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Gonadal dysfunction and metabolic alterations in a survivor of bilateral Nephroblastoma: A case report

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Abstract
Advances in pediatric oncology have markedly improved survival rates; however, long-term endocrine and metabolic sequelae remain frequent among survivors. Gonadal dysfunction and metabolic disorders represent significant late effects, particularly in patients exposed to intensive chemotherapy, radiotherapy, and hematopoietic stem cell transplantation at an early age. We report the case of a male adolescent survivor of bilateral nephroblastoma diagnosed in infancy and treated with surgery, high-dose chemotherapy, and autologous bone marrow transplantation, who later developed hypergonadotropic hypogonadism, azoospermia, obesity, insulin resistance, dyslipidemia, and hepatic steatosis. This case highlights the complex interplay between gonadal failure and metabolic complications in childhood cancer survivors and underscores the importance of long-term, multidisciplinary follow-up. Early identification of endocrine dysfunction, timely hormonal replacement, metabolic intervention, and counseling regarding fertility preservation are essential to optimize health outcomes and quality of life in this growing population.

Keywords: Childhood cancer survivor, gonadal failure, hypergonadotropic hypogonadism, fertility preservation, metabolic complications, nephroblastoma

Introduction
Advances in the development of effective therapies for the treatment of paediatric cancer have resulted in remarkable improvements in survival rates over recent decades. Currently, approximately 80% of cancers arising in childhood and adolescence are diagnosed and successfully treated, with variations related to the economic capacity of each country [1, 2]. Consequently, there is a growing number of survivors of childhood cancer who face long-term sequelae. These depend not only on the treatment received but also on age at diagnosis, tumour type, and genetic polymorphisms [2]. Approximately 40–50% of childhood cancer survivors develop disorders of the endocrine system throughout their lifetime [1, 2]. These alterations may compromise growth, puberty, thyroid function, fertility, bone metabolism, among others. Radiotherapy may interfere with the endocrine system depending on the total dose received and treatment duration, as may chemotherapy depending on the agents used and their cumulative doses [2]. Gonadal dysfunction is a possible complication of both radiotherapy and chemotherapy. The testicular germinal epithelium is highly sensitive to radiation. Elevation of Follicle-Stimulatin Hormone (FSH) is observed with radiation doses as low as 0.1 Gy, and recovery of spermatogenesis is highly unlikely when doses exceed 4–6 Gy. [2] More than 83% of cancer survivors treated with combined modalities (chemotherapy and abdominal/pelvic radiotherapy) may develop azoospermia, and approximately 17% of these may show potential recovery of spermatogenesis up to 15 years after completion of treatment [2].
Chemotherapy is also responsible for long-term gonadal dysfunction [2]. Chemotherapeutic agents can be divided into cell cycle–specific agents (e.g., vincristine) and cell cycle–nonspecific agents (e.g., actinomycin). Cell cycle–specific agents inhibit mitosis by altering DNA synthesis, thereby affecting cells with a high proliferation rate. Germ cells involved in spermatogenesis during puberty are the most affected. Spermatogonia and Sertoli cells also display moderate proliferative activity during childhood and may be affected by these drugs. In contrast, cell cycle–nonspecific agents cause direct DNA and RNA damage in both highly proliferative and quiescent cells, rendering all types of gonadal cells susceptible to these agents at any age [1].

Fertility preservation in children undergoing chemotherapy and radiotherapy is an increasingly important topic. It is estimated that approximately one third of childhood cancer survivors experience infertility due to oncological treatments. Fertility preservation offers survivors the possibility of choosing parenthood in the future, which may positively impact psychological and emotional well-being. In post-pubertal males, sperm cryopreservation before treatment initiation is a standard procedure for fertility preservation. [2]. In prepubertal boys, spermatozoa are immature and therefore cryopreservation techniques are not an option in this age group. At present, reimplantation or transplantation of testicular tissue remains experimental. Thus, testicular tissue containing spermatogonia is cryopreserved before oncological treatment with the potential for future reimplantation, benefiting from more effective and safer techniques.

