Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Radiation Oncology

Testicular Embryonal Carcinoma: A Case Report

Souraya Bricha[1*], Sara Amimi[1], Samir Barkiche[1], Nezha Oumghar[1], Mouna Darfaoui[1], Abdelhamid El Omrani[1], Mouna Khouchani[1]

[1]Radiation Oncology Department, Oncology and Hematology Hospital; Mohamed VI University Hospital, Marrakech, Morocco

DOI: https://doi.org/10.36347/sjmcr.2024.v12i09.001 | **Received:** 25.07.2024 | **Accepted:** 29.08.2024 | **Published:** 02.09.2024

***Corresponding author:** Souraya Bricha
Radiation Oncology Department, Oncology and Hematology Hospital; Mohamed VI University Hospital, Marrakech, Morocco

Abstract **Case Report**

Embryonal carcinoma is a rare and aggressive type of non-seminomatous germ cell tumor, usually affecting young or middle-aged people. It is often discovered by the patient or during routine medical examinations as a painless or sometimes painful mass. The aim of this article is to present the case of a 25-year-old patient with embryonal carcinoma, who presented to the clinic complaining of pain and swelling of the right testicle. Scrotal ultrasound revealed a hypoechoic, heterogeneous solid lesion. Histopathological and immunohistochemical analysis of this case led to the diagnosis of pure embryonal carcinoma. Although pure embryonal carcinoma is rare, it is one of the tumors that can be confused clinically and histopathologically with other testicular tumors and should be considered in patients presenting to the clinic with complaints mainly of a painless mass in the testis. Multidisciplinary collaboration between urologist, radiologist, oncologist and pathologist is essential to ensure rapid diagnosis and implementation of the most appropriate therapeutic approach in these difficult cases.

Keywords: Testicular Neoplasms, Non-Seminoma, Embryonal Cell Carcinoma, Young, Metastasis, Orchidectomy, Chemotherapy, BEP.

INTRODUCTION

Testicular neoplasms account for approximately 5% of all urological tumors and 1% of all cancers in the global male population. Notably, the age-standardized incidence is higher in Western Europe, reaching 7.8% in some reports [1, 2].

Seminomas predominantly present in men aged 25 to 40 years, while non seminomatous tumors are more frequently diagnosed in younger individuals, typically ranging from adolescence to 30 years [3, 4].

Embryonal carcinoma, a non-seminomatous germ cell tumor (GCT), ranks as the second most common GCT of the testis after seminoma. Despite this, its pure form is relatively rare, occurring in only 1-5% of cases [5-12].

Since it was established as an entity in 1946 [13, 14], Embryonal carcinoma has generally been considered to have 3 major patterns: glandular, solid, and papillary, with more pleomorphic cytology than seminoma in addition to differing immunohistochemical properties.

This type of tumor tends to be seen in young to middle-aged individuals, with an average age at diagnosis of 31-32 years [6-8].

Embryonal carcinoma is known for its aggressive clinical course, primarily due to its early propensity for hematogenous spread [7]. Approximately 66% of cases, including those with an embryonal carcinoma component, present with metastasis at the time of diagnosis [8]. This underscores the critical importance of early detection and prompt initiation of treatment in managing embryonal carcinoma.

Like many testicular tumors, embryonal carcinoma is frequently detected by the patient or during routine examinations, presenting as a painless or occasionally painful lump [15]. However, it is uncommon for embryonal carcinoma to present with symptoms such as left lumbar pain or renal colic.

Ultrasound is the initial imaging modality of choice in these cases, typically revealing a well-defined, hypoechoic and heterogeneous lesion [15].

The highly malignant nature of embryonal carcinoma was once reflected in a 60% two-year mortality rate, persisting until the 1970s [16, 17].

Despite evidence in the 1960s of the tumor's sensitivity to various cytotoxic drugs, significant improvements in patient outcomes were not realized until the mid-to-late 1970s. During this period, the introduction of newly discovered agents such as cisplatin, vinblastine, and bleomycin into combination chemotherapy regimens led to high complete remission rates and long-term disease-free survival in patients with disseminated disease [18-20].

