

Relapse of unusual localization of classic seminoma with post-chemotherapy transformation

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Case Report

Abstract

Germ cell tumor is the most common cancer among males in the 20–39 year-old age range, representing 21% of invasive cancer diagnose. The vast majority of testicular tumors in this age range are germ cell tumors. There are two types of malignant tumors, the pure seminoma cell and non-seminomatous germinal cell tumors (NGCT). We present the case of a patient who underwent a testicular tumor surgery, classic seminoma stage I, receiving two cycles of adjuvant carboplatin chemotherapy. During the follow up, an elevation on the alpha-fetoprotein level was observed, thus the final diagnosis was adenopatic recurrence of the Yolk Sac tumor.

Keywords: Classic Seminoma; Alpha-fetoprotein; Vitelline tumor

Introduction

Testicular tumors are the most common malign solid neoplasias affecting young males, representing less than 1% of male tumors. The number cases have a peak in the age range 20–39 years, then decline; therefore it is considered a prototypic malignancy of young adults. The incidence of germ cell tumors in males is relatively steady through the age range 20–39 years. From 2001 to 2005, the incidence of germ cell tumor in the US was estimated to be 11.8 per 100,000 males aged 20–39.1 years. Overall, there are about 8200 new cases of testicular germ cell tumor in the United States annually.¹

There are two types of malignant tumors, the pure seminoma cell and non-seminomatous germinal cell tumors (NGCT). In clinical practice, three types of tumoral markers are quantified in blood analysis: alpha-fetoprotein, (AFP), beta

subunit of chorionic gonadotropin, (hCG), and lactate dehydrogenase (LDH). Levels of AFP and/or hCG show an increase in 80–85% of the NGCTs, even in non-metastatic disease. However, the hCG is elevated in less than 20% of the seminoma cells and showing not AFP level increase in these tumors.² Before the development of the effective chemotherapy, the 5-years survival rate in patients with germinal tumors was 64% whereas this was improved to the current 95% for seminoma cells and non-seminomatous cells.

After the initial treatment, the follow up must be carried out with periodic hCG and AFP determinations. An increase in tumoral markers represents the first evidence of disease, including those ones that have normal levels at the time of the initial diagnosis.³ Relapsed patients with pure seminoma stage-I after the orchiectomy can be treated with radiotherapy (RT) or cisplatin-based chemotherapy.⁴ In case of residual masses, patients must be only observed, except for tumors larger than 3 cm, in this case, neoplasia removal will be performed or a biopsy if the surgery was not possible. Currently, positron emission tomography (PET) computed axial tomography application is recommended and if the outcome is positive (increased SUV) it is mandatory to remove the neoplasia. Relapsed patients with CGNT stage-I

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after an orchiectomy must be treated with cisplatin chemotherapy and underwent surgery of the residual masses, except in cases when the primary tumor was an embryonic carcinoma, with or without seminoma. Monitoring is recommended in patients under chemotherapy when the tumor volume decreased at least 90%.

Clinical case

We report the case of one patient, a 45-years-old male, without relevant medical history, underwent vasectomy, showed up at the emergency service in November 2011 for painless tumor in left testicle. Blood analysis was performed yielding the following results, human chorionic gonadotropin (hCG) level was 61 mU/mL (normal level <5 mU/mL), alpha-fetoprotein (AFP) level of 12 ng/mL (normal range: 0 – 10 ng/mL) and LDH level of 494 U/L (normal range: 230-460 U/L).

A surgery was performed, on November 18, 2011 according to germinal tumor diagnosis by left inguinal orchiectomy. Anatomopathologic (AP) study shows a 4.8 x 2.2 cm classic seminoma that invades both testicular membranes (T2NxMx) without lymphovascular presentation and with resection borders free. The post-surgery analysis showed hCG 0.1 mU/mL, AFP 14 ng/mL and LDH 321 U/L levels. The thoracic and abdominal computed axial tomography showed no visceral or lymph node involvement.

Because of the type of tumor, a classic high risk testicular seminoma stage-I, (larger than 4cm) with good prognosis, the patient received two cycles of adjuvant carboplatin (AUC7) every 21 days, finishing on January 20, 2012, and followed by regular monitoring.

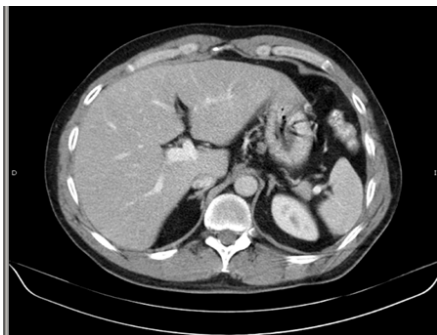


FIG. 1: Abdominal computed axial tomography May 2012: adenopathy of 8 mm in minor axis at high gastrohepatic level

On January 2012, the blood analysis showed an AFP increase (34.2 ng/mL). Due to this elevation, the patient was assessed closely. A re-evaluation was performed by clinical examination, thoracic and abdominal computed axial tomography, PET computed axial tomography, cranial RMN, lumbar puncture and bone marrow biopsy. The obtained outcomes could not explain the AFP increase. The primary

tumor biopsy was reviewed by the Pathological Anatomy Service confirming the initial diagnosis of classic seminoma. On May 2012, the AFP showed a level of 107 ng/mL and the computed axial tomography showed an adenopathy of 8 mm of lower axis at the gastrohepatic high level, (**Figure 1**).

