Diffuse Embryoma of the Testis
- A Case Report -

Diffuse embryoma of the testis is a very rare, distinct form of mixed germ cell tumor. I report here on a case of diffuse embryoma in a 22-year-old male who presented with painful scrotal swelling. The resected testis was entirely occupied by a non-encapsulated tumor mass. The cut surface of the tumor was grey or whitish pink, soft and granular with foci of hemorrhage and necrosis. Microscopically, the tumor was characterized by a diffuse, orderly arrangement of embryonal carcinoma and yolk sac tumor in almost equal proportions. The yolk sac tumor component was diffusely wrapped around the embryonal carcinoma. Syncytiotrophoblasts were scattered throughout the tumor. Minor foci of immature teratoma, seminoma and intratubular germ cell neoplasia were observed. The yolk sac tumor (YST) component was emphasized by immunoreactivity for alpha fetoprotein, whereas the embryonal carcinoma was reactive for CD30. The strong reactivity for cytokeratin in the YST component formed an outstanding contrast to the weak cytokeratin reactivity in the embryonal carcinoma.

Key Words : Testis; Mixed germ cell tumor; Embryonal carcinoma; Yolk sac tumor

Won Ae Lee
Department of Pathology, Dankook University College of Medicine, Cheonan, Korea

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Diffuse embryoma of the testis was first described by Cardoso de Almeida and Scully in 1983. This tumor is a very rare, distinct form of mixed germ cell tumor (MGCT) that is often separately categorized because of its unique histologic features. Histologically, it is characterized by a diffuse, orderly arrangement of embryonal carcinoma (EC) and yolk sac tumor (YST) with scattered trophoblastic elements. To the best of my knowledge, only 5 cases of diffuse embryoma of the testis have been reported in the English Medical literature. In a recent report, Zamecnik and Sultani described a case of diffuse embryoma with intratubular germ cell neoplasia (ITGCN) in residual testicular tissue, indicating that diffuse embryoma arises from ITGCN, like the other postpubertal GCTs of the testis.

CASE REPORT

A 22-year-old male presented with painful swelling on the right scrotum for 1 month. Ultrasound examination of the scrotum revealed an ill defined inhomogeneous hyperechoic mass in the right testis. On abdominopelvic computed tomography (CT), multiple lymph nodes enlargements were noted, and these were suspected to be tumor metastasis. His preoperative serologic examination revealed elevated levels of alpha fetoprotein (AFP) (714 ng/mL) and the beta subunit of human chorionic gonadotrophin (222 mIU/mL). He underwent right orchiectomy.

The resected testis was enlarged and it was almost completely occupied by a non-encapsulated tumor mass that measured 7 cm at the greatest dimension. The cut surface of the tumor was grey or whitish pink soft and granular with foci of hemorrhage and necrosis (Fig. 1). Microscopically, the tumor was characterized by a diffuse infiltration of EC and YST in almost equal proportions. The YST cells were diffusely wrapped around the EC or they were closely intermingled with EC in more than 95% of the tumor volume (Fig. 2A). The EC component was characterized by irregular glands and thick ribbons. The cells showed typical appearance of EC, with hyperchromatic nuclei containing prominent nucleoli, and active mitotic activity was revealed. The YST component was characterized by its typical reticular pattern and the thin ribbons that covered the hyalinized fibrovascular trabeculae. The YST cells were cuboidal to flat with small nuclei. Syncytiotrophoblasts, which consisted of multinucleat-
ed giant cells, were scattered individually or in small groups throughout the tumor. Small foci of immature spindle cells were scattered within the tumor, indicating a minor immature ter-

Fig. 1. Grossly, the cut surface of the tumor is grey or whitish pink soft and granular with foci of hemorrhage and necrosis.

Fig. 2. Microscopically, yolk sac tumor (YST, triangles) component enwraps around embryonal carcinoma (EC, asterisks) component. A few syncytiotrophoblasts (arrows) are scattered (A). YST component is emphasized by positivity for alpha fetoprotein (B). EC component is reactive for CD30 (C). The strong cytokeratin immunoreactivity in YST component contrasts with weak reactivity in EC component (D).

