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PURE EMBRYONAL CARCINOMA OF THE TESTIS IN AN ADULT MALE PATIENT: CASE REPORT

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Abstract

As a case presentation, the present paper aims to present a patient with pure embryonal carcinoma, which is rarely seen, together with the relevant literature. The case is a 36-year-old male patient, who applied to the clinic with complaints of pain and swelling in the left testis. In the scrotal doppler ultrasonography, hypoechoic solid lesion contoured to the lobule almost filling the left testis and having the size of 25x60 mm were observed. Histopathological and immunohistochemical analysis of the this case was diagnosed with pure embryonal carcinoma. All the patients with complaint of pain-free mass in testis should be investigated. Although the pure embryonal carcinoma is rarely seen, it is one of the tumors that can be clinically and histopathologically confused with other testis tumors and should be considered for the patients applying to the clinic with complaints of pain-free mass in testis.

Keywords: *Testis, embryonal carcinoma, orchiectomy, adult*

Rezumat

Carcinom embrionar pur al testicului la un pacient adult de sex masculin: raport de caz

Lucrarea prezintă cazul, mai rar întâlnit, de carcinom embrionar pur la un pacient de sex masculin, însoțit de literatura relevantă. Pacientul, în vârstă de 36 de ani, a aplicat la clinică cu acuze de durere și umflături la nivelul testicului stâng. În ultrasonografia scrotală doppler, s-au observat leziuni solide hipoecogene conturate până la lobul, aproape umplând testiculul stâng și având dimensiunea de 25x60 mm. Analiza histopatologică și imunohistochimică a acestui caz a fost diagnosticată cu carcinom embrionar pur. Toți pacienții cu acuze de masă nedureroasă în testicule ar trebui investigați. Deși carcinomul embrionar pur se întâlnește rar, el rămâne una dintre tumorile care pot fi confundate clinic și histopatologic cu alte tumori ale testiculului și ar trebui luat în considerare în cazul pacienților care se adresează cu acuze de masă fără durere în testicule.

Cuvinte-cheie: *testicul, carcinom embrionar, orchiectomie, adult*

Резюме

Эмбриональный рак яичка у взрослого пациента мужского пола: отчет о клиническом случае

В качестве презентации клинического случая, настоящая статья имеет целью представить пациента с чистой эмбриональной карциномой, которая редко встречается, вместе с соответствующей литературой. Пациент, 36 лет, обратился в клинику с жалобами на боль и припухлость в левом яичке. При ультразвуковом допплеровском исследовании мошонки наблюдались твердые гипоэхогенные очаги, очерченные долькой, почти заполняющие левое яичко и имеющие размер 25x60 мм. Гистопатологический и иммуногистохимический анализ этого случая выявил чистую эмбриональную карциному. Все пациенты с жалобами на безболезненное образование яичек должны быть обследованы. Хотя чистая эмбриональная карцинома встречается редко, это одна из опухолей, которую клинически и гистопатологически можно спутать с другими опухолями яичка, и ее следует учитывать пациентам, обращающимся в клинику с жалобами на безболезненное образование в яичках.

Ключевые слова*: яичко, эмбриональная карцинома, орхиэктомия, взрослый*

Introduction

Embryonal carcinoma is a non-seminomatous germ cell tumor and seen in only 1-5% [1-8]. In general, following the seminoma, it constitutes the second-most frequently (80%) seen tumor component of mixed germ cell tumors [2]. Embryonal carcinomas tend to be seen in youth and young-middle-age period and the average age is 31-32 years [2, 4]. Metastasis is detected at the moment of diagnosis in approx. 66% of embryonal carcinoma cases and cases with embryonal carcinoma component [4]. These tumors follow an aggressive course because of the early hematogenous invasion of embryonal carcinoma [3]. For this reason, early diagnosis and treatment of embryonal carcinoma cases are very important [3]. As in many testicular tumors, embryonal carcinoma is also detected by the patient or coincidentally in examination in form of pain-free or (less frequently) painful palpable mass [5-10]. When pain or mass is detected in testis, the first imaging method to be used is USG. In USG, the embryonal carcinoma cases are characteristically seen in form of well-circumscribed, hypo-echoic, and heterogeneous lesions [5].