Currently, there are no well-defined protocols for the evaluation of the endocrine system in childhood and adolescent cancer survivors. Given the complexity of oncological treatments and their potential long-term adverse effects, active involvement of paediatric endocrinology in the follow-up of these patients is essential. Regular monitoring allows early detection of abnormalities, enabling timely interventions that promote healthier development, prevent future complications, and improve quality of life.

Case Report

A 13-year-and-2-month-old male adolescent was referred to the Paediatric Endocrinology consultation for obesity (body mass index 28.1 kg/m², z-score +2.53 Standard Deviation Score) and hepatic steatosis. His past medical history included bilateral nephroblastoma diagnosed at 8 months of age, treated with left nephrectomy, right tumour excision, and chemotherapy (cumulative doses: vincristine 51 mg/m², actinomycin 855 µg/kg, and doxorubicin 300 mg/m²). He subsequently underwent autologous bone marrow transplantation at 2 years of age. At 6 years, he developed thrombosis of the right transverse and sigmoid sinuses in the context of acute otitis media and pansinusitis, with partial recanalization on follow-up magnetic resonance imaging and no associated deficits. He remained under follow-up in primary care and paediatric oncology and immunoallergology outpatient clinics. His usual medication consisted of daily intranasal corticosteroids.

Dietary errors and sedentary lifestyle were identified during history taking. Physical examination revealed signs of insulin resistance (acanthosis nigricans in cervical and axillary folds), abdominal striae, buffalo hump, and pubertal development at Tanner stage 4. Laboratory evaluation showed a normal complete blood count. Renal function (urea 45 mg/dL, creatinine 0.77 mg/dL), thyroid function, and liver enzymes (aspartate aminotransferase 28 U/L, alanine aminotransferase 46 U/L) were normal. Fasting glucose was impaired (109 mg/dL) with glycated haemoglobin of 5.3%. Dyslipidaemia was present (triglycerides 239 mg/dL, total cholesterol 163 mg/dL, high-density lipoprotein [HDL] cholesterol 35 mg/dL, low-density lipoprotein [LDL] cholesterol 110 mg/dL). Endocrine evaluation revealed hypergonadotropic hypogonadism (Luteinizing Hormone [LH] 9.43 mIU/mL, FSH 26.7 mIU/mL, testosterone 9.45 pg/mL). A dietary plan and daily physical activity were recommended.

Due to worsening metabolic abnormalities of glucose and lipid profiles, at 15 years of age he started metformin 1000 mg twice daily and liraglutide (maximum dose 0.6 mg). He developed adverse effects associated with liraglutide administration, including epigastric pain, nausea, and vomiting, leading to treatment discontinuation.

With further analytical worsening of hypogonadism (LH 14.4 mIU/mL, FSH 34.4 mIU/mL, testosterone 2.18 ng/mL) and absence of pubertal progression, he was evaluated in a reproductive medicine clinic, and semen analysis was compatible with azoospermia. Testosterone replacement therapy was initiated (50 mg/month for 6 months, subsequently titrated to 200 mg every 6 weeks).

During follow-up in the Paediatric Endocrinology consultation, he showed good clinical and laboratory evolution. Final height was not compromised. Body composition improved with a reduction in BMI under metformin therapy and non-pharmacological measures promoting healthy eating and physical activity. Laboratory tests showed slight improvement in lipid profile (total cholesterol 146 mg/dL, HDL cholesterol 40 mg/dL, LDL cholesterol 101 mg/dL, triglycerides 100 mg/dL), and fasting glucose remained controlled. He remained under follow-up until 18 years of age, when he transitioned to adult Endocrinology care.

