Mixed Germ Cell Tumor Presenting as a Multifocal Mass within the Testis and Spermatic Cord

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Introduction

Testicular cancer is overall a rare malignancy seen in males, but has been on the rise in the Western world due to unknown reasons. Testicular neoplasms fall into two major categories which are germ cell tumors (95%) and sex-cord stromal tumors.[1] Neoplasms arising in the testis are almost always of germ cell origin and are divided into two main groups based on the new World Health Organization (WHO) 2016 classification: tumors occurring predominately in prepubertal patients, not derived from germ cell neoplasia *in situ* (GCNIS); and tumors derived from GCNIS.[2] GCNIS, previously termed intratubular germ cell neoplasia (IGCN), is the most widely accepted precursor lesion of adult malignant testicular germ cell tumors. Germ cell tumors typically are seen in the 15 to 34-year age group and account for less than 1% of all malignancies in males.[1] Typically, germ cell tumors are capable of rapid and wide dissemination due to their aggressive nature, but with proper treatment most can be cured.[3] Testicular germ cell tumors are very sensitive to chemotherapy and considered one of the most curable solid tissue tumors. Chemotherapy is routinely given to patients with metastatic seminomas or NSGCTs and patients with serum tumor markers that remain elevated after orchiectomy.[3] Mixed germ cell tumors account for about 60% of all testicular tumors and common combinations include teratoma, embryonal carcinoma and yolk sac tumor; seminoma with embryonal carcinoma; and embryonal carcinoma with teratoma.[1]

Patient Case

The patient is a 51-year old male with no previous significant medical history and no past significant surgical history, who presented to his primary care physician after noticing a fullness in his left inguinal area. The patient was then referred to a urology clinic by his primary care physician for an ultrasound of his left testis, which confirmed a hypoechoic mass. A left, inguinal radical orchiectomy and left inguinal hernia repair was performed. Upon surgery, two separate masses were noted, one in the left testicular area and a second within the left spermatic cord. Pre-orchiectomy, the patient was found to have elevated levels of beta-human chorionic gonadotropin (hCG) at 108 mIU/mL, alpha-fetoprotein (AFP) levels were normal at 4.7 ng/mL, and lactase dehydrogenase (LDH) levels were high at 336 U/L. Post-orchiectomy, his beta-hCG levels remained elevated at 129 mIU/mL, which prompted a computed tomography (CT) scan for cancer staging of the chest, abdomen, and pelvis with intravenous (IV) contrast. The CT scan revealed a left para-aortic metastatic lymph node and two additional positive nodes.

Materials and Methods

Cassettes submitted by the Pathologists' Assistant for microscopic examination included the:

- spermatic cord margin
- three representative sections of mass number one with one section including the epididymis
- two sections of mass number one extending towards mass number two
- two representative sections of mass number two
- two sections of mass number two extending towards mass number one
- one section of unremarkable testicle with underlying epididymis
- an additional cross section of the spermatic cord.

In this case the most important diagnostic factor is to submit all areas of the mass that are grossly different.[5] The most important prognostic factor the Pathologists' Assistant can contribute is to ensure that sufficient cassettes of the tumor are submitted. At the absolute minimum, one cassette should be submitted per one cm of tumor.[5] The extent of invasion and relationship of the tumor to the attached organs and structures is also extremely important for the Pathologists' Assistant to mention in their gross dictation.

Results

Gross Findings

The surgical pathology laboratory received the patient's left testis with attached spermatic cord. The specimen was 94 grams with the left testis measuring 4.8 x 3.1 x 1.2 cm and attached spermatic cord measuring 7.5 x 2.0 cm. The tunica vaginalis appeared to be grossly intact and the spermatic cord margin appeared to be grossly viable. The entire specimen was bivalved to reveal two masses. Mass number one, which was located within the testis, consisted of a well-defined firm mass with focal areas of hemorrhage measuring 3.2 x 2.7 x 2.7 cm (Figure 1). The first mass appeared to grossly invade through the tunica albuginea and extended into the spermatic cord, but did not involve the overlying tunica vaginalis. Further sectioning of mass number one revealed yellow, chalky areas of possible necrosis. Mass number two, located within the spermatic cord, consisted of a firm, variegated in color ranging from tan-yellow to hemorrhagic with areas of possible necrosis and measuring 2.7 x 2.1 x 2.1 cm (Figure 1). A distance of 2.5 cm was measured in between the two masses. Both masses collectively did not appear to involve the tunica vaginalis. The vas deferens appeared to be grossly dilated and the remaining uninvolved testicular parenchyma was unremarkable. Lymph nodes were not found upon gross dissection.

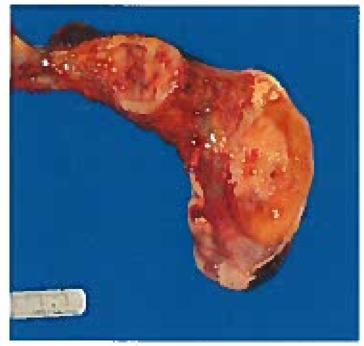

Figure 1. Gross photograph of the bivalved left testis with two separate masses, mass number one is within the testis and mass number two within the spermatic cord.