Concurrently, advancements in diagnostic radiographic techniques and the development of radioimmuno-assays capable of detecting nanogram quantities of tumor-secreted alpha-fetoprotein and human chorionic gonadotropins in the sera of testicular cancer patients revolutionized the diagnosis of metastatic disease [21]. These innovations facilitated earlier and more effective use of chemotherapy, resulting in increased complete remission rates and improved patient survival.

This medical case report highlights the clinical presentation, diagnosis process, and therapeutic approach of a 25- year-old patient with testicular embryonal carcinoma.

Case Presentation: Male patient with metastatic testicular Embryonal Carcinoma

A 25-year-old patient, whose medical history was characterized by chronic smoking for 5 years, i.e., 20 packs per year, presented in consultation complaining of dysuria evolving for 1 year, associated with pain and swelling of the right testicle, as well as penile pain on micturition.

On physical examination, the patient was found to be in good general condition with normal vital signs, afebrile, and a body mass index of 22.9 kg/m². Clinical assessment revealed tenderness in the left lumbar region. Examination of the external genitalia identified a solid, mildly painful mass in the right testicle, which the patient noted had caused episodes of testicular heaviness and significant discomfort. The remainder of the clinical examination was unremarkable.

An ultrasound scan of the scrotum was then performed, showing a hypoechoic lesion measuring 48x45x40 mm and 20 ml with scalloped contours, vascularized with micro-calcifications on the right testicle, associated with the presence of a small layer of fluid in the tunica albuginea, in addition to thickening and infiltration of the scrotal envelopes; the left testicle was normal. There was no evidence of testicular torsion.

The tumor markers were assessed, revealing elevated levels of alpha-fetoprotein (AFP) at 4060 ng/ml, human chorionic gonadotropin (HCG) at 1619.33 UI/ml, and lactate dehydrogenase (LDH) at 418 U/L.

It was decided to proceed with a right inguinal orchiectomy, and the patient was scheduled for surgery 72 hours later, following a comprehensive cardiological and biological evaluation.

Anatomopathological examination demonstrated a tumor exhibiting partial necrosis and characterized by proliferation organized into tubular and glandular structures with microcysts **(Figure 1)**. The tumor cells were large, cuboidal, with relatively abundant cytoplasm, round hyperchromatic nuclei, and numerous mitotic figures. The stroma is partially fibrotic, interspersed with hemorrhagic and necrotic foci **(Figure 2)**, and infiltrated by both mononuclear and polymorphonuclear inflammatory cells, including altered polymorphonuclear leukocytes and areas of dystrophic calcification. This tumor proliferation extensively infiltrated and disrupted the testicular parenchyma, with only scattered epididymal ducts maintaining a regular border at the periphery. The tumor extended into the spermatic cord excision slice and peripheral adipose tissue. Additionally, the tunica albuginea was thickened due to fibrotic changes and tumor invasion. No neoplastic vascular emboli were detected.

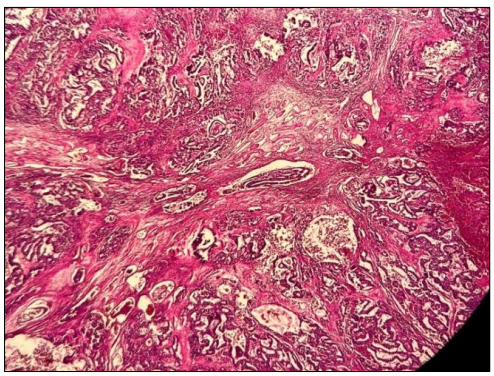

Figure 1: Photomicrographs showing a proliferation arranged in glandular and micrkystic structures (HE, ×25)

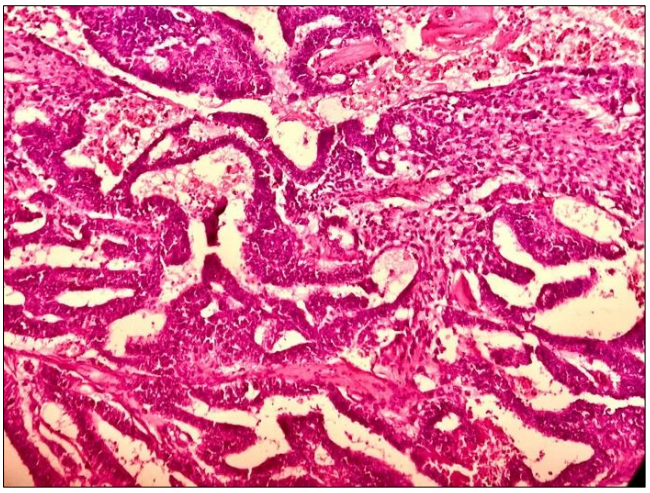

Figure 2: Photomicrographs showing a tumor proliferation dissociated by hemorrhagic and necrotic foci (HE, ×100)

