

## NATURAL PROGRESSION OF EMBRYONAL CARCINOMA

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**Summary.-** *OBJECTIVE:* We report a rare case of advanced testicular cancer that describes the natural progression of testicular cancer without medical treatment. This study also describes the effectiveness of chemotherapy, which was the approach used for treatment.

*METHODS:* 37 year old male with history of mental retardation, presented to the emergency room with an ulcer on his right scrotum that had been present for a few months. He was diagnosed of pT4 embryonal carcinoma by biopsy. CT scan showed multiple lung nodes. He was treated with five cycles of Bleomycin/Etoposide/Cisplatin with complete response after treatment.

*RESULTS:* Testicular tumors are the most frequent solid tumors in males between the ages of 20 and 39 years old. Testicular tumors represent 1% of all neoplasias diagnosed in males and 0.1% of all male deaths due to cancer. Several studies have reported the current real incidence rate of testicular tumors has increased to 3%, which accounts for the diagnosis of 450 new cases of testicular cancer a year in Spain.

*CONCLUSIONS:* The cure rate for patients with intermediate risk non-seminoma is around 70% following a conventional treatment approach of four cycles of BEP. The present case is noteworthy because, in our experience, testicular tumors are diagnosed at an early stage without extensively affecting the skin or simulating another type of epithelial tumor. As a result, the present study describes the natural progression of testicular cancer.

**Keywords:** Embryonal carcinoma.

**Resumen.-** *OBJETIVO:* Presentamos el caso de un varón de 37 años con un carcinoma embrionario en una forma poco frecuente en su debut, y que representa la historia natural de la enfermedad sin recibir atención sanitaria así como la efectividad del tratamiento con quimioterapia.

*MÉTODOS:* Paciente de 37 años con antecedentes de retraso mental desde el nacimiento, acude a urgencias por presentar una masa escrotal ulcerada maloliente de meses de evolución. Tras biopsia es diagnosticado de carcinoma embrionario pT4; en el estudio de extensión se evidencian múltiples nódulos pulmonares compatibles con metástasis. Recibió un total de cinco ciclos de Bleomicina/Etoposido/Cisplatino con una respuesta total tras el tratamiento.

*RESULTADOS:* Los tumores testiculares representan el tumor maligno sólido más frecuente en varones entre 20 y 39 años. Comprenden el 1% de todas las neoplasias masculina, y son responsables del 0,1% de todas las muertes por cáncer. Algunos autores apuntan que la incidencia real del tumor testicular ha aumentado y se sitúa alrededor del 3% y se estima en 450 nuevos casos al año en España.

*CONCLUSIONES:* Con respecto al pronóstico de los tumores no seminomatosos, se acepta que la tasa de curación de los pacientes de riesgo intermedio se sitúa alrededor del 70% con tratamiento convencional con cuatro ciclos de BEP. El caso que presentamos resulta muy llamativo puesto que en nuestro medio los tumores testiculares son diagnosticados en estadios iniciales, sin afectación cutánea extensa, ni simulando otros tipos de tumores epiteliales y muestra la historia natural de la enfermedad.

**Palabras clave:** Carcinoma embrionario.

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## INTRODUCTION

Testicular tumours are the most frequent solid tumour in males between the ages of 20 and 39 years old (1, 2). Testicular tumours represent 1% of all neoplasias diagnosed in males (3, 4) and 0.1% of all male deaths due to cancer. Several studies have reported that the current real incidence rate of testicular tumours has increased to 3% (5), which accounts for the diagnosis of 450 new cases of testicular cancer a year in Spain (6). Here, we report a rare case of advanced testicular cancer that describes the natural progression of testicular cancer without medical treatment. This study also describes the effectiveness of chemotherapy, which was the approach used for treatment.

## CASE REPORT

A 37-year-old male, with a history of mental retardation, went to the emergency room with an ulcer on his right hemiscrotum that had been present for a few months (Figure 1).