Case:

The case was a 36-year-old male, who applied to the clinic with complaints of pain and swelling in the left testis and chilling-shivering. In the physical examination of the patient, hardness, swelling, and

sensitivity were detected in the left testis. In scrotal ultrasonography (USG), an increase in point echogenicity in the right testis parenchyma, miliary-type echogenicity, increase in liquids in left testis, miliary hyper-echogenicities, areas that are suspicious for local irregular hypo-echoic bilobular mass, and increase of vascularity of left testis were detected. In the scrotal doppler USG, an increase in the left peritesticular liquids, micro-lithiasis in both testis, and hypoechoic solid lesion contoured to the lobule almost filling the left testis and having the size of 25x60 mm were observed. In laboratory examinations, high levels of leukocytosis, CRP, LDH, and GGT were detected. In unenhanced abdominal computed tomography (CT) examination, stones were observed in spleen, left kidney, and right kidney. Then, in the macroscopic examination of left high radical orchiectomy material, the left orchiectomy material incorporating a spermatic cord with weight of 86g and dimensions of 3.7x2 cm and epididymis with dimensions of 3.7x1.5x1.5 cm was measured to have dimensions of 6.6x5.7x4 cm. In cross-sections, a hemorrhagic, necrotic, off-white/skin-colored, and solid tumoral area having dimensions of 6x5.7x3.7 cm, macroscopically involving most of testis and tunica albuginea, approaching to the epididymis, and showing no spermatic cord involvement was observed (*figure 1*). We applied hematoxylin–eosin (H&E) staining to one of the 3 imprint samples that we made with the touch and scraping method, and we did Giemsa staining to the others. In the examination of the imprint example; a tumor group showing pleomorphism, having non-clearly definable cellular borders, having apparent nucleoli and coarse chromatin structure on a necroinflammatory background (*figure 2*). In histopathological examination, infiltrative and solid tumoral islets incorporating inflammatory cells at the bottom, as well as large necrotic and hemorrhagic areas, and creating a tubular, papillary, and syncytial pattern were observed. Tumor cells were large and pleomorphic cells with a vesicular nucleus and apparent nucleolus and having typical and atypical mitotic figures, and non-clearly definable cytoplasmic borders (*figure 3-4*). Moreover, there were extensive lymphovascular invasion – tumor embolies and spermatic cord and tunica albuginea involvement. In the immunohistochemical examination, CD30, PLAP, and OCT4 were positive and AFP, CD117, and LCA were negative *(figure 5-10)*. Ki 67 value was found to be 80-85%. Given the morphological and immunohistochemical findings, the case was diagnosed with „Pure Embryonal Carcinoma". Our patient received surgical treatment with left high orchiectomy and chemotherapy. The informed consent form was obtained from patient.

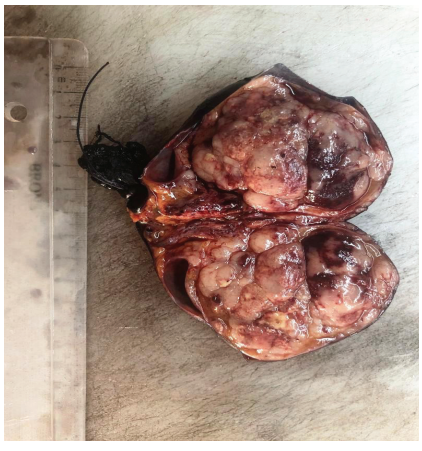

Figure 1. *A macroscopic specimen from soft and solid embryonal carcinoma sample with hemorrhagic and necrotic foci and mildly irregular borders*