Immunohistochemical studies were performed on the formalin-fixed, paraffin-embedded tissue sections via the avidin-biotin peroxidase complex method. The primary antibodies used were AFP (1:200, Biogenix, San Ramon, CA, USA), CD30 (1:100, Dako, Carpentry, CA, USA), CD117 (1:200, Dako) and cytokeratin (1:50, Novocastra, Newcastle, UK). Immunohistochemically, the YST component was emphasized by positivity for AFP (Fig. 2B) and negativity for CD30, whereas the EC was positive for CD30 (Fig. 2C) and negative for AFP. The strong immunoreactivity for cytokeratin in the YST component formed an outstanding contrast to the weak reactivity in the EC (Fig. 2D). The minute foci of the seminoma component were positive for CD117 (Fig. 3D) and they were negative for AFP and CD30.
Extensive tumor necrosis and intravascular tumor thrombi were found. No tumor invasion to the tunica vaginalis or the epididymis was seen. Although lymph node dissection was not performed, multiple lymph node enlargements that were suspected to be metastasis were noted in the aortocaval and left paraaortic areas and in both inguinal areas on abdominopelvic CT. The patient underwent adjuvant chemotherapy and he has survived after the operation without evidence of recurrence or metastasis for 15 months up to now.

**DISCUSSION**

MGCTs are the second most common testicular GCT following seminoma, and they account for 40-50% of all primary testicular GCTs.\(^5,6\) The various types of GCT can occur in any combination.\(^6\) The clinical features and behavior of MGCT are similar to those of nonseminomatous GCTs depending on the proportion and composition of each GCT component.\(^6\) The most frequent histological element in MGCTs was EC in 84.4% of the reported cases, followed by teratoma in 69.7% and YST in 60.1%.\(^5\) Polyembryoma and diffuse embryoma are rare variants of MGCT. Polyembryoma consists of small, scattered, embryonic bodies that have a central core of EC cells (resembling the embryonic plate), an associated amnion-like cavity and a YST component that resembles the embryonic yolk sac.\(^3,7\) Diffuse embryoma is apparently differentiated from polyembryoma because, in diffuse embryoma, there is a diffuse intermingling of approximately equal amounts of EC and YST elements with scattered trophoblastic elements.\(^1,5\)

Cardoso de Almeida and Scully\(^1\) first described two cases of diffuse embryoma of the testis. Only 5 cases of diffuse embryoma of the testis have been reported to date.\(^1,4\) The previously reported cases are summarized in Table 1. When considering

![Fig. 3. Minor components of the tumor consist of scattered immature spindle cells (asterisks) indicating immature teratoma (A), uniform polygonal cells arranged in cord-like fashions indicating seminoma component (B), and intratubular germ cell neoplasia (C). Seminoma component is immunoreactive for CD117 (D).](image-url)
all the reported cases, including the present case, the patients were young adults (age range: 22-38 years old) and the size of the tumors ranged from 5 to 8 cm. In Cardoso de Almeida and Scully’s report, a few small foci of smooth muscle differentiation were also present within the specimens, indicating a minor mesodermal teratomatous component. In the present case, minute foci of immature teratoma as well as foci of the seminoma component were noted. These minor GCT components occupied less than 5% of the total tumor volume. The seminoma component accompanied by diffuse embryoma was not described in any of the five previously reported diffuse embryomas.

It is well known that immunohistochemistry can be useful for making the differential diagnosis of the various elements of MGCT. In the present case, the immunohistochemistry for AFP, CD30 and CD117 was also helpful to accentuate each GCT component. AFP distinctly highlighted the YST component, which would be easily ignored on routine hematoxylin-eosin staining. The EC and seminomatous components were specifically reactive for CD30 and CD 117 respectively. The strong cytokeratin reactivity in the YST component was distinct from the weak cytokeratin reactivity in the EC component. All these results were consistent with the report of de Peralta-Venturina.

Diffuse embryoma of the testis is exclusively seen in postpubertal man. Postpubertal GCTs of the testis usually accompany ITGCN. Zamcnik and Sultani recently reported on a case of diffuse embryoma with the presence of ITGCN in the residual testicular tissue, and this indicated that like the other postpubertal GCTs of the testis, diffuse embryoma arises from ITGCN. The present case, in which ITGCN was found in the periphery of the tumor, is also an additional case that supports the opinion of Zamcnik and Sultani.

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