Dysgerminoma with An Underlying Bilateral Gonadoblastoma: Immunohistochemical Study

GONADOBLASTOMA ZEMİNİNDE GELİŞEN DİSGERMİNOMA OLGUSU: İMMUNOHİSTOKİMYASAL ÇALIŞMA

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SUMMARY

Scully described the gonadoblastoma as a tumor of ovary composed of germ cells and sex cord derivatives in 1953. The gonadoblastoma have frequently been detected in patients with gonadal dysgenesis and most of the patients whose karyotype has been determined were found to have a Y chromosome. We identified a 12 years old patient with bilateral dysgermioma developed in a gonadoblastoma. The tumor has been stained for vimentin and cytokeratin using immunohistochemical methods. It has been determined that sex cord cells in solid nests showed focal strong positive staining for vimentin and weak focal positive staining for cytokeratin and germ cells did not react to vimentin and cytokeratin. In this report, we discussed our histopathologic and immunohistochemical findings with review of the literature.

Kay Words: Gonadoblastoma, Cytokeratin, Vimentin

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ÖZET

Overin miks germ hücreli sex kord stromal tümörlerinden olan gonadoblastoma Scully tarafımdan 1953 yılında tanımlanmıştır. Bu tümörler sıklıkla disgenetik gonadlı kişilerde gözlenmekte olup, olguların çoğunda karyotipik olarak Y kromozomu mevcuttur. Biz, kliniğimizde oniki yaşında bir hastada bilateral gonadoblastoma zemininde gelişen disgerminoma saptadık. Tümöre immunhistokimyasal olarak sitokeraiin ve vimentin uyguladık. Sonuçta solid adaların içindeki seks kord hücrelerinde fokal olarak vimentin ile kuvvetli, sitokeratin ile zayıf pozitif boyanma saptanmış, germ hücrelerinde ise boyanma izlenmemiştir.

Bu çalışmada, histopatolojik ve immunohistokimyasal bulgularımızı literatür eşliğinde tartışmayı amaçladık.

Anahtar Kelimeler: Gonadoblastoma, Sitokeratin, Vimentin

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The gonadoblastoma is one of the rare tumors of the ovary. Talerman has reported that there are 200 cases in the literature between 1977 and 1989 (1). Most of the gonadoblastoma tumors have been detected in patients with gonadal dysgenesis and 96% of the patients' karyotype have a **Y** chromosome (2). The majority (80%) of patients with gonadoblastoma are phenotypic females and the other 20% are male pseudohermaphrodites. The patients consult to the physician frequently with a complaint of primary amenore, virilization, external genital anomaly or abdominal mass (1).

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The gonadoblastoma which is bilateral in 50% of the patients is a being tumor but the dysgerminoma accompanies in at least 50% of the cases (3). In some studies it has been emphasized the positive staining of the tumor for vimentin and cytokeratin using immunohistochemical methods (4-8). Here, we describe a case of patient with a bilateral dysgerminoma developed in a bilateral gonadoblastoma.

CASE REPORT

A 12 years old girl was admitted to Gynecology and Obstetric Clinics for her complaint of abdominal mass. Her menarche was 6 months ago and her menses were irregular. Her physical exemination revealed famele phenotype and virilization. Gynecologic examination findings were hypoplaslc and anteverted uterus with bilateral adnexial mass. Abdominal ultrasonography showed a 17x11 cm left ovarian mass and a

