

# Synchronous Bilateral Testicular Tumors With Discordant Histopathology: A Rare Case in an Infertile Male

Review began 11/17/2023

Review ended 11/24/2023

Published 12/03/2023

© Copyright 2023

Dalla Ali et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Saif Dalla Ali <sup>1</sup>, Ibrahim A. Khalil <sup>2</sup>, Bara Wazwaz <sup>3</sup>, Nagy Younes <sup>2</sup>, Khalid Al Rumaihi <sup>2</sup>

1. Department of Education, Hamad Medical Corporation, Doha, QAT 2. Department of Urology, Hamad Medical Corporation, Doha, QAT 3. Department of Pathology, Hamad Medical Corporation, Doha, QAT

Corresponding author: Ibrahim A. Khalil, ikhalil1@hamad.qa

## Abstract

Testicular cancer, accounting for 1-1.5% of male malignancies, rarely presents bilaterally, with only 2-3% of cases being bilateral and a mere 10% being synchronous, typically sharing histological patterns in both testes. Discordant histological presentation is exceedingly rare, with only a few reported cases. In this report, we detail a case involving a 35-year-old infertile male with bilateral synchronous testicular tumors, each exhibiting different histopathologies. This case highlights the diagnostic intricacies and the necessity for tailored management in the face of such uncommon presentations. The implications of oncological treatment and fertility preservation significantly affect the patient's overall quality of life.

**Categories:** Urology

**Keywords:** discordant histopathology, embryonal carcinoma, seminoma, bilateral testicular cancer, testicular germ cell tumor

## Introduction

Testicular cancer, a rare malignancy, represents approximately 1-1.5% of all male-related malignancies. Despite its infrequency, it stands out as the most prevalent cancer affecting males in the age range of 15-44 years [1]. While around 2-3% of testicular tumors manifest bilaterally, the majority of these occurrences are metachronous. However, synchronous bilateral testicular tumors, constituting just 10% of bilateral cases, are characterized by shared histological patterns, with bilateral seminoma being the most commonly observed presentation [2,3]. Though exceedingly rare, discordant histological presentations have significant implications for treatment and follow-up plans. In this context, we present a rare case of bilateral synchronous testicular tumor with different histopathologies in a male with a history of infertility, shedding light on the challenges and complexities of managing such unique clinical scenarios.

## Case Presentation

A 35-year-old male patient presented with left testicular swelling that had persisted for 2 months. Physical examination revealed a hard, mobile mass in the left testis, along with an atrophied right testis. The patient's history included infertility, but he successfully conceived via in-vitro fertilization six years prior to the current presentation. He also underwent sleeve gastrectomy one year before this presentation. Otherwise, his medical history is unremarkable. Given the newly discovered testicular swelling, an urgent ultrasound and tumor marker tests were ordered. The patient's lab tests showed elevated tumor markers and low testosterone levels with high gonadotropins, leading to a diagnosis of primary hypogonadism (Table 1).

### How to cite this article

Dalla Ali S, Khalil I A, Wazwaz B, et al. (December 03, 2023) Synchronous Bilateral Testicular Tumors With Discordant Histopathology: A Rare Case in an Infertile Male. Cureus 15(12): e49874. DOI 10.7759/cureus.49874

Test (Units)	Results	Normal reference Range
LDH (U/L)	1212	135-225
AFP IU/mL	38	0-6
BhCG (mIU/mL)	19	0-2
FSH (IU/L)	47	1.5-12.4
LH (IU/L)	40.5	1.7-8.6
Testosterone (nmol/L)	4.8	10.40-37.44
Albumin (gm/L)	39	35-50
ALT(U/L)	20	0-41
AST (U/L)	18	0-40
Alk Phos (U/L)	79	60-80

TABLE 1: Laboratory test results and reference ranges.

LDH: Lactate dehydrogenase; AFP: Alpha fetoprotein; BhCG: Beta human chorionic gonadotropin; FSH: Follicle-stimulating hormone; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Alk Phos: Alkaline phosphatase.