A High technology imaging in digestive endoscopy, (HDE), was implemented and no malicious adenopathies were noted. On July 2012, due to the rise of AFP, (2400 ng/mL), and in absence of macroscopic disease chemotherapy was started with BEP schedule (Cisplatin 20 mg/m² days 1-5, Etoposide 100 mg/m² days 1-5 and Bleomycin 30 mg days 1, 8 and 15) every 21 days during 3 cycles, AFP level was reduced to 350 ng/mL. After two months of follow up, AFP level increased again and computed axial tomography showed an increase to 17 mm in the gastrohepatic adenopathy previously observed (**Figure 2**). On 14 February of 2013, the patient underwent a laparotomy showing an adenopathy at the celiac trunk (2 cm) in close contact with pancreas. The AP result was compatible with solid Yolk Sac Tumor, with a significant AFP expression. After lymph node metastasis surgical removal, AFP dropped to 44.7 ng/mL level and two additional cycles of carboplatin and etoposide were administered, currently the patient maintains this treatment.

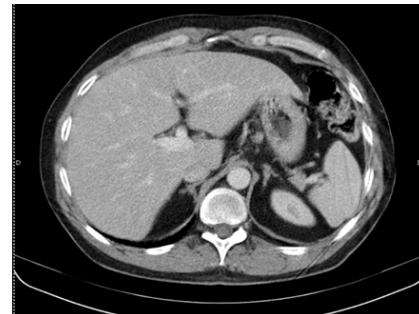


FIG. 2: Abdominal computed axial tomography January 2013: adenopathy of 17 mm in minor axis at high gastrohepatic level.

Discussion

In most cases of germinal tumors stage-I, a clinical follow up is performed. The recurrence incidence is around 16-20% and the median of time is 12-18 months, and the most common site is the retroperitoneum, followed by pelvic and lung lymph nodes. In contrast, in this patient, the radiological relapse happens at gastrohepatic level without other adenopathies at retroperitoneal level. Carboplatin has an effect in the metastatic seminoma, (although lower than cisplatin), and with an acceptable tolerability profile. Most of the patients with stage-I seminoma were treated with one or two cycles or adjuvant carboplatin obtaining excellent results. The relapse index achieved by treatment is smaller than after radiotherapy and the 5-years-survival rate is almost 100%, therefore it is recommended in high-risk patients, (size greater than 4 cm or with Rete testis invasion).^{5,6}

In this case, the minimum AFP elevation prior and after surgery, (12 and 14 ng/mL respectively), questioning the non-seminomatous nature of the tumor. Although, anatomopathological findings after over 10 histological slides in the primary testicular tumor showed a classic pattern seminoma, (**Figure 3**), with clear lymphocitic infiltration and lack of pseudoglandular patterns.

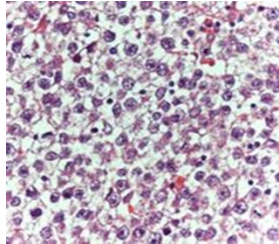


FIG. 3: Original tumor: classic seminoma with minimal lymphocitic infiltration.

The immunohistochemical analysis showed a classic immunophenotype with OCT3+ and AFP-, cytokeratins- and hCG-. However, the ganglionic metastasis showed a different histology, showing a solid vitelline tumor with glandular areas, (**Figure 4**), the immunophenotype was completely different from the original tumor, being AFP + (**Figure 5**) and showing SALL4 expression.

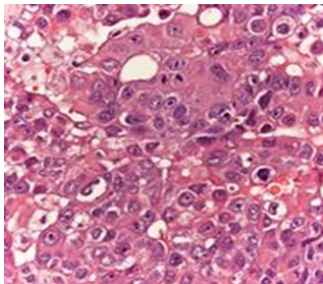


FIG. 4: Lymphatic ganglion: metastasis of vitelline tumor with solid pattern and in the glandular part. Observe hyaline globules.

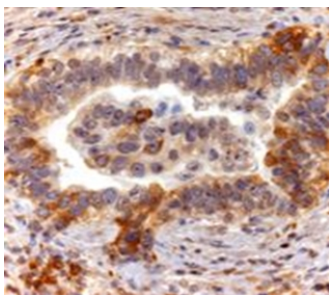


FIG. 5: Vitelline tumor, glandular area with clear secretion of alpha-fetoprotein.

The classical conception that seminoma cannot evolve towards other tumoral types has been controversial, previous data showing the seminoma pluripotentiality with similar characteristic to primary germinal cells. This evidence is supported by immunohistochemical and ultra-structural studies that showed somatic differentiating aspects,

(cytokeratin, blood antigens), in primitive germinal cells of the seminoma. This assumption is shown for both testicular and ovarian germinomas.^{7,8,9} This conversion from primary germinal cells is just a particular type of maturation process, in this case induced by chemotherapy or spontaneously.

Conclusion

The relapse of classic seminoma stage-I is rare and usually appears in retroperitoneum or lungs. In case of metastasis, the histology is similar to primary tumor but, occasionally, it can suffer cellular transformation, induced by chemotherapy. In other cases, the transformation occurs on the histology alone, without chemotherapy.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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