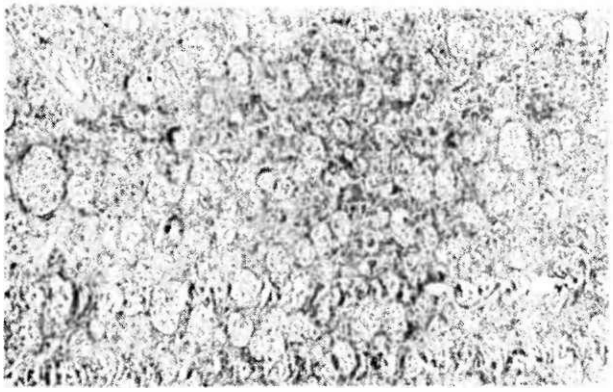

Figure 1 **Pure dysgerminoma (H&E, X40)**

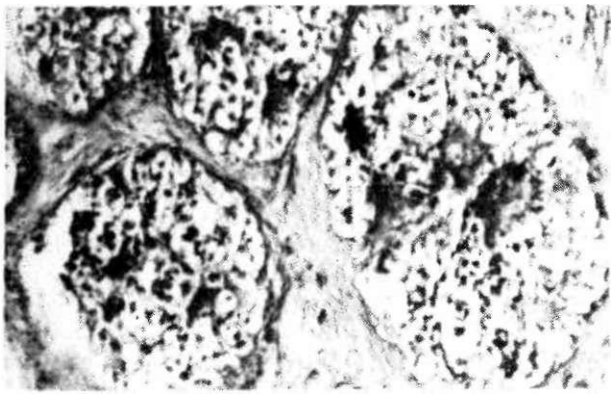

Figure 2**Tumoral cellular nests (H&E, X100)**

6x4 cm right ovarian mass. Pelvic X-ray revealed areas of small calcification in bilateral ovaries. The karyotype of the patient was 46XY and the buccal smear was negative for sex chromatin. The first surgical procedure was left ovarial mass extirpation and right ovary wedge resection. After histopathologic examination right salpingooophorectomy, left salpingectomy, omentectomy and lymph node dissection was performed.

MATERIAL AND METHODS

Tissue samples from the histerectomy material was fixed in formalin, embedded in farafin, sectioned at 5 um and stained with H&E. Immunohistochemical studies were performed in 5 um sections of formalin fixed and parafin embedded tissues with monoclonal vimentin and cytokeratin antibodies (DAKO) using the peroxidase-antiperoxidase complex (PAP) method. In this study, positive staining for vimentin and cytokeratin has been described as yellow-brown and granular staining in cytoplasm.

PATHOLOGIC FINDINGS

MACROSCOPIC FINDINGS: The left ovarian mass was solid, gray-yellow in color and partially hemorragic and the tumor was measured 17x12x7 cm. The right ovarian mass was firm, solid, gray-yellow and measured 7x5x3 cm. Both tuba uterina and omentum were within normal limits in macroscopic examination.

MICROSCOPIC FINDINGS: Histologic examination of both ovaries in H&E slides were similar. There were two areas with different types of histological characteristics. Most of the tumor composed of areas containing large, rounded cells with large nucleus, prominent nucleoli and inconspicuous cytoplasmic borders resembling those of the pure dysgerminoma with lymphositic cell infiltration in connective tissue stroma (Figure 1). In other hand, in the small areas we saw the tumoral cellular nests had been composed of two different type cells. The first type of cell was germ cells with broad vesicular nuclei and inconspicuous cytoplasmic borders. The latter cells were more fusiform with scanty cytoplasm and dark nucleoli resembling immature Sertoli or granulosa cells. These cells line the periphery of the nest in a coronal pattern and surrounded large pale cells and smalll eosinophilic hyaline bodies, resembling Call-Exner bodies (Figure 2). There were laminated calcific concretions within some of the nests and the surrounding connective tissue stroma. Some cells with eosinophilic broad cytoplasm and vesicular nuclei like Leydig or theca-lutein cells were present within the stroma in some areas.

IMMUNOHISTOCHEMICAL FINDINGS: The immunohistochemical study using cytokeratin and vimentin showed focal strong positive staining for vimentin (Fig 3) and focal weak positive staining for cytokeratin in sex cord cells within the solid nests (Fig 4). In our study, germ cells did not react to vimentin or cytokeratin.

According to these histologic finding the patient was diagnosed as "DYSGERMiNOMA WITH AN UNDERLYING BILATERAL GONADOBALSTOMA".

DISCUSSION

The gonadoblastoma, a mixed germ cell sex cord stromal tumor of the ovary, have frequently occured in phenotypic females with pure or mixed gonadal dysgenesis. 96% of the patients with gonadoblastoma have a Y chromosome. The chromosomal analysis of the patients showed that 50% of the patients have 46XY and 25% of the patients have 45X\46XY mozaisizm (1, 2). Our patient had a 46XY karyotype and sex chromatin analysis in buccal smear was negative.