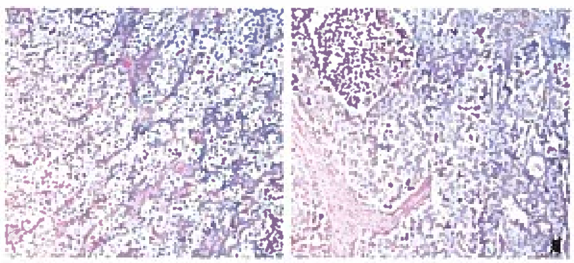

Figure 2. A- Seminoma, H&E x 40 B- Embryonal carcinoma, H&E x10

Microscopic Findings

The tissue was stained with H&E and revealed two separate histological components consistent with seminoma and embryonal carcinoma (Figure 2). The seminoma presents in a very classical manner with large cells, varying from round to polyhedral, with a moderate amount of clear cytoplasm, pale nuclei, prominent nucleoli, and distinct cell borders separated by fibrovascular septa with scant lymphocytic infiltrates (Figure 2A).[1,6,7] The embryonal carcinoma component resembles large primative epithelial cells with abundant, amphophilic or clear cytoplasm (Figure 2B).[1,6,8] The nuclei of embryonal carcinoma cells tend to be hyperchromatic, have prominent nucleoli, pleomorphic and have a greater degree of crowding than seminomas which makes their appearance very distinct.[6,8] The cell borders of embryonal carcinoma are less distinct than those seen in seminoma.[1,8]

	Seminoma	Spermato-cytic Seminoma	Embryonal Carcinoma	Yolk Sac Tumor	Choriocar-cinoma	Patients Results
OCT4	+ (strong)	-	+ (strong)	-	-	+
SALLA 4	+ (strong)	+	+ (strong)	+ (strong)	+ (variable)	+
PLAP	+			+		+
D2-40	+ (strong)	-	- / focal weak +	-	-	+
HCG	- (hCG+ in ST GC)	-	-	-	+ (ST)	+ (few cells)
EMA	-		-	occasionally +		+ (rare focal cells)
AFP	-	-	-	+ (often focal)	-	-
CD 117	+	-	-	-	-	focal + in seminoma
CD 30	-	-	+	-	-	+ in embryonal
CK	- / focal dots	- / focal dots	+	+	+	+ focally in embryonal

Figure 3. Immunohistochemical stains and results of the tests based on what type of testicular germ cell tumor is present. Seminoma and embryonal carcinoma are highlighted to compare with the patients results. ST GC: syncytiotrophoblast giant cells ST: syncytiotrophoblast

Ancillary Studies

Immunohistochemical studies were done on formalin fixed, paraffin embedded tissues to confirm the diagnosis of a mixed germ cell tumor composed of seminoma and embryonal carcinoma. Immunohistochemical tests included octamer-binding transcription factor 4 (OCT4), sal-like protein 4 (SALLA 4), placental alkaline phosphatase (PLAP), podoplanin (D2-40), human chorionic gonadotropin (HCG), epithelial membrane antigen (EMA), alpha fetoprotein (AFP), CD 117, CD 30 and Cytokeratin (CK). Results of patient immunohistochemical tests and common presentation of immunohistochemical tests in germ cell tumors can be seen in Figure 3.[7,9,10] The immunohistochemical tests coupled with gross findings and histological findings are important for the differential diagnosis. The most useful immunohistochemical markers in this case would be the use of OCT4, CD 30, CD 117, hCG and CK.[6,10]

Discussion

Diagnosis

Overall, gross and histopathological findings were consistent with the diagnosis of a mixed germ cell tumor consisting of 95% seminoma and NSGCT with 5% embryonal carcinoma involvement.

Staging

The patient was initially staged as pT2b, pNx, and M1 but was corrected to pT3, cN2, and M1 after a CT scan and correction based on the new AJCC 8th Edition. The patient was staged as a IIB according to the Royal Marsden Staging System, which takes into account only the extent of the disease.[11] A stage IIB is indicative of having positive nodes 2 cm in size or more, but less than 5 cm.[11] The secondary discrete mass in the spermatic cord along with the vascular-lymphatic involvement upstaged the patient from a pT2 to a pT3. A tumor in the testicle is classified as a pT3 when it invades the spermatic cord with or without vascular/lymphatic invasion.[3,12] After the CT scan the patient's N category went from the original Nx to N2 because of metastasis to the left para-aortic lymph node which was greater than 2 cm in greatest dimension and two other positive nodes with one greater than 2 cm in greatest dimension.[3] The patient was staged as M1 due to the non-continuous, discrete, distant mass in the spermatic cord.

Treatment

The patient is not a candidate for retroperitoneal lymph node dissection (RPLND) based on the diagnosis of stage IIB NSGCT with bulky lymph nodes and beta-HCG levels that didn't normalize after the radical orchiectomy procedure. The patient agreed to start treatment with cisplatin and etoposide for a total of 4 cycles every 21 days.

Prognosis

The patients prognosis is good with about a 90% cure rate after being treated with chemotherapy. The outcome of this case is unknown.

Acknowledgments

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References

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