Immunohistochemical analysis revealed positive staining for CD30, PLAP, and OCT4 **(Figure 3,4,5)**, while CD117 and LCA were negative (figure). Based on the morphological and immunohistochemical findings, a diagnosis of embryonal carcinoma was established.

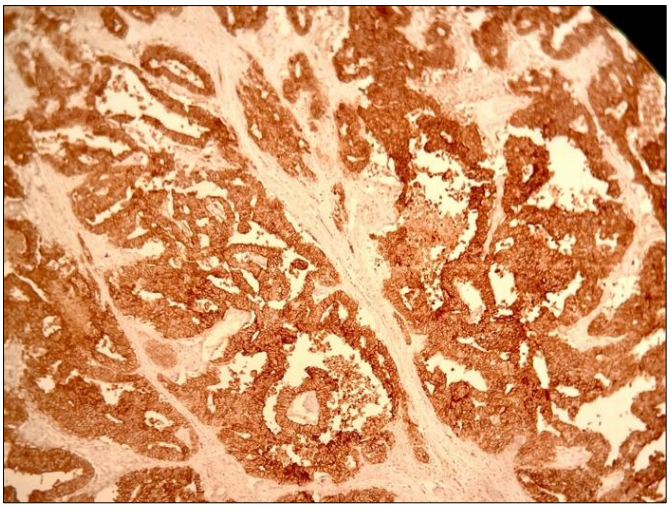

Figure 3: CD30 positivity in Immunohistochemical staining

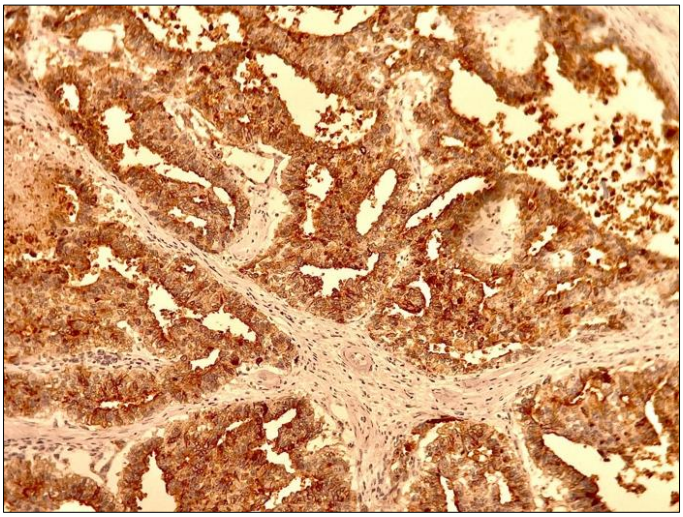

Figure 4: PLAP positivity in Immunohistochemical staining

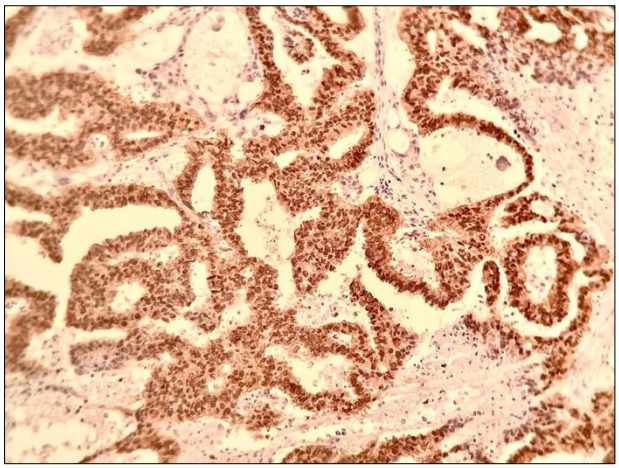

Figure 5: OCT 3/4 positivity in Immunohistochemical staining

The tumor marker levels post-operatively were still elevated: Alpha-fetoprotein (AFP) at 16965 ng/ml, Human chorionic gonadotropin (HCG) at 2226 UI/ml, and Lactate dehydrogenase (LDH) at 340 Ul/L.