### Physical examination and analyses:

The lesion possessed an odour, as well as necrotic regions. The bilateral inguinal lymph nodes were swollen to pathologic size and were tender. The corporal temperature was normal, and there were no signs of systemic sepsis.

The patient underwent an emergency operation to drain the suspected scrotal abscess. The patient was believed to have an abscess vs Fournier gangrene. During the surgery, a large bleeding tumour mass was found. The tumour originated in the scrotum, but had invaded into the right testicle. The anatomic structures within the



FIGURE 1. The scrotal mass at the time of diagnosis in the emergency room. A biopsy revealed the presence of an embryonal carcinoma with vascular invasion and a skin ulcer (AJCC stage T4).

testicle could no longer be identified. Only superficial biopsies were taken from the mass

### Pathological Anatomy:

An analysis of the mass revealed an embryonal carcinoma with evidence of vascular invasion and a skin ulcer (classified using the American Joint Committee on Cancer (AJCC) guidelines as stage pT4 testicular cancer). Immunohistochemistry (IHC) was performed, and the tumour was positive for cytokeratin (determined using the pan-cytokeratin antibody AE1/AE3), placental alkaline phosphatase (PLAP), CD30 and p53. Furthermore, as detected using IHC, the tumour was negative for human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP; Figure 2).

### Tumour markers:

The tumour expressed lactate dehydrogenase (LDH) at a concentration of 748 IU/L (230-460), AFP at a concentration of 17.6 ng/mL and HCG at a concentration of 3 IU/L.

### Computed tomography (CT) scan:

The patient's lungs were examined using CT scan. A large node, 2 cm in diameter, was found in the anterior segment of the upper left lobe of the lung, confirming metastasis. Five additional nodes were found in the right lung, and three nodes were found in the left lung. A large scrotal mass affecting the pelvis on both sides with subcutaneous cellular tissue in the prevesical area, which also affected the bilateral lymph nodes, was present (Figure 3).

The patient began chemotherapy treatment after diagnosis with a germinal tumour, not a seminoma with intermediate risk. The treatment scheme included three cycles of bleomycin/etoposide/cisplatin (BEP) and two cycles of etoposide/cisplatin. After the third cycle, a new CT scan was performed.

### CT scan after three cycles of chemotherapy:

After three cycles of chemotherapy, the affected inguinal and scrotal masses were reduced by more than 50% compared to the first CT scan. Additionally, the lung nodes were reduced to 3 mm and the lung mass in the upper right lobe was less than 7 mm.

### CT scan after five cycles of chemotherapy:

After five cycles of chemotherapy, the lung nodes were smaller than those seen in the previous CT scan, with a size of less than 4 mm. The scrotal mass showed a significant reduction in size.

Two months after the fifth cycle of chemotherapy, a surgical examination of the inguinal and testicular area was performed. A large fibrosis in the inguinal area was observed, along with a fibrous string (a rest of spermatic cord) that was dried out. A biopsy of the left testicle revealed that it was negative for malignant cells.