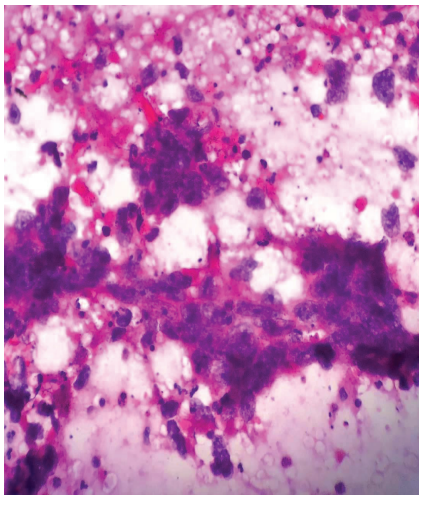

Figure 2. *A tumor group showing pleomorphism, having non-clearly definable cellular borders, having apparent nucleoli and coarse chromatin structure on a necroinflammatory background (H&E x 100, imprint, cytology)*

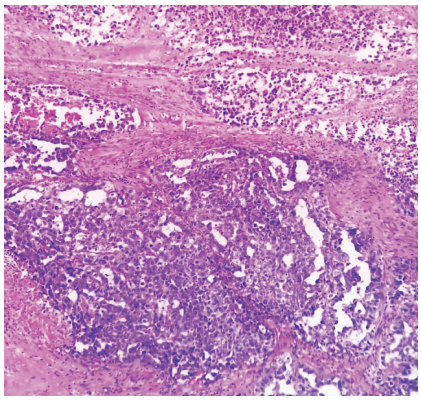

Figure 3**.** *An infiltrative tumoral structure with necrotic foci, creating solid, pseudo-glandular, and tubular patterns, and locally divided by fibrous bands (H&E x 20)*

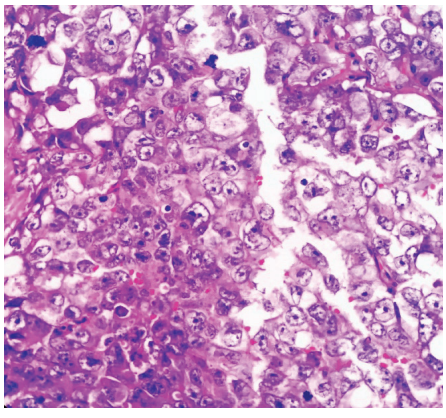

Figure 4. *A sample of embryonal carcinoma consisting of pleomorphic cells, having solid and pseudo-glandular pattern, non-clearly definable cellular borders, amphophilic cytoplasm, apparent nucleoli, and coarse chromatin structure (H&E x 40)*

