which highlights the importance of adjusting levels to the patient's age[6]. In a meta-analysis conducted by Guo et al.[7], the αFP value at diagnosis was not found to have prognostic value; however, a high postoperative value is associated with a poor prognosis. It was also shown that tumor stage is an important prognostic factor, but it is independent of the αFP level[7,8].

Kramarova et al.[9], in a systematic review of the EUROCARE initiative, a European multicenter registry that records the survival of cancer patients, suggest that the survival rates for these tumors vary from 50% to 90%, mainly due to factors such as the clinical stage at diagnosis and the surgical complexity of the resection[9].

Other cases reported in the literature, such as that of Samaila et al.[15], show a later diagnosis in terms of age of onset, as well as a more advanced form, in the context of an indigenous patient in Nigeria who was treated at a center with limited resources, where it was impossible to measure all immunohistochemical markers, but they managed to perform both surgical and chemotherapeutic treatment, with a fatal outcome within 3 months, reaffirming the biopsychosocial determinants in the prognosis of these patients[15].

There are a few reports in Latin America. Bautista Moreno et al.[16] report their 20 years of experience with GCT in Colombia, with a survival rate of 96%, where 98.7% of patients were treated surgically and 58.2% also received chemotherapy[16].

Currently, treatment involves cytoreductive surgery with the aim of complete macroscopic resection, with postoperative chemotherapy based on a combination of bleomycin, etoposide, and platinum deriv-

atives, although there is currently controversy over which platinum to use in pediatrics. In addition, the use of bleomycin is associated with potential pulmonary toxicity, requiring specialized monitoring. In the specific case of endodermal sinus tumors, the role of radiotherapy is not clearly established and is not usually indicated[8-10].

Due to the variety of metastasis locations and the different degrees of tissue infiltration, surgical resection may be ineffective, negatively impacting outcomes by failing to achieve complete resection[11]. In the case presented, there was a discrepancy between the imaging studies and the definitive surgical findings, attributable to the complex anatomy of the penile/inguinal region and the proximity of the structures involved. Currently, radical orchiectomy in addition to pelvic dissection is not considered to improve clinical outcomes compared to conservative surgery, but it can have consequences such as infertility and psychological implications due to the cosmetic impact on the patient[17].

In cases of proven peritoneal, retroperitoneal, and gonadal involvement, radical orchiectomy and even penectomy are indicated. However, function and structure preserving surgeries, with lymphadenectomy, in the adolescent population, where complete resection of the tumor lesion is achieved, they have a survival rate of 96%, reaching up to 99% at 5 years[17].

The case presented illustrates the complexity of the diagnostic challenge, starting with clinical suspicion, as well as the challenges that may arise, such as the discrepancy between imaging and surgical findings. It also allows for a consistent comparison with the literature on the diagnostic value and clinical follow-up of αFP. Regarding the treatment, a conservative procedure was successfully performed, thus avoiding orchiectomy and penectomy, with a favorable outcome for the patient.

Conclusion

Germinal cell tumors, especially endodermal sinus tumors, have a significant morbidity burden. Although extragonadal presentation is rare, a high index of suspicion should be maintained in the presence of midline masses in order to establish an early diagnosis and treatment, thus positively impacting survival outcomes. The presence of positive αFP supports the diagnosis, but a high value at the time of diagnosis is not related to prognosis; its measurement is considered very useful for monitoring these patients in terms of response to surgical and chemotherapeutic treatment. We encourage the continuous report of these cases to enrich the knowledge and experience of managing these patients.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the parents (tutors) of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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References