Additionally, a thoracic abdominal pelvic CT scan was performed, revealing multiple nodular lesions in both lung fields at the thoracic level. The largest lesions measured 23 mm in the left basal region, 25 mm in the right basal region, and 20 mm in the inferior lingular region. These findings were associated with mediastinal adenopathies, including one measuring 20 × 12 mm at the barium lodge level, 13 × 23 mm at the right latero-aortic level, and 12 × 16 mm at the left hilar level. At the abdomino-pelvic level, multiple retroperitoneal adenopathies were observed, with inter-aorto-caval adenopathies measuring 38 × 42 mm and 40 × 50 mm, and inter-hepato-renal adenopathies measuring 39 × 49 mm. Additionally, a right primitive iliac adenopathy measuring 28 × 35 mm, a right external iliac adenopathy measuring 21 × 18 mm, and a mass infiltrating the right spermatic cord, measuring 19 × 22 mm and extending over 54 mm, were noted. No associated peritoneal effusion was detected. The bone window images did not reveal any abnormal lesions.

The patient was referred to the laboratory for sperm preservation and subsequently started on adjuvant chemotherapy. He underwent 4 cycles of the BEP regimen, which included Bleomycin at 30 mg administered on days 1, 8, and 15; Cisplatin at 20 mg/m² from days 1 to 5; and Etoposide at 100 mg/m² from days 1 to 15, administered every 21 days.

The follow-up thoraco-abdominopelvic CT scan, performed after the fourth course of chemotherapy, showed an increase in the size of pre-existing pulmonary lesions, as well as supra- and sub-diaphragmatic adenopathies and the previously noted spermatic cord infiltrating mass, compared with the initial scan, with the association of a moderate right hydronephrosis, concluding with an estimated resistance of 52.97%. A small pelvic peritoneal effusion was also observed. After multidisciplinary discussion, it was decided to proceed with second-line chemotherapy using the VIP regimen, which included Etoposide 75 mg/m² on days 1 to 5, Ifosfamide 1.2 g/m² on days 1 to 5, Cisplatin 20 mg/m² on days 1 to 3, and Mesna 1.5 g/m², administered every 21 days.

DISCUSSION

Embryonal Carcinoma (EC) is a well-known type of germ cell tumor (GCT) that affects the testis and is the second most prevalent type of GCT, following Seminoma [22].

Although embryonal carcinoma is most commonly diagnosed between the ages of 25 and 35, with an average age of 31-32 years, it is rarely observed in infants or individuals over 50 years old [5-9]. Patients typically present with a painless testicular mass, though 10% may exhibit hormonal symptoms [5-23]. At the time of diagnosis, approximately two-thirds of cases show lymph node involvement and distant metastases [6]. The aggressive nature of embryonal carcinoma is largely due to its propensity for early hematogenous spread [7]. The lungs are the primary site of metastasis, but the liver, brain, and bones can also be affected [24]. Lymphatic invasion significantly contributes to metastasis, with initial spread to retroperitoneal para-aortic lymph nodes, followed by involvement of mediastinal and supraclavicular nodes [25, 26]. The median survival time is 5 months, with 1-, 2-, and 5-year survival rates of 41%, 34%, and 34%, respectively [11].

With the widespread use of testicular ultrasonography (USG) today, the detection of small, non-palpable tumors has significantly increased compared to the past [7]. When pain or a mass is detected in the testis, scrotal USG is the first imaging method of choice. In cases of embryonal carcinoma, USG typically reveals well-circumscribed, hypoechoic, and heterogeneous lesions [9].

Thoracic abdominal pelvic CT should be conducted primarily to assess for potential metastatic sites, especially if the mass detected during the physical examination suggests a malignant course based on the patient's age. Additionally, the scan can help identify the cause of the ureteral hydronephrosis observed on ultrasound [27].