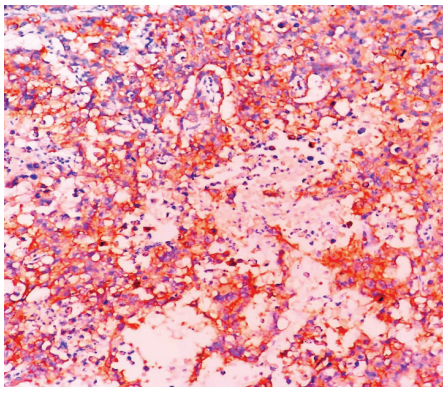

Figure 5. *CD 30 positivity in immunohistochemical staining (x 40)*

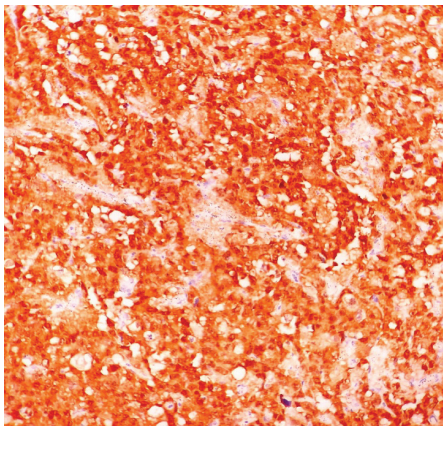

Figure 6. *OCT4 positivity in immunohistochemical staining (x 40)*

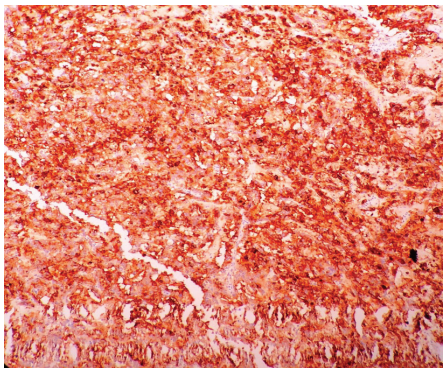

Figure 7. *PLAP positivity in immunohistochemical staining (x 40)*

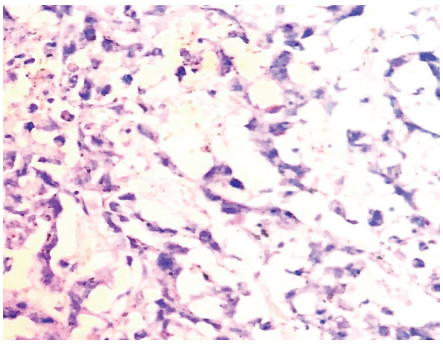

Figure 8. *CD 117 negativity in immunohistochemical staining (x 40)*

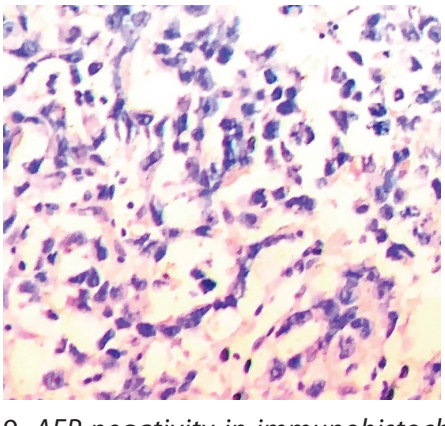

Figure 9. *AFP negativity in immunohistochemical staining (x 40)*

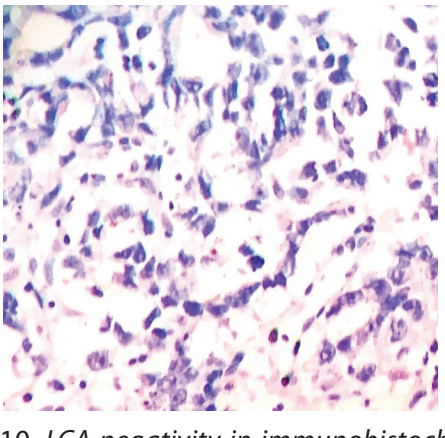

Figure 10. *LCA negativity in immunohistochemical staining (x 40)*

Discussion

Embryonal carcinoma is a non-seminomatous germ cell tumor and pure embryonal carcinoma is seen in only 1-5% [1-8]. Even though it is most frequently seen between the ages of 25 and 35 years, the average age is 31-32 years. It is rarely seen in infants and those older than 50 years [1-5]. The cases generally apply to the clinic with complaints of pain-free testicular mass and (10%) hormonal symptoms [1-3, 10]. In approx. two-thirds of cases, lymph node and distant metastasis are detected at the moment of diagnosis [2]. The main reason for embryonal carcinoma's aggressiveness is the tendency of early hematogenous invasion [3]. The median survival time was 5 months and 1, 2 and 5 year survival rates of 41%, 34% and 34%, respectively [7].The case was a 36-year-old male, who applied to the clinic with complaints of pain and swelling in the left testis and chilling-shivering. In the physical examination of the patient, hardness, swelling, and sensitivity were found in the left testis.

Widespread use of testicular USG today, the detection of small and non-palpable tumors significantly increased when compared to the past [3].The first imaging method to use when pain or a mass is detected in testis is scrotal USG. In embryonal carcinoma cases, generally well-circumscribed, hypoechoic, and heterogeneous lesions are characteristically observed in USG [5]. In the present case, an increase in point echogenicity in the right testicular parenchyma, miliary-type echogenicity, increase in liquids in left testis, miliary hyper-echogenicity, areas suspicious for local irregular hypo-echoic bilobular mass, and increase of vascularity of left testis were detected in scrotal USG. An increase in peritesticular liquid on the left, micro-lithiasis in both testis, and hypoechoic solid lesion contoured to the lobule almost filling the left testicle and having the size of 25x60 mm were observed in the scrotal Doppler USG imaging.