The patient’s record included a previous ultrasound of both testes. Starting with the left testis, there was a significant change from the previous size of 6 x 4 x 3.8 cm (49 mL) (Figure 1A) to 8.4 x 5.4 x 5.4 cm (127 mL). This was accompanied by diffuse heterogeneity and nodularity with calcifications and increased vascularity (Figure 1B), all consistent with a left testicular tumor. Regarding the right testis, the size remained unchanged from the previous ultrasound. However, there were diffuse parenchymal heterogeneity and calcifications, along with increased vascularity. Notably, a newly formed irregular hypoechoic area measuring 15mm, not present in the previous ultrasound, raised suspicion for another testicular tumor (Figures 1C-1D).

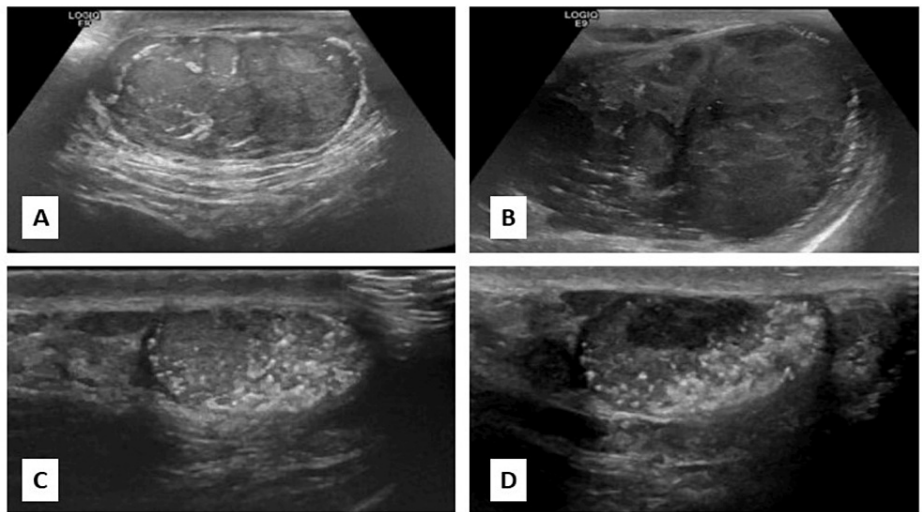
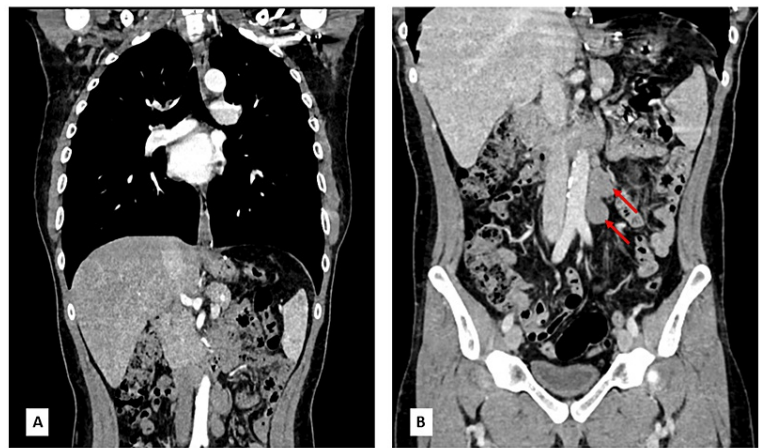


FIGURE 1: Ultrasound images showing development of new bilateral testicular masses.

Ultrasound of the left testis showing the development of a new heterogeneous mass (B) that was not evident in the previous ultrasound (A). Ultrasound of the right testis showing a small testis (C) with the development of a small heterogeneous mass in the new ultrasound, without any change in testis size (D).