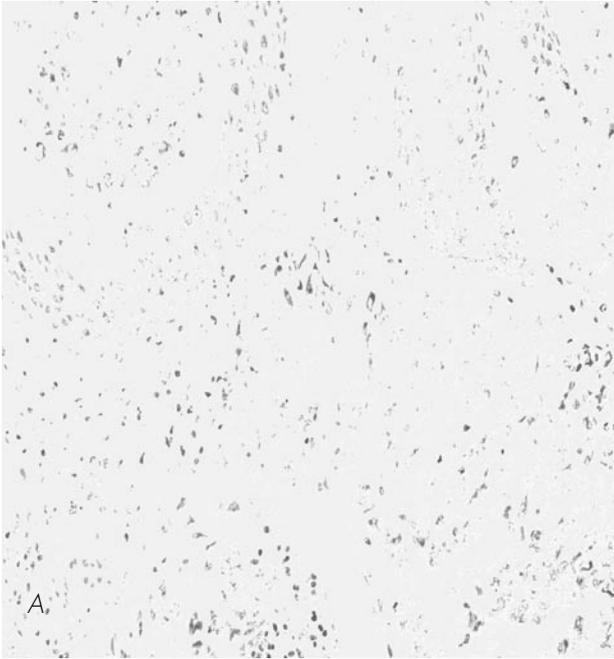


FIGURE 2A. Skin infiltration of the solid tumour with polygonal cells containing clear and large cytoplasm, vesicular nuclei and prominent nucleoli (HE stain at 20X magnification).

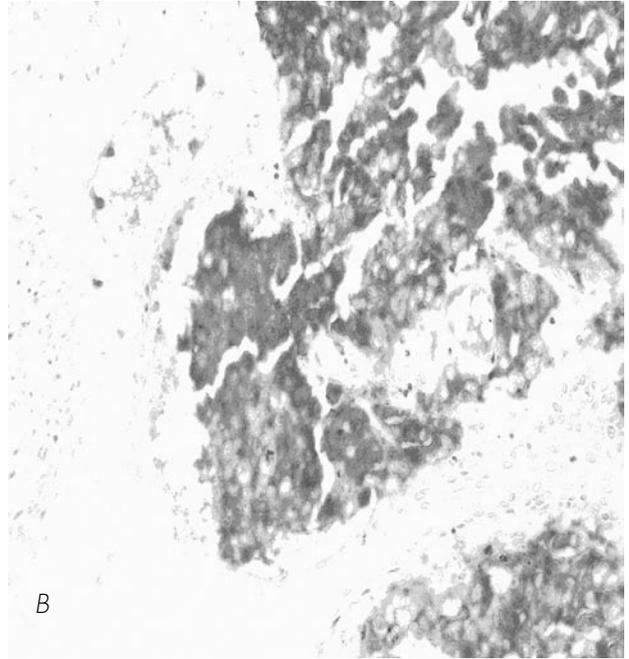


FIGURE 2B. CD30 positive staining in the tumour cells.

#### Pathological anatomy:

A fragment of tissue including a deferent conduct associated with connective tissue, as well as inflammatory changes associated with necrosis, was examined. No residual carcinoma was seen in this specimen. Additionally, no testicular tissue was identified.

Three months after surgery, the patient was re-evaluated by CT scan and for tumour markers. A 1 mm subpleural lung node of a stable size in the upper right lung was observed. The tumour markers had returned to normal (Figure 4).

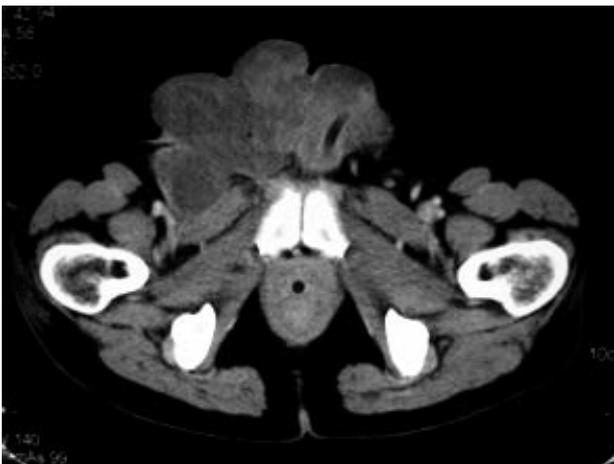


FIGURE 3. Pelvic CT scan prior to diagnosis.



FIGURE 4. Current image of the patient.

#### DISCUSSION

Germ cell tumours are more frequent in white males and in the Scandinavian population; only a few cases have been diagnosed in Africa and Asia. Two of the most important risk factors for germ cell tumours are cryptorchidism and Klinefelter syndrome (7-9).