In the macroscopic examination, the tumor was found to have unclear borders, soft consistency, grey color, and a cross-sectional surface incorporating hemorrhage and necrosis on the large areas [2]. Spermatic cord and epididymis invasion are frequently seen. In testis of present case, a hemorrhagic, necrotic, off-white/skin-colored, and solid tumoral area with dimensions of 6 x 5.7 x 3.7 cm, macroscopically invading majority of the testicular area and tunica albuginea, approaching to the epididymis, and showing no spermatic cord involvement was found. In histopathological examination, tumor is observed in various patterns and it generally involves multiple patterns at once. Solid, syncytial, tubular, and tubulo-papillary patterns are the most frequently observed ones. Tumor cells are the cells with polygonal, undifferentiated, and epithelial appearance, having apparent anaplasia, many atypical mitosis, vesicular nucleus, thick nuclear membrane, dense-thin granular, and cytoplasm with non-definable borders. Moreover, apoptotic particles, extensive necrosis areas, and single-cell necrosis draw attention. Besides that, histological patterns are not related with the prognosis [2, 3]. In the present case, the tumor had solid, tubular papillary, and syncytial pattern. Tumor cells were large and pleomorphic and had apparent nucleolus and non-clearly definable cytoplasmic borders. In the background, many typical and atypical mitotic figures, widespread hemorrhage, intra-tumoral necrosis, and local inflammatory cells were found. Moreover, extensive lymphovascular invasion – tumor embolies and spermatic cord and tunica albuginea involvement were also detected.

The differential diagnosis of EC includes large cell lymphoma and germ cell neoplasms such as seminoma and yolk sac. Since the treatment protocols are significantly different, the neoplasia should be distinguished. For this reason, high number of samples should be taken from specimens in order to make the "pure embryonal carcinoma" diagnosis and exclude the mixed germ cell neoplasia [2, 3]. While embryonal carcinoma is frequently positively stained with cytokeratin, they are negative with epithelial membrane antigen (EMA) and it is useful in distinguishing a metastatic embryonal carcinoma from a somatic carcinoma. On the contrary with seminoma that is tumors specified in the differential diagnosis, both of placental-like alkaline phosphatase (PLAP) and OCT3/480 are positive in embryonal carcinoma. D2-40 is stained in seminoma but not in EC. CD30 is negative in seminoma or yolk sac tumor but it is a sensitive marker for EC. However, it is interesting that the loss of CD30 expression is widely seen in metastatic EC cases that have received chemotherapy. Carcinoembryonic antigen (CEA), hCG, and CD117 (c-Kit) are generally negative in EC. In differential diagnosis, especially in distinguishing EC with solid pattern from seminoma, CK cocktail, CD30, D2-40, and CD117 immunohistochemical panel are used as support for differential diagnosis. Besides that, detection of immunohistochemical staining with AFT in focal areas and increase in serum AFP level can be used as evidence for yolk sac differentiation [2]. Seminoma, yolk sac tumor, and lymphoma were involved in the differential diagnosis of the present case and CD30, PLAP, OCT4, AFP, CD117, Ki67, and LCA were immunohistochemically performed. The case was found to be positive for CD30, PLAP, and

OCT4 and negative for AFP, CD117, and LCA. Ki 67 index was found to be 80-85%.

As in other non-seminomatous tumors, the treatment of embryonal carcinoma is based primarily on the chemotherapy [6] but typical treatment for a suspicious testicle mass is orchiectomy. Considering that embryonal carcinoma is resistant to radiation, treatment protocol consists of orchiectomy and chemotherapy [5, 9]. Our patient received surgical treatment with left high radical orchiectomy and chemotherapy.

In conclusion, all the patients applying with complaint of pain-free mass in testis should be examined first using ultrasound and then, depending on the findings, using histopathological analysis. Although pure embryonal carcinoma is rarely seen, it is one of the tumors that can be clinically and morphologically confused with other testicular tumors and should be considered for the patients applying to pain-free testicular mass.

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