Case Report

**Mixed germ cell tumor of the testicle with raviomuosarcomatous component: a case report**

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**Abstract**

**Introduction:** Testicular tumors can be classified as seminomatous and non-seminomatous germ-cell tumor (NSGCT) types. Mixed germ cell tumors contain more than one germ cell component and are much more common than any of the pure histologic forms representing 32%-60% of all germ cell tumors. The composition of these tumors varies. Here we present a rare case of a mixed germ cell tumor composed of seminoma, Yolk sack tumor and teratoma containing a sarcoma component of somatic type malignancy.

**Case presentation:** A 32-year-old Caucasian male presented with history of right-sided scrotal swelling since 6 months. Backache was present since 2 months and a history of right epididimitis was also present since 8 months. Alpha-Fetoprotein, beta-HCG and LDH values were found abnormal. USG of the scrotum revealed a large right testis swelling characterized by scarce cystic elements and calcifications. CT scan of the abdomen showed nodular metastasis involving the interaortocaval, precaval, and right para-aortic lymph nodes. The block of enlarged lymph nodes infiltrated the psoas muscle. The patient underwent right-sided high orchidectomy and was given chemotherapy of the BEP regimen. After the 2nd cycle the patient discontinued the chemotherapy and when he came for follow-up after a gap of 3 months, despite the normalisation in tumor markers values, the retroperitoneal mass was relapsed. CT scan of the chest showed multiple lung metastases.

**Conclusion:** More than 50% of germ-cell tumors include more than 2 basic germ-cell tumor types, with the exception of spermatocytic seminoma. About 90% of the patients with nonseminomatous tumors can achieve complete cure with aggressive chemotherapy and most of them can be cured. Although prognosis of testicular tumors depends largely on clinical stage, histological type and adhesion to the treatment influence the prognosis as well.
Background

Testicular cancer is a respectively rare neoplasm; It make up approximately two percent of all malignant cancers in men and account for up to ten percent of all malignant disease occurring within the male genitourinary system. Most of these tumors occur in three age groups - infancy, late adolescence and early adulthood. More importantly, testis tumors are the most common malignant disease, developing in men between 20 and 40 years of age and are the third leading cause of death among men of this age group [1].

Pathologically, testis cancers are divided into two classes; germ cell tumors which are derived from germinal epithelium and non-germinal tumors which are of gonadal stroma origin. Tumors of germ cell origin comprise about 95% of all testis cancer. Germ cell tumors are divided into two basic groups: seminomas which occur in approximately 40% of the population and non-seminomatous tumors (NSGC) which may be seen in pure or mixed form [2].

NSGCs are further divided into the following five groups:

1) embryonal carcinoma with or without seminoma, which occurs in about 25% of the group;

2) teratoma with or without seminoma, which occurs in about 7% of the group;

3) teratocarcinoma including teratoma with embryonal carcinoma, choriocarcinoma, or both with or without seminoma occurring in about 25% of the group;

4) choriocarcinoma with or without seminoma or embryonal carcinoma or both account for the remaining 1-3%.

Mixed germ cell tumors contain more than one germ cell component and are much more common than any of the pure histologic forms representing 32%-60% of all germ cell tumors. Essentially, any admixture of the germ cell tumors as seen in pure form may be seen, one of the most common admixtures being embryonal carcinoma and teratoma [3]. Minor foci of yolk sac tumor are common, although it is usually overshadowed by other components, such as embryonal carcinoma. As is typical of embryonal carcinoma when seen in pure form, epithelium is often associated with syncytiotrophoblast giant cells when seen as part of a mixed germ cell tumor. Although seminoma may be seen as part of a mixed germ cell tumor, in some cases one sees seminoma separate from a dominant mass of non-seminomatous mixed germ cell neoplasia, and in such cases it is probably truly multicentric neoplasia, although for sign-out purposes it is probably sufficient to consider the seminoma together with the other neoplastic components under the one designation of mixed germ cell tumor with the traditional rough quantitation of the various components in descending order of frequency. The average age of presentation for patients with mixed germ cell tumors is 30 years. Unfortunately, many of these patients present late, usually with some or the other complications which are difficult to treat and carry bad prognosis. Still, if they can complete the chemotherapy they have a reasonable survival period, depending on the complications they have. We report on a patient who represents this unusual mixed variety of germ cell tumor.