Macroscopic examination of the tumor reveals blurred margins, a soft consistency, a gray coloration, and a cross-sectional surface with extensive areas of hemorrhage and necrosis [6]. Invasion of the spermatic cord and epididymis is commonly observed. Histopathologically, the tumor appears in various forms, often exhibiting multiple patterns simultaneously. The most frequently observed patterns include solid, syncytial, tubular, and tubulo-papillary structures. The tumor cells are polygonal, undifferentiated epithelial cells displaying marked anaplasia, numerous atypical mitoses, vesicular nuclei with thick nuclear membranes, dense fine granules, and cytoplasm with indistinct borders. Additionally, apoptotic bodies, extensive necrosis, and single-cell necrosis are prominent features. However, these histological characteristics are not predictive of prognosis [6, 7].

The differential diagnosis of embryonal carcinoma (EC) includes large cell lymphoma and other germ cell neoplasms such as seminoma and yolk sac tumor. Due to the significant differences in treatment protocols, it is crucial to accurately distinguish these neoplasms. To ensure a diagnosis of 'pure embryonal carcinoma' and to rule out mixed germ cell neoplasia, a large number of samples should be taken from specimens [6,7]. Embryonal carcinoma typically shows positive staining for cytokeratin but is negative for epithelial membrane antigen (EMA), which aids in differentiating metastatic embryonal carcinoma from somatic carcinoma. Unlike seminoma, which is one of the tumors in the differential diagnosis, embryonal carcinoma is positive for both placental-like alkaline phosphatase (PLAP) and OCT3/4. Seminoma, however, stains positive for D2-40, whereas embryonal carcinoma does not. CD30 is a sensitive marker for embryonal carcinoma and is typically negative in seminoma and yolk sac tumors. Interestingly, the loss of CD30 expression is commonly observed in metastatic embryonal carcinoma cases that have undergone chemotherapy.

In the context of embryonal carcinoma, the expression of carcinoembryonic antigen (CEA), human chorionic gonadotropin (hCG), and CD117 (c-Kit) is typically absent. When differentiating EC with a solid pattern from seminoma, a panel of immunohistochemical markers including cytokeratin cocktail, CD30, D2-40, and CD117 can be employed to assist in the diagnosis. Notably, the detection of alpha-fetoprotein (AFP) immunostaining in focal areas, coupled with elevated serum AFP levels, serves as a strong indicator of yolk sac differentiation within the tumor [6].

Given embryonal carcinoma's resistance to radiation, the treatment protocol typically involves surgical resection of the mass, tailored according to whether the tumor is pure or mixed, followed by chemotherapy [9-29]. Our patient underwent surgical treatment with a right inguinal orchiectomy followed by four cycles of chemotherapy using the BEP regimen.

Despite effective initial treatment, about 10% to 30% of patients with testicular cancer experience recurrence, usually within the first two years after achieving a complete response [30]. In a pooled analysis of 5,880 patients with testicular cancer, Oldenburg *et al*., reported late relapses in 3.2% of non-seminomas and 1.4% of seminomas [31]. Late recurrences of non-seminomatous germ cell tumors are resistant to chemotherapy, with the best outcomes achieved through complete surgical resection of localized tumors. This approach should be a key component of the treatment strategy [31]. Given the challenges associated with lifelong follow-up, it is important not to underestimate the potential for late metastasis in patients with a history of embryonal carcinoma.

A primary mediastinal tumor, non-lung visceral metastasis, or post-orchiectomy markers such as AFP > 10,000 ng/mL, beta-hCG > 50,000 IU/L, and LDH > 10 times the upper limit of normal are considered unfavorable prognostic factors for non-seminoma [32]. Patients classified within the IGCCG group with a poor prognosis are estimated to have a 5-year survival rate of approximately 50% [33].

CONCLUSION

Embryonal carcinoma is the most common non-seminomatous germ cell tumor of the testis, whether occurring as a pure form or as part of a mixed germ cell tumor. It ranks as the second most common germ cell tumor, following seminoma. This aggressive subtype predominantly affects individuals aged 20 to 30 and is often detected by the patient or during routine medical examinations as a painless, or occasionally painful, lump.