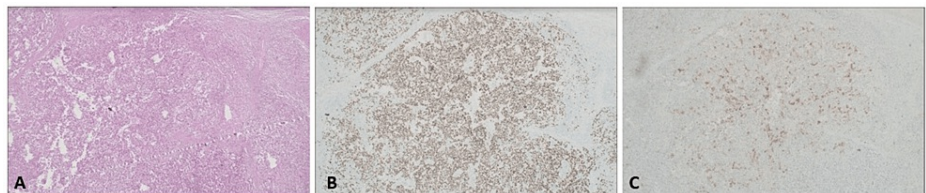
Staging chest, abdominal, and pelvic computed tomography (CT) scans revealed two enlarged lymph nodes in the left para-aortic region at the level of the left renal hilum, with a maximum diameter of 30 mm. There was no other evidence of metastatic disease (Figure 2).



**FIGURE 2: Staging chest, abdomen, and pelvis CT scan.**

A: Unremarkable CT of the chest with no metastatic lesions. B: CT of the abdomen showing two enlarged lymph nodes in the left para-aortic region (indicated by red arrows).

Following the aforementioned findings, the patient underwent bilateral radical orchiectomy with the insertion of bilateral testicular prostheses and sperm extraction. Histopathological diagnosis: Grossly, the cut surface of the left testicle revealed a 7.2 x 5.2 x 4.8 cm tan-yellow homogenous nodular soft mass replacing the entire testicle, while the right testicle exhibited a tan-white, smooth, rubbery, infiltrative mass measuring 1.9 x 1.4 x 0.8 cm, abutting the tunica albuginea. Microscopically, the mass in the left testicle was mainly composed of sheets of seminoma tumor cells with focal polygonal cells representing an embryonal carcinoma component (Figure 3A). Both components were positive for Sal-like transcription factor 4 (SALL4) (Figure 3B), while CD30 highlighted the embryonal carcinoma component (Figure 3C). Conversely, the right testicular mass showed a pure seminoma tumor. These findings correlate with a pathological stage of T3 in the left testicle and T1 in the right.



**FIGURE 3: A: H&E stain showing sheets of seminoma tumor with focal polygonal cells representing embryonal carcinoma. B: Nuclear staining positive for Spalt-like transcription factor 4 (SALL4). C: Immunohistochemistry: CD30 highlighting the embryonal carcinoma component.**

In order to plan adjuvant therapy for the patient, the highest stage was determined based on the pathology, tumor markers, and radiological findings. He was classified as having a pT3cN2M0 (STAGE IIb) tumor. Accordingly, he received adjuvant chemotherapy, which consisted of 4 cycles of Etoposide plus Cisplatin. Upon follow-up, the tumor markers normalized, and a CT scan showed complete resolution of the left paraaortic lymph nodes (Figure 4).



**FIGURE 4: The CT scan of the abdomen showed resolution of the lymph nodes following adjuvant chemotherapy.**

## Discussion

The WHO delineated testicular germ cell tumors in 2016 into two primary categories: prepubertal-type tumors, unrelated to germ cell neoplasia in situ (GCNIS), and postpubertal-type tumors, derived from GCNIS, commonly found in young men. The latter group comprises seminomas and non-seminomatous germ cell tumors, including embryonal carcinoma, yolk sac tumor, teratoma, and choriocarcinoma [4]. In our case study, an infertile adult presented with synchronous bilateral testicular tumors of distinct histopathologies. Upon examination, the right testis contained a pure seminoma, while the left testis harbored a mixed germ cell tumor.

Historically, the pathogenesis behind the development of synchronous bilateral testicular germ cell tumors (TGCTs) has been a controversial and yet-to-be-determined topic. Initially, when this subject was debated, researchers were divided over whether bilateral cancers were caused by metastasis or if separate oncologic mechanisms occurred concurrently. The latter possibility gained acceptance following a proposition by Matsushima M et al. in 1987. They argued that synchronous bilateral TGCTs resulted from separate oncologic mechanisms, citing the lack of vascular or lymphatic connections between the testes as evidence [5]. This proposition finds support in the varied activation, de-repression, and repression of distinct genes during the development of tumors with diverse histological subtypes [6]. As a result, it has been accepted that bilateral synchronous tumors of different histology follow a similar mechanism and occur as the development of two independent primary tumors.