Case reports

A 32-year-old Caucasian male presented with history of right-sided scrotal swelling since 6 months. According to the patient, it was a right -sided painless swelling which had progressively increased in size to its present dimensions. There was heaviness in the right side of the scrotum. There was no skin involvement. Backache was present since 2 months, more on walking and on straining. A history of right epididimitis since 8 months was also present. The patient was averagely built and nourished. Vital parameters were stable. The abdomen was soft on palpation with no obvious organomegaly. The chest was clear on auscultation. On local examination, a large right-sixed scrotal swelling was found. The scrotal skin was normal. No scar, sinuses or dilated veins were seen. On palpation, local temperature was normal and testicular sensations were absent on the affected side. It was a painless, non tender, non transilluminant swelling with variegated consistency. Per-abdominal examination did not reveal any abnormality. Virchow's nodes were negative.

Hematocrit was 42.5%, WBC:7100, PLT:213000, Glu:92, Ur:41 mg/dL, Cr:0,9 mg/dL, CPK:132.

Tumor markers: Alpha-Fetoprotein (AFP):2628 ng/ml, Beta-HCG:6,96 IU/ml, LDH:979

USG of the scrotum revealed a large right testis swelling of 45 × 37 × 53 mm. The eco architecture of the affected testis was promiscuous characterized by scarce cystic elements and calcifications. No dilated veins were seen.

USG of the abdomen showed a large right retroperitoneal mass corresponding to para-aortic lymph node block.

CT scan of the abdomen showed nodular metastasis involving the interaortocaval, precaval, and right paraaortic lymph nodes. The block of enlarged lymph node was filling almost the entire right retroperitoneal space infil-
The patient underwent right-sided high orchidectomy.

On gross pathological examination, there was a solitary, non encapsulated tumor measuring $4 \times 3 \times 26$ cm located mainly to the originating area of the spermatic cord. The tumor was hard in palpation. On cut section, it had a grating feel and hoary colour. There were areas of hemorrhage and necrosis with yellowish discoloration. Histopathology showed a mixed germ-cell tumor with predominant yolk sac tumor (45%) containing areas of necrosis (figure 3). The tumor also contained a typical seminoma component (25%) (figures 4 and 5) and immature teratomatous element (30%). The last was consisted of mature keratinized columned squamous epithelium (figure 6), respiratory epithelium, cartilage and immature rhabdomyoblastic element that was finally diagnosed as rhabdomyosarcoma (figures 7 and 8).

The tumor infiltrated the tunica albuginea. In close proximity to the tunica albuginea a small number of vascular spaces containing neoplasmatic embolus. Epididimis was free of malignant component while diffuse hyperemic spaces were observed along the spermatic cord.

The patient was given chemotherapy of the BEP regimen, i.e. Bleomycin, Etoposide, and Cisplatin. He showed good response after the 1st cycle. At the time of starting the second cycle, AFP had decreased to 98 IU/ml and was accompanied by a moderate reduction of the dimensions of the retroperitoneal mass. However, after the 2nd cycle the patient discontinued the chemotherapy due to personal family problems. When he came for follow-up after a gap of 3 months, he presented with complications of breathlessness, loose motions and loss of weight. Despite the normalisation in tumor markers values, the retroperito-
neal mass was relapsed. CT scan of the chest showed multiple lung metastases. After oncology evaluation, the patient was found unfit for further chemotherapy. The poor prognosis was explained to him and to his relatives. He was treated symptomatically. However, finally he succumbed to death after two months due to complications.

Discussion and conclusion
About 99% of neoplasms of the testis are malignant and they are one of the commonest forms of cancers in young adult males. Two decades ago testis tumors were the most common solid tumor cause of death in young males. Advances in clinical pathology, progress of radiologic and diagnostic testing and the development of novel chemo-therapies, allowed for a more accurate staging and treating of testis cancer.

Today, chemotherapy is generally highly effective and achieves some of the highest successes in the field of oncology.

Despite the progress in the diagnosis and treatment, testis cancer continues to present a formidable challenge. In fact, ten percent of patients present with symptoms of metastasis at diagnosis and up to thirty-five percent of patients have evidence of metastatic disease when first seen. It is noteworthy how such an easily accessible and superficially palpable tumor escapes detection till a very late stage of its presentation. The most probable explana-
tion for the delay in diagnosis from the time of initial rec-
ognition to the time of treatment is the insidious
presentation and lack of overt signs. This delay not
uncommonly exceeds six months. It should be noticed
however that some testis cancers progress rapidly either
because of their rapid growing rate or because of their
ability to metastasize. With the exception of spermatocytic
semimoma, germ-cell tumor types usually develop retro-
peritoneal lymph-node metastases -especially NSGCs [4].