All patients presenting with a painless testicular mass should initially undergo ultrasound examination, followed by histopathological analysis based on the findings. Although pure embryonal carcinoma is rare, it can be clinically and morphologically similar to other testicular tumors and should be considered in differential diagnosis. Recognizing the atypical clinical presentations of embryonal carcinoma is crucial, underscoring the need for clinicians to be vigilant about these entities.

Prompt diagnosis and treatment can also help prevent complications, such as ureteral hydronephrosis.

Significant improvements have been seen in the survival rates of patients with distant metastases, a group that historically had a particularly poor prognosis.

Multidisciplinary collaboration between urologist, radiologist, oncologist and pathologist is essential to ensure rapid diagnosis and implementation of the most appropriate therapeutic approach in these difficult cases.

BIBLIOGRAPHY

1. EAU Guidelines. Edn. Presented at the EAU Annual Congress Barcelona, 2019. ISBN 978-94-92671-04-2.
2. Rosen, A., Jayram, G., Drazer, M., & Eggener, S. E. (2011). Global trends in testicular cancer incidence and mortality. *European urology*, *60*(2), 374-379.
3. Garner, M. J., Turner, M. C., Ghadirian, P., & Krewski, D. (2005). Epidemiology of testicular cancer: an overview. *International journal of cancer*, *116*(3), 331-339.
4. Moch, H., Humphrey, P. A., Ulbright, T. M., & Reuter, V. E. (Eds). (2016). WHO Classification of Tumours of the Urinary System and Male Genital Organs, 4th Edition.IARC Press, Lyon.
5. Petrescu, A., Berdan, G., Muresan, A., Damian, D., Bengus, F., Paranici, C., ... & Vasilescu, F. (2019). Pure embryonal carcinoma of the testis in young male patients–case reports. *European Urology Supplements*, *18*(2), e2370.
6. Bahrami, A., Ro, J. Y., & Ayala, A. G. (2007). An overview of testicular germ cell tumors. *Archives of pathology & laboratory medicine*, *131*(8), 1267-1280.
7. Jagtap, S. V., Bisht, T. V., Jagtap, S. S., & Huddedar, A. (2015). Pure embryonal carcinoma of testis presenting with extensive metastasis. *International Journal of Medical Science and Public Health*, *4*(1), 145-147.
8. Khan, L., Verma, S., Singh, P. K., & Agarwal, A. (2009). Testicular embryonal carcinoma presenting as chest wall subcutaneous mass. *Journal of Cytology*, *26*(1), 39-40.
9. Martin, A., & Anderson, S. (2019). Combined embryonal cell carcinoma and granulomatous orchitis of the testis. *Journal of Diagnostic Medical Sonography*, *35*(5), 413-417.
10. Ohkubo, N., Ogihara, T., Miura, T., Soejima, K., Iyori, S., Akasaka, Y., & Tashiro, M. (1993). Primary embryonal carcinoma of the retroperitoneum. *Internal Medicine*, *32*(4), 295-297.
11. Rescigno, P., Di Lorenzo, G., Raimondo, L., D'Aniello, C., Matano, E., Damiano, V., ... & Palmieri, G. (2012). Primary Embryonal Lung Carcinoma and Testicular Seminoma in the Same Patient Ten-Years Later: Case-Report and Literature Review.
12. Barmon, D., Kataki, A. C., Sharma, J. D., & Hafizur, R. (2011). Embryonal carcinoma in androgen insensitivity syndrome. *Indian Journal of Medical and Paediatric Oncology*, *32*(02), 105-108.
13. Friedman, N. B., & Moore, R. A. (1946). Tumors of the testis; a report on 922 cases. *Mil Surg*, *99*, 573–593.
14. Young, R. H. (2005). A brief history of the pathology of the gonads. *Modern pathology*, *18*, S3-S17.
15. Kucuk, S., Kucuk, I. G., Mizrak, B., & Öngel, K. (2021). Pure embryonal carcinoma of the testis in an adult male patient: case report. *Общественное здоровье, экономика и менеджмент в медицине*, (1 (88)), 26-30.
16. Mostofi, F. K., & Price, E. B. Jr. (1973). Tumor soft hemalegenital system In: Atlas of Tumor Pathology, series 2. Washington, DC: *Armed Forces Institute of Pathology*, 40-52.
17. Dixon, F. J., & Morre, R. A. (1953). Testicular tumors: A clinicopathological study. *Cancer*, *6*, 427-454.
18. Li, M. C., Whitmore, W. F., Golbey, R., & Grabstald, H. (1960). Effects of combined drug therapy on metastatic cancer of the testis. *Jama*, *174*(10), 1291-1299.
19. Einhorn, L. H. (1981). Testicular cancer as a model for a curable neoplasm: The Richard and Hinda Rosenthal Foundation Award Lecture. *Cancer Research*, *41*(9_Part_1), 3275-3280.
20. VUGRIN, D., HERR, H. W., WHITMORE Jr, W. F., SOGANI, P. C., & GOLBEY, R. B. (1981). VAB-6 combination chemotherapy in disseminated cancer of the testis. *Annals of Internal Medicine*, *95*(1), 59-61.
21. Javadpour, N. (1979, March). The value of biologic markers in diagnosis and treatment of testicular cancer. In *Seminars in Oncology* (Vol. 6, No. 1, pp. 37-47).
22. Kao, C. S., Ulbright, T. M., Young, R. H., & Idrees, M. T. (2014). Testicular embryonal carcinoma: a morphologic study of 180 cases highlighting unusual and unemphasized aspects. *The American journal of surgical pathology*, *38*(5), 689-697.
23. Syu, S. H., Chang, C. L., & Shih, H. J. (2019). Testicular mixed germ cell tumor presenting with seizure as the initial symptom: a case report and literature review. *International braz j urol*, *45*(3), 629-633.
24. Poulopoulos, A. K., Antoniades, K., Kiziridou, A., & Antoniades, V. (2001). Testicular embryonal carcinoma metastatic to the labial mucosa of the upper lip. *Oral oncology*, *37*(4), 397-399.
25. Ayala, A. G., & Ro, J. Y. (1998, May). Testicular tumors: clinically relevant histological findings. In *Seminars in urologic oncology* (Vol. 16, No. 2, pp. 72-81).
26. Dunphy, C. H., Ayala, A. G., Swanson, D. A., Ro, J. Y., & Logothetis, C. (1988). Clinical stage I nonseminomatous and mixed germ cell tumors of the testis. A clinicopathologic study of 93 patients