Germ cell tumours originate in the testicle in 90% of all cases and are of extragonadal origin in 10% of cases. Histologically, seminomas represent around 50% of the germinal tumours (10).

Embryonal carcinoma is the most undifferentiated type of germ cell tumour. Embryonal carcinomas are characterized by large areas of necrosis and bleeding. Embryonal carcinomas are formed by epithelial cells, which are organized into glands or strings. Typically, embryonal carcinomas will present as a solid painless mass in the scrotum. Quite frequently, patients will suffer from some form of scrotal trouble or an increase in the volume of the scrotum. These symptoms suggest epididymitis and/or orchitis. Sometimes, patients will present with acute testicular pain similar to testicular torsion. Most patients will be diagnosed after one of these symptoms. As a result, very seldom is a mass that had infiltrated the skin of the scrotum observed. Here, we report such a case.

In general, it is accepted that the median time to diagnosis is around three months (12). The delay in testicular tumour diagnosis is due to the long time it takes for patients to seek medical assistance and sometimes in the delayed diagnosis by the physician. A delay in the diagnosis can affect the staging of the disease. There is a linear correlation between the time to diagnosis and clinical stage of the disease (13,14). In the present case, the history of mental retardation may have influenced the length of time that the patient waited before consulting a medical professional.

To correctly classify the tumour, a thorough physical exam is necessary. The AFP, beta-HCG and LDH levels and diagnostic image tests are important. The local extension of the tumour, whether distant organs are affected, the tumour marker levels and whether the patient presents with an elevated LDH establish the different prognostic group (Table I), treatment and duration (15).

In general, the germ cell tumours that are not seminomas disseminate through the lymph system. Cells from the primary lesion travel to the retroperitoneal lymph nodes and then to distant locations in the following order: lung, posterior mediastinum and left supraclavicular fossa. The retroperitoneum is the initial place of metastasis in 70–80% of patients with testicular cancer. Contralateral dissemination is frequent in tumours of the right side and, in general, is associated with a large tumour mass. Metastasis in the lowest places usually show a retrograde dissemination to the distal iliac lymph nodes and inguinal area secondary to a large volume of the tumour, or less commonly to an aberrant lymph drainage of the testicle (16). In the case presented here, the bilateral conglomerate inguinal lymph nodes were emphasized.

A CT scan is an optimal image test for the detection of distant metastasis (11). The AFP and beta-HCG levels

TABLE I. GERM CELL TESTICULAR TUMOUR- CLASSIFICATION OF THE RISK ASSOCIATED BASED ON AJCC STAGING.

Risk	No Seminoma
Low	Testicular tumour or primary retroperitoneal. No evidence of visceral metastasis, nodes not found in the lung. Tumour markers: AFP: <1000 ng/mL HCG: <5000 IU/mL LDH: <1.5 times the normal upper level.
Intermediate	Testicular tumour or primary retroperitoneal. Visceral metastasis not in the lung. Tumour markers: AFP: between 1000 and 10,000 ng/mL HCG: between 5000 and 50,000 IU/mL LDH: between 1.5 and 10 times the normal upper level.
High	Primary tumour with mediastinum localization. Visceral metastasis not in the lung. Tumour markers: AFP: >10,000 ng/mL HCG: >50,000 UI/L LDH: >10 times the normal upper level.

are increased in 60% and 40% of patients, respectively, who do not have an advanced seminal tumour. The LDH level reflects the growth pattern and cellular proliferation of the tumour independent of cell type (17). An increase in the LDH level is considered an independent prognostic factor (18). Of the patients who do not have a seminoma, 60% have an increase in the LDH level (19,20).

## CONCLUSIONS

The cure rate of patients without seminomas and with an intermediate risk is around 70% following a conventional treatment approach of four cycles of BEP.

The case presented here is noteworthy because, in our experience, testicular tumours are diagnosed at an early stage without extensively affecting the skin or simulating another type of epithelial tumour. As a result, the present study describes the natural progression of testicular cancer.

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