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Case Report

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Thirty-Year-Old Male Patient with Non-Seminoma and Coincidental Rectal Cancer

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Non-seminoma · Rectal cancer · BEP chemotherapy · TP53 mutations

Abstract
We present the case of a 31-year-old male patient with non-seminoma (90% embryonal carcinoma, 10% teratoma) pT1b L1 V0 Pn0 R0 cN2 cM0, Clinical Stage IIb and "good prognosis group" according to IGCCCG of the left testis. According to EAU guidelines, he received three cycles of BEP. After the second cycle, he developed recurrent, clinically not significant rectal bleeding, which we associated with deep thrombocytopenia. Following chemotherapy, there was one lymph node in the CT scan left, with a diameter of 0.9 cm at the inferior mesenteric arteria and the rectal bleeding did not stop; so coloscopy and staging revealed rectal cancer (adenocarcinoma) with peritoneal carcinosis. The patient was scheduled for radio-chemotherapy. Next-generation sequencing of the adenocarcinoma showed two mutations in KRAS and TP53 genes. To our knowledge, this is the first case of non-seminoma and coincidental rectal cancer. Furthermore, this case underlines the significance of molecular biological studies for the development of individualized targeted therapies, especially in younger patients and in chemo- and/or platin-resistance.

Introduction

Testicular cancer is relatively rare accounting for approximately 1–1.5% of all cancers in men. At diagnosis, 1–2% are bilateral, and the predominant histology is germ cell tumor. Most malignant postpubertal testicular germ cell tumor originates from the germ cell neoplasia. They are clinically and histologically subdivided into seminomas and non-seminomas. Non-seminomas include elements of embryonal carcinoma, yolk sac, choriocarcinoma, and teratoma. Peak incidence is in the third decade of life for non-seminoma. Epidemiological risk factors for the development of testicular cancer are components of testicular dysgenesis syndrome, which encompasses cryptorchidism, hypospadias, decreased spermatogenesis evidenced by sub- or infertility, or disorders/differences of sex development. Additional risk factors include family history among first-grade relatives, the presence of a contralateral tumor or carcinoma in situ [1].

We present the case of a 31-year-old patient with a non-seminoma of the left testis and coincidental rectal cancer. To our knowledge, this was never described before and underlines the necessity for further molecular biological research in young patients to develop targeted therapy, especially in chemoresistance.

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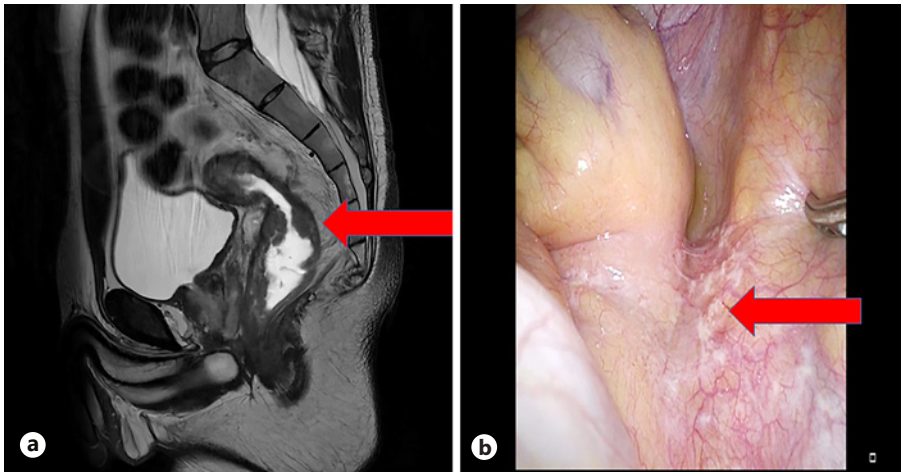

Fig. 1. Illustration of the clinical findings of rectal cancer. **a** MRI scan of the pelvis. **b** Laparoscopic protective ileostomy surgery revealing peritoneal carcinosis.