on a surveillance protocol after orchiectomy alone. *Cancer*, *62*(6), 1202-1206.

27. Youness, T., Othman, M., Mokhtari, M., Mohammed, R., Miry, N., Amal, B., & Barki, A. (2023). Unusual Presentation of Embryonal Carcinoma of the Testis: A Case Report. *Cureus*, *15*(2).
28. Cassell, A., Jalloh, M., Ndoye, M., Yunusa, B., Mbodji, M., Diallo, A., ... & Gueye, S. (2020). Review of testicular tumor: diagnostic approach and management outcome in Africa. *Research and reports in urology*, 35-42.
29. Sagalowsky, A. I. (2000, October). Treatment options for clinical stage 1 testis cancer. In *Baylor University Medical Center Proceedings* (Vol. 13, No. 4, pp. 372-375). Taylor & Francis.
30. Flora, M., Costigliola, A., Lavoretano, S., Mollica, M., Tranfa, C. M., Perrotta, F., & Calabrese, C. (2020). Pulmonary metastasis: very late relapse of testicular embryonal carcinoma. *Monaldi Archives for Chest Disease*, *90*(1).
31. Oldenburg, J., & Fossa, S. D. (2009). Late relapse of germ cell malignancies: incidence, management, and prognosis. Methods of Cancer Diagnosis, Therapy, and Prognosis: General Overviews, Head and Neck Cancer and Thyroid Cancer. *Springer*, Dordrecht. 10.1007/978-90-481-3186-0_15
32. Leman, E. S., & Gonzalgo, M. L. (2010). Prognostic features and markers for testicular cancer management. *Indian Journal of Urology*, *26*(1), 76-81.
33. Mead, G. M., & Stenning, S. P. (1997). The International Germ Cell Consensus Classification: a new prognostic factor-based staging classification for metastatic germ cell tumours. *Clinical oncology (Royal College of Radiologists (Great Britain))*, *9*(4), 207-209.