A systematic review was conducted to assess the clinicopathological characteristics of bilateral TGCTs. It was found that synchronous bilateral TGCTs were associated with more advanced disease and a worse prognosis compared to metachronous bilateral TGCTs. The five-year survival rate for synchronous bilateral TGCTs was 88%, while it was 95% for metachronous bilateral TGCTs. Additionally, discordant histology was found to negatively impact the overall survival of the group with synchronous tumors [1].

Although it presents many complications, such as erectile dysfunction, infertility, and psychological distress, bilateral radical orchiectomy remains the standard of care for patients presenting with synchronous testicular cancer. Over the past decade, there has been increased focus on research into the treatment of bilateral testicular cancer. The aim is to identify approaches that preserve fertility and eliminate the need for

lifelong androgen treatment, thereby significantly enhancing a patient's quality of life. Extensive research has also explored the viability of testicular-sparing surgery as an alternative to radical orchiectomy. Nonetheless, radical orchiectomy continues to be the standard of care, pending further advancements in understanding. In our case, the patient underwent bilateral radical orchiectomy, followed by adjuvant chemotherapy.

## Conclusions

It is known that bilateral primary synchronous testicular germ cell tumors (TGCTs) typically present with similar histology; however, it is rare for them to present with different histopathologies. Our patient presented with a case of primary synchronous bilateral testicular cancer, exhibiting discordant histology in each testis. The treatment of this condition should be based on the tumor with the highest stage and most malignant features.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Ibrahim A. Khalil

**Acquisition, analysis, or interpretation of data:** Ibrahim A. Khalil, Bara Wazwaz, Nagy Younes , Khalid Al Rumaihi, Saif Dalla Ali

**Drafting of the manuscript:** Ibrahim A. Khalil, Bara Wazwaz, Nagy Younes , Khalid Al Rumaihi, Saif Dalla Ali

**Critical review of the manuscript for important intellectual content:** Ibrahim A. Khalil

**Supervision:** Nagy Younes , Khalid Al Rumaihi

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Zequi Sde C, da Costa WH, Santana TB, Favaretto RL, Sacomani CA, Guimaraes GC: Bilateral testicular germ cell tumours: a systematic review. *BJU Int.* 2012, 110:1102-1109. [10.1111/j.1464-410X.2012.11056.x](https://doi.org/10.1111/j.1464-410X.2012.11056.x)
2. Shanmugalingam T, Soultati A, Chowdhury S, Rudman S, Van Hemelrijck M: Global incidence and outcome of testicular cancer. *Clin Epidemiol.* 2013, 5:417-427. [10.2147/CLEP.S34430](https://doi.org/10.2147/CLEP.S34430)
3. Symeonidis EN, Tsifountoudis I, Anastasiadis A, Mutomba WF, Kotakidou R, Hatzichristou D, Dimitriadis F: Synchronous bilateral testicular cancer with discordant histopathology occurring in a 20-year-old patient: a case report and review of the literature. *Urologia.* 2023, 90:434-441. [10.1177/03915603211028556](https://doi.org/10.1177/03915603211028556)
4. Tourne M, Radulescu C, Allory Y: [Testicular germ cell tumors: histopathological and molecular features]. *Bull Cancer.* 2019, 106:328-341. [10.1016/j.bulcan.2019.02.004](https://doi.org/10.1016/j.bulcan.2019.02.004)
5. Matsushima M, Fukasawa K, Kawahara M, et al.: Synchronous bilateral testicular tumors of different cell types on each side. *Urology.* 1987, 30:180-182. [10.1016/0090-4295\(87\)90192-0](https://doi.org/10.1016/0090-4295(87)90192-0)
6. Reinberg Y, Manivel JC, Zhang G, Reddy PK: Synchronous bilateral testicular germ cell tumors of different histologic type. Pathogenetic and practical implications of bilaterality in testicular germ cell tumors. *Cancer.* 1991, 68:1082-1085. [10.1002/1097-0142\(19910901\)68:5<1082::aid-cnrcr2820680529>3.0.co;2-x](https://doi.org/10.1002/1097-0142(19910901)68:5<1082::aid-cnrcr2820680529>3.0.co;2-x)