A review of the literature revealed a few case reports of
mixed germ cell tumor of the testicle with sarcomatous
component [5-8]. Theories about its pathogenesis include
derivation of the tumor cells from pluripotential germ
cells and malignant transformation from teratomatous
elements [9]. The last is somehow controversial since tes-
ticular teratomas themselves represent the end stage of a
differentiation process from other types of malignant
germ cell tumor [10]. This concept is being supported by
the following observations: Firstly, prepubertal testicular
teratomas are benign, yet their morphologically similar
counterparts in the postpubertal testis are malignant,
whether mature or immature. In fact, postpubertal testic-
ular teratomas have a more disordered arrangement, fre-
nently show significant cytological atypia and may have
widespread mitotic activity [10]. Secondly, genetic anal-
sis has shown that the teratomatous elements in postpu-
bertal mixed germ cell tumors of the testis have strikingly
parallel allelic losses compared to the nonteratomatous
components of the same tumor [10].

Notably, it is very unusual for an embryonal rhabdomy-
osarcoma to develop on purely teratoma. In addition the
sarcomatous element can be present in the primary exci-
sion or it can appear after chemotherapy in the metastases
[11]. Both facts are indicating that factors other than
malignant transformation from teratomatous elements
contribute to the development of sarcoma.

Approximately 60% of the patients with NSGC tumors
present with advanced clinical disease, i.e. metastasis
through the lymphatic as well as hematogenous routes.
The most important predictor of metastases is the pres-
ence of vascular/lymphatic invasion in the primary tumor
and the amount and degree of aggressiveness of a distinct
component as well [12]. In fact, about 60% of NSGC
tumors are composed of more than one of the pure pat-
tterns. The metastasis usually reflects the histology of the
basic primary tumor. However, different histologic cell
types are found more often in metastases than in primary
tumors. This may be due to maturation of one germ-cell
type into another cell type. This might not be the case in
our patient because of the normalisation in tumor mark-
ers values after chemotherapy. To our knowledge, elevated
levels of AFP are seen almost exclusively in tumors con-
taining yolk sac elements. AFP is demonstrable in approx-
imately 92% of both primary and metastatic yolk sac
tumors. In rare cases, AFP may not be demonstrable in a
metastatic viable yolk sac tumor even though the primary
tumor is positive for AFP.

In general, 90 to 100% of patients with localized tumors
can be cured and up to 70% with metastatic disease can be
cured. The therapy and prognosis of testicular tumors can
depend largely on clinical stage and on histological type.
According to the above criteria our patient would be clas-
sified to the intermediate risk group [NSGC tumor, pri-
mary location on testis-retroperitoneal space, AFP 1000-
10.000, HCG 5000-50.000, LDH > 500, no brain, liver
and bone metastases] having an 80% possibility of com-
plete cure. However, the histologic subtype appears to
critically influence the prognosis: It is the choriocarci-
noma component which is the most aggressive as it
spreads rapidly through the hematogenous route, thus
leading to a poorer prognosis of patients carrying mixed
NSGCs as compared to seminomas [13]. The presence of
embryonal carcinoma comprising over 40% of the pri-
mary tumor has been also associated with a tendency to
metastasize [12]. It is also well documented that the pres-
ence of yolk sac elements is highly associated with precoc-
ious metastases [14], while accumulative evidence
suggests that teratomas with somatic-type malignancies
are associated with a poor prognosis [4]. Similarly, the
occurrence of sarcomatous elements in germ cell tumors
is considering a poor prognostic sign [15]. Actually the
development of sarcomas in patients with germ cell
tumors is rare and for this reason, in patients with mixed
NSGC tumors, metastases composed purely of sarcoma.
are rare also [5], however, prognosis is usually dependent on the degree of aggressiveness of the sarcomatous component.

In our case, this unusual combination not commonly reported in the literature (yolk sac tumor and immature teratomatous element consisted of rhabdomyosarcoma), appears to have influenced the prognosis.

Another important factor significantly contributing to the definite cure is completion of treatment and regular follow-up of the patient. As demonstrated in our case, any break in the treatment can and will lead to flaring up of the complications and carries very poor prognosis.

Conclusion
More than 50% of germ-cell tumors include more than 2 basic germ-cell tumor types, with the exception of spermatocytic seminoma. About 90% of the patients with non-seminomatous tumors can achieve complete cure with aggressive chemotherapy and most of them can be cured. Although prognosis of testicular tumors depends largely on clinical stage, histological type and adhesion to the treatment influence the prognosis as well.

Consent
The authors would like to thank the patient’s relatives for providing informed consent for the publication of this case report.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
SK, PP and GP were involved in the case directly. SK drafted the manuscript. NG and MO took part in the care of the patient PP contributed in the preparation of the manuscript. TV contributed in carrying out the medical literature search. SK was involved in conception of the manuscript. TV contributed in carrying out the medical literature search. SK, PP and GP were involved in the case directly. SK

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