1. Van den Akker M, Vervloessem D, Huybrechs A, Declercq S, Van der Werff Ten Bosch J. Yolk sac tumor in the abdominal wall of an 18-month-old girl: a case report. J Med Case Rep. 2017;11(1):47. https://doi.org/10.1186/s13256-017-1216-4.
2. Ministerio de Salud (Chile). Registro Nacional de Cáncer Infantil (RENCI). Tasa e incidencia de tumores de células germinales en menores de 15 años. Informe RENCI 2007-2019. Santiago, Chile; 2024. (Registro nacional).
3. National Cancer Institute. SEER Pediatric Monograph: Germ Cell, Trophoblastic, and Other Gonadal Neoplasms. In: Cancer Incidence and Survival among Children and Adolescents, 1986-1995, SEER Program. Bethesda (MD): NCI; 2012.
4. Rodríguez P, Godoy JI. Tumor de células germinales. Rev Med. 2008;16(2):200-14. Available from: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0121-52562008000200008.
5. Nakazawa R, Soneda S, Kinoshita A, Kitagawa H, Koike J, Chikaraishi T. A case report: primary extragonadal yolk sac tumor of penile shaft in a 2-year-old child. Int J Urol. 2009;16(4):413-5. https://doi.org/10.1111/j.1442-2042.2009.02264.x.
6. Pierce JL, Frazier AL, Amatruda JF. Pediatric germ cell tumors: a developmental perspective. Adv Urol. 2018;2018:9059382. https://doi.org/10.1155/2018/9059382.
7. Guo YL, Zhang YL, Zhu JQ. Prognostic value of serum α-fetoprotein in ovarian yolk sac tumors: a systematic review and meta-analysis. Mol Clin Oncol. 2015;3(1):125-32. https://doi.org/10.3892/mco.2014.417.
8. Wang X, Zhao S, Zhao M, Wang D, Chen H, Jiang L. Use of targeted therapy and immunotherapy for the treatment of yolk sac tumors in extragonadal pelvic sites: two case reports. Gland Surg. 2021;10(10):3045-52. https://doi.org/10.21037/gs-21-663.
9. Kramárová E, Mann JR, Magnani C, Corraziari I, Berrino F. Survival of children with malignant germ cell, trophoblastic and other gonadal tumours in Europe. Eur J Cancer. 2001;37(6):750-9. https://doi.org/10.1016/S0959-8049(01)00047-8.
10. Dällenbach P, Bonnefoi H, Pelte MF, Vlastos G. Yolk sac tumours of the ovary: an update. Eur J Surg Oncol. 2006;32(10):1063-75. https://doi.org/10.1016/j.ejso.2006.07.010.
11. Sudour-Bonnange H, Orbach D, Kalfa N, Fasola S, Patte C. Germ cell tumors in atypical locations: experience of the TGM 95 SFCE trial. J Pediatr Hematol Oncol. 2014;36(8):646-8. https://doi.org/10.1097/MPH.0000000000000083.
12. St. Jude Children's Research Hospital. (s. f.). AGCT1532: A Randomized Phase 3 Trial of Accelerated Versus Standard BEP Chemotherapy for Patients with Intermediate and Poor-Risk Metastatic Germ Cell Tumors. Recuperado de https://www.stjude.org/care-treatment/clinical-trials/agct1532-germ-cell-tumors.html
13. Karan S, Mukherjee R, Singha Roy P, Mohin M, Firdous W, Chatterjee U. Yolk Sac Tumour Arising in the Glans Penis an Achondroplasic Child: A Case Report with Summary of Prior Published Cases. Fetal Pediatr Pathol. 2023 Oct;42(5):820–824. doi:10.1080/15513815.2023.2242941. Epub 2023 Aug 3
14. Alurkar SS, Dhabhar BN, Jambhekar NA, Kulkarni JN, Advani SH. Primary endodermal sinus tumour of the penis: a case report. J Urol. 1992 Jul;148(1):131-3. doi:10.1016/S0022-5347(17)36534-5
15. Samaila MO, Maitama HY, Abdullahi K, Mbibu H, Waziri GD. Yolk sac tumour of the penile shaft: a rare primary extra-gonadal presentation. Afr J Paediatr Surg. 2011 May-Aug;8(2):241-3. doi:10.4103/0189-6725.86074
16. Bautista Moreno D, Ariza-Varon M, Medina-Vega DL, et al. Tumores germinales gonadales en niños: experiencia de 20 años en un centro de referencia pediátrico. Rev Fac Med. 2015;63(1):47–56. https://doi.org/10.15446/revfacmed.v63n1.44794.
17. De Campos Vieira Abib S, Chui CHH, Cox S, et al. International Society of Paediatric Surgical Oncology (IPSO) surgical practice guidelines. ecancer. 2022;16:1356.