The gonadoblastoma have been seen most ferquently during second decade and somewhat less frequently during third and first decade, in that mode (1). The patients consult to the physician frequently with a complaint of virilization, primary amenore, external genital organ developmental anomalies or abdominal mass (1). The gonadoblastoma is an active tumor which secrete many hormones especially testosterone and estradiole (9).

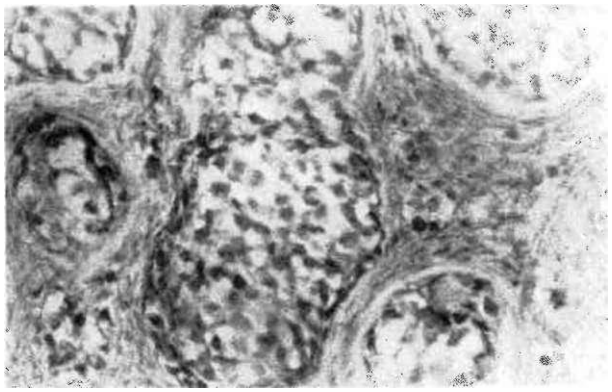

Figure 3Focal strong positive staining for vimentin in sex cord stromal cells (X100)

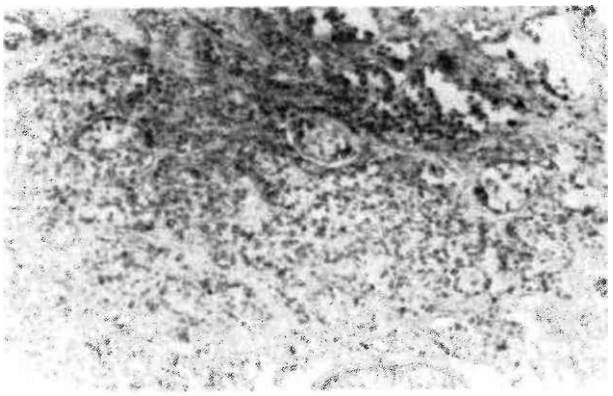

Figure 4Focal weak positive staining for cytokeratin in sex cord stromal cells (X40)

The pure gonadoblastoma Is a small lesion varying in size from microscopic up to 8 cm diameter, most of the lesions measuring between 1 and 2 cm. When a gonadoblastoma becomes overgrown by a germ cell tumor which is seen in about 60% of cases, the tumor may reach larger sizes (3). Our case had a left adnexial mass measuring 17 cm and right adnexial mass measuring 7 cm diameter.

Histopathologic features of the gonadoblastoma is distinctive as seen in our case and it is easy to diferentiate histopathologlcally the gonadoblastoma from other gonadal neoplasms. Because the tumor is frequently seen together with germ cell tumors (especially dysgerminoma), it has been suggested that careful examination of the lesion with many samplings has a prognostic significance when the histopathologic lesion is dysgerminoma.

In many studies, it has been reported the importance of tumorectomy and histologic examination of the other ovary because the tumor is 50% bilateral and carries potential risk for malignancy In 50% of the cases, as seen in our patient (3).

Several studies with vimentin and cytokeratin antibodies using immunohistochemical techniques have been reported in germ cell, sex cord and stromal tumors in recent years. Miettinen firstly reported in a Sertoli Leydig cell tumor that the tumor stained only for vimentin and not with epidermal keratin (4). In 1979, Franke et al have determined staining only for vimentin in the Sertoli cell of rat testis (5). Recently Miettinen have reported cytokeratin-posltive cells in seminiferous tubules and the tubular structures considered to represent Sertoli cell differentiation of seven Sertoli-Leydig cell tumors stained for cytokeratin, whereas 12 granulosa cell tumors were negative (6). In another study, the investigators were able to demonstrate only focal cytokeratin positivity in two of seven granulosa cell tumors, whereas vimentin staining occured more diffusely in six of seven cases (7). Some authors have suggested that the type of cytokeratin antibody used may be the cause of the different staining seen In Sertoli-like cells. In another report consisting a patient with gonadoblastoma the sex cord cells reacted with both vimentin and cytokeratin and it has been suggested that this may be a reflection of a stage of cellular differentiation (8). In our case, sex cord cells reacted focally with both markers but more strongly with vimentin and these findings