

Metastatic and Synchronous Melanoma in the Testicle and Paratesticular Region

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Abstract

Background: Metastatic tumors of the testicles are rare (0.8%) and preferably located in the testicular parenchyma or, much more rarely, in the para-testicular region. The melanoma of the skin represents the third primary site of metastases and the patients may present with increased scrotum volume, heterogeneous testicle mass beside local pain and tenderness.

Objective: To show the rare case of metastatic and synchronous melanoma in the testicle and para-testicular region.

Description of the case: Case reports of a 74-year-old male patient who was undergone an extended acral melanoma resection in the left calcaneus. The micro stage showed Clark level IV and Breslow depth of 3 mm. The treatment was complemented with homolateral inguinal-iliac lymphadenectomy. Three years later a crossed metastasis was diagnosed in the opposite inguinal region that required another lymphadenectomy. The patient developed a perineal lymphedema that was managed clinically. He was then carried to oncologist who starts high-dose interferon per one year as adjuvant therapy. Two years later, the patient showed an increased size and irregularity of the right testicle along with pain and loss of elasticity. An ultrasound confirmed an increased testicle diameter and increased vascularization associated with parenchyma heterogeneity. The measurements of LDH, alpha-fetoprotein and β HCG were normal. A staging computed tomography scans showed bilateral pulmonary nodules and increased diameter of periaortic lymph nodes representative of metastatic disease. A radical right orchiectomy via the inguinal route was then expedited. The histopathology diagnosed synchronous metastatic melanoma in the testicle and paratesticular region.

Conclusion: The presence of a testicular mass in patients with previous clinical history of melanoma represents a warning sign. It should be considered a metastatic disease at first time and an accurate diagnostic restage is mandatory.

Keywords: Melanoma; Secondary testis tumours; Paratesticular metastasis

Introduction

Metastatic solid tumors of the testicles are rare and represent only 0.8% of the neoplasias for this organ. The most important primary sites involved are prostate (29%), followed by lungs (16%), skin (melanoma, 11%), kidney (9%), adrenal gland (neuroblastoma, 7%), and colon and rectum (7%) and the most cases are diagnosed after autopsy. The melanoma of the skin therefore represents the third primary site and its incidence has been reported to vary between 9% and 41% [1-3].

The patients may present increased scrotum volume followed by irregularities, local pain and tenderness. Metastatic tumors of the testicles are preferably located in the testicular parenchyma or, much more rarely, in the para-testicular region, determining solitary or multiple nodules. A relevant clinical aspect is the differentiation from primary neoplasias of the testicles. Patient age, previous malignant disease and higher biochemical markers (LDH; alpha-fetoprotein and β HCG) contribute to the differential diagnosis [4].

Description of the Case

Case reports of a 74-year-old male patient who was undergone an extended acral melanoma resection in the left calcaneus. The micro stage showed Clark level IV and Breslow depth of 3 mm. The treatment

was complemented with homolateral inguinal-iliac lymphadenectomy. Three years later a crossed metastasis was diagnosed in the opposite inguinal region that required another lymphadenectomy.

The patient developed a perineal lymphedema that was managed clinically. He was then carried to oncologist who starts, per one year, high-dose interferon as adjuvant therapy. Two years later, the patient showed an increased size and irregularity of the right testicle along with pain and loss of elasticity. An ultrasound confirmed an increased testicle diameter and increased vascularization associated with parenchyma heterogeneity (Figure 1).

The measurements of LDH, alpha-fetoprotein and β HCG were

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normal. A staging computed tomography scans showed bilateral pulmonary nodules and increased diameter of periaortic lymph nodes representative of metastatic disease. Faced with the diagnostic suspicion of testicular metastatic melanoma, a radical right orchiectomy via the inguinal route was expedited (Figure 2 A-B). The histopathology diagnosed synchronous metastatic melanoma in the testicle and paratesticular region (Figure 3 A-B).

The research was approved by the Ethics Commission at Monte Sinai Hospital in Juiz de Fora – Minas Gerais – Brazil. The own patient signed up an informed consent term to participate in the study conformed to the Helsinki Declaration and to local legislation.

Discussion

The reasons that justify the low incidence of testicular and paratesticular metastatic tumors are not well established yet. Speculations focus on the fact that the low temperature of the scrotum could reduce the probability of tumor cells being carried to the testicles and compromise its capacity to establish ways of secondary growth [4]. Even so, testicles can be affected by metastatic disease from arterial, retrograde venous and lymphatic dissemination as well as deferens ductus and epididymis. In general, for primary tumors that are located



Figure 1: Ultrasonography of right scrotum showing testicular atrophy parenchyma and several heterogeneous nodules.

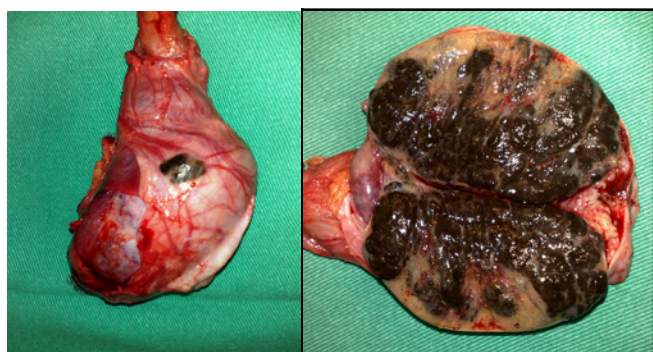


Figure 2: (A) Surgical specimen showing melanoma synchronous metastasis in the paratesticular region (tunica vaginalis) and testicular parenchyma (B). During histopathological study, no extravasation was evidenced in the testicular tumor for the tunica albuginea.

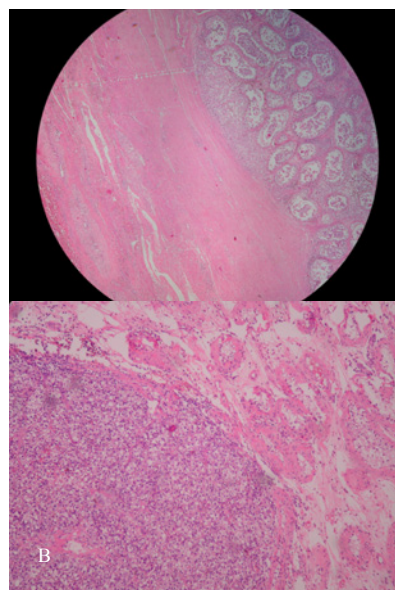


Figure 3: (A) 20X photomicrography on Hematoxylin- and Eosin-stained slide showing two distinct metastatic nodules restricted to the testicular parenchyma with intact tunica albuginea. (B) 40X photomicrography on Hematoxylin- and Eosin-stained slide showing a sole node in tunica vaginalis. Neoplastic epithelioid cells, melanin-compatible intracellular pigments and nucleolus with multiple figures of mitosis are present.

outside the pelvic and abdominal cavity, arterial dissemination seems to be the preferred route [5].

Moreover, It is also believed that the chronic stasis secondary to congenital or surgical acquired lymphedema, produce local changes in the lymphatic protein composition (decreased alpha-2 globulin fraction and increased albumin-globulin ratio), and delaying protein transport from the interstitial space into the lymphatic tissue, might change the tissular antigenic composition and/or regional immunological competence, allowing the growth of tumors. These evidences may explain, at least in part, the development of metastatic disease in the scrotum area [6,7].

The testicles and para-testicular region (inguinal-scrotal region independent from the testicle including the spermatic cord, epididymis and scrotal tunics) are known as uncommon regions for melanoma metastases. Aslam et al. [8] described the first case of metastatic malignant melanoma involving para-testicular tissues solely in 2008. In their case report the widely metastatic disease was identified based on histopathologic examination of the excised scrotal mass [8]. In fact, the Initial presentation of the melanoma as a testicular or para-testicular mass is very rare, and in the majority of cases represents a disseminated disease that was not diagnosed yet. Like this, the presence of a testicular mass in patients with previous clinical history of melanoma represents a warning sign and demands imaging testes and systematic effort to re-stage the disease [8,9].

Our case report is unique and call attention to a curiosity not described yet that was photographically documented after right testicle resection. The diagnosis of metastatic synchronous melanoma at right testicle and the tunica vaginalis without involvement of any other adjacent structure (Figure 2 A-B). In fact, this simultaneous involvement can be easily explained as local extension of the disease;

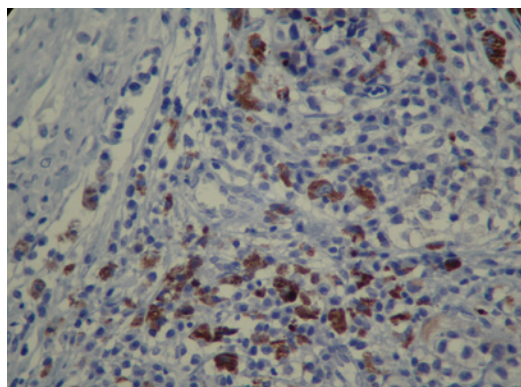


Figure 4: 400X photomicrography on a slide for which an immunohistochemical study shows an injury in the testicular parenchyma with strong and focal Melan-A positivity.

however what is not true in this case, the histopathology shows two distinct anatomical points of metastatic implant (parenchyma and tunica vaginalis) without contiguous dissemination. Another point that deserves commentary is related to the inguinal approach to correctly managing the patient. Surgical approach via the scrotal route should be avoided due to the risk of a metastatic implant in the scrotum.

The histopathologic study confirmed the testicular tissue atrophy due to the compression from multiple nodules embraced by an intact tunica albuginea. In addition, it was diagnosed in the tunica vaginalis only one metastatic implant. It was also possible to observe in epithelial neoplastic cells with vacuolized and eosinophilic cytoplasm the presence of melanin-compatible intracellular pigment and prominent nucleolus with multiple mitosis images (Figure 3 A-B). The Immunohistochemistry (Figure 4) study demonstrated the melanocytic lineage of the cells which expressed group GP100 (HMB-45) proteins, a condition that was confirmed by the Melan-A marker [10,11].

The presence of metastatic testicular and/or para-testicular melanoma carry out a dismal prognosis with a life expectancy after orchiectomy ranged from 2 to 14 months [12]. Chemotherapy (dacarbazine or the nitrosureas carmustine and lomustine) and immunotherapy with interleukin-2 or interferon Alfa represent the current treatment options for metastatic melanoma [13,14]. Despite multiple trials evaluating potential new therapies, high-dose interferon remains the only FDA-approved therapy for stage IIB and III melanoma. The therapeutic efficacy of interferon appears to exceed other regimens, when associated with treatment of 1 year's duration. Our patient has been previously managed with high-dose interferon and completed the planned regimen two years later. Two months after the operation, he had a quickly declined in his performance status that precluded any other adjuvant therapy. The patient died at his home three months later.

In conclusion, the presence of a testicular mass in patients with previous clinical history of melanoma represents a warning sign. It should be considered a metastatic disease at first time and an accurate diagnostic restage is mandatory.

Competing Interest Statement

The authors Carlos Augusto Gomes, Cleber Soares Junior, Emilio Augusto

Campos Pereira de Assis, Thais Aparecida de Souza Silva, Cecília Maria Stroppa Faquin, Leonardo de Paula Vilela, Camila Couto Gomes and Igor Vitoi Cangussu declare there was not financial support or relationships that may pose conflict of interest.

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Study design: Carlos Augusto Gomes / Emilio Augusto Pereira Campos de Assis

Definition of intellectual content: Carlos Augusto Gomes / Cleber Soares Junior

Literature research: Thais Aparecida de Souza Silva / Cecília Stroppa Faquin

Data acquisition: Carlos Augusto Gomes / Leonardo de Paula Vilela

Data analysis: Carlos Augusto Gomes / Camila Couto Gomes / Igor Vitoi Cangussu

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Manuscript editing: Leonardo de Paula Vilela / Camila Couto Gomes

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