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A 31-year-old otherwise healthy patient without risk factors for germ cell tumors and without a family history of malignancies presented with a tumor of the left testis. Tumor markers were LDH negative, beta-HCG 75.1 mU/mL, AFP 13.2 mU/mL; so, we scheduled him for radical orchiectomy. Pathology revealed non-seminoma (90% embryonal carcinoma, 10% teratoma) pT1b L1 V0 Pn0 R0 cN2 cM0. Tumor markers returned to normal values after surgery. CT scan of the thorax and abdomen revealed clinical stage IIb disease, and the patient therefore fell into the good prognosis group according to IGCCCG. Considering the EAU guidelines on testicular cancer the patient received three cycles of BEP (cisplatin, etoposide, bleomycin) [1]. During the second cycle, he developed thrombocytopenia (<20 GpT/L) with recurrent but clinically not significant rectal bleeding. After the three cycles of chemotherapy, he received a restaging CT scan which showed one lymph node with a diameter of 0.9 cm below mesenteric arteria left and tumor markers were still negative. Thus, it was decided to perform an early restaging after 6 weeks. However, rectal bleeding did not clear even with normalization of platelet count. Consequently, we scheduled him for a coloscopy in an outpatient clinic. This coloscopy revealed histologically confirmed rectal cancer (adenocarcinoma) 10 cm ab ano. For further evaluation, the patient received an MRI of the pelvis and a laparoscopic protective ileostomy surgery. Furthermore, this surgery found histologically confirmed peritoneal carcinosis of the adenocarcinoma. Figure 1 illustrates the MRI scan as well as the peritoneal carcinosis during laparoscopic surgery. Interdisciplinary discussion in the tumor board decided on radio-chemotherapy according to the RAPIDO protocol[2].

Additionally, molecular pathology assessment was performed from the adenocarcinoma using the from the Cancer Hotspot Panel v2 amplicons with iSeq 100 (Illumnina; San Diego, CA, USA) next-generation sequencing technology. This analysis showed two mutations: a KRAS Gene point mutation pG12D (Coverage 3085; Variant-allele-frequency 6.8%) and a TP53 Gene in-frame-deletion pI252_I254del (Coverage 1493; Variant-allele-frequency 10.6%). Consequently, human genetic counselling was carried out, even while no germline mutation was found.

In summary, human genetic counselling stated: no evidence for relevant germline mutation from whole blood in the established and known colon cancer genes. Therefore, there is no increased risk for the development of cancer in relatives.

Discussion

This case represents non-seminoma with coincidental rectal cancer. To the best of our knowledge, this is the first report of such a case according to a search using MEDLINE via PubMed using the Mesh terms "non-seminoma" and "rectal cancer." It is remarkable that the rectal adenocarcinoma grew during the BEP chemotherapy. It is also important to note the significance of the molecular pathology assessment that was performed. Especially in young cancer patients, this knowledge is essential to develop targeted individualized therapies. Furthermore, these therapies are of special interest in chemo- and/or platin-resistant cancer [3–5]. Interestingly, Hacioglu et al. [3] described in their retrospective analysis that 15% of non-seminomas also carry KRAS mutations. Unfortunately, no molecular information on the non-seminoma could be retrieved, as the quality of the respective archival tissue sample was considered not sufficient for next-generation sequencing. This is a limitation of this case report.

In summary, further studies about genomic profiling in germ cell tumors are needed to develop targeted therapies especially in platin-resistance [3, 4]. This fact is also underlined by this case since the patient might have developed a secondary cancer under a platin-based therapy.

Statement of Ethics

According to our ethics review board, an ethics approval is not necessary for a case report; so ethical approval is not required for this study in accordance with local guidelines. All procedures performed in this case report were in accordance with the ethical standards of the institutional and/or national research committee and with the 1,964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare regarding this case report.

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Author Contributions

Julia Nolting, Desiree Louise Dräger, Oliver W. Hakenberg, and Laila Schneidewind took care of the patient, analyzed and presented the data, and wrote the manuscript.

Data Availability Statement

All data generated or analyzed during this case report are included in this article. Further inquiries can be directed to the corresponding author.

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