Discussion

Healthcare professionals must be aware of the risks that chemotherapy and radiotherapy pose to spermatogenesis, testosterone deficiency, and sexual dysfunction. Chemotherapy with alkylating agents and anthracyclines, combined with autologous bone marrow transplantation, constitutes one of the main risk factors for primary testicular failure. Studies in survivors of neuroblastoma and nephroblastoma treated with similar regimens show that up to 70% of boys develop primary gonadopathy and persistently elevated FSH levels, requiring androgen replacement therapy [1, 3, 4]. Utriainen *et al*. demonstrated that gonadotoxicity is more severe in patients undergoing autologous transplantation, even in the absence of testicular irradiation, and that fertility is preserved only in a minority of cases [5]. Exposure to radiotherapy, particularly at testicular doses above 12 Gy, is also associated with gonadal dysfunction.

Therefore, monitoring of growth, pubertal progression, and gonadotropin and testosterone levels is recommended in these patients. Hormonal therapies for pubertal induction may be required, and in adolescents who have completed puberty, semen analysis is strongly recommended to identify abnormalities in spermatogenesis.

Sperm cryopreservation is the method of choice for post-pubertal adolescents prior to chemotherapy [3, 4]. When this is not possible as in the present case due to young age and early treatment testicular tissue cryopreservation represents an alternative strategy. Although still experimental, it has shown promising results with *in vitro* maturation of spermatogonia and potential restoration of spermatogenesis [4]. Early discussion with the patient and family about gonadal risks and fertility preservation options before initiating oncological treatment is essential.

Hypergonadotropic hypogonadism reflects irreversible testicular damage. Testosterone replacement is recommended according to Endocrine Society guidelines, with progressive doses that mimic physiological pubertal development [6]. In the present case, therapy improved clinical symptoms and metabolic profile, reinforcing the

importance of individualized treatment and regular monitoring.

The obesity, dyslipidaemia, and hepatic steatosis observed are well-documented metabolic complications in childhood cancer survivors, often associated with alterations of the Growth Hormone – Insuline-like Growth Factor-1 axis and insulin resistance [1, 2]. Metformin therapy was effective, and liraglutide, although poorly tolerated, represents a valid option in obese adolescents with insulin resistance.

The risk of multiple endocrinopathies increases with age and time since initial treatment. Current recommendations suggest annual endocrine evaluation and multidisciplinary follow-up, including endocrinology, nutrition, reproductive medicine, and psychology [1, 2, 6].

Conclusion

This case highlights the importance of long-term endocrine follow-up in survivors of paediatric malignancies. Early detection of hypogonadism, insulin resistance, and dyslipidaemia allows timely intervention, improving metabolic prognosis and quality of life. Fertility should be discussed at all stages of follow-up, even when available options remain experimental.

References

1. Lopez Dacal J, Grinspon RP, Rey RA. Review of the function of the hypothalamic-pituitary-gonadal axis in children and adolescents with cancer. Touch Reviews in Endocrinology. 2022;18(2):122–132.
2. Casano-Sancho P, Izurieta-Pacheco AC. Endocrine late effects in childhood cancer survivors. Cancers. 2022;14(11):2630.
3. Pasten González A, Salvador Alarcón C, Mora J, Martín Gimenez MP, Carrasco Torrents R, Krauel L. Current status of fertility preservation in pediatric oncology patients. Children. 2024;11(5):537.
4. Jing YX, Zhang LL, Li HX, Yue F, Wang NH, Xue SL, *et al*. Fertility preservation in cancer patients. Reproductive and Developmental Medicine. 2021;5:44–54.
5. Utriainen P, Suominen A, Mäkitie O, Jahnukainen K. Gonadal failure is common in long-term survivors of childhood high-risk neuroblastoma treated with high-dose chemotherapy and autologous stem cell rescue. Frontiers in Endocrinology. 2019;10:555.
6. Sklar CA, Antal Z, Chemaitilly W, Cohen LE, Follin C, Meacham LR, *et al*. Hypothalamic–pituitary and growth disorders in survivors of childhood cancer: An Endocrine Society clinical practice guideline. Journal of Clinical Endocrinology and Metabolism. 2018;103(8):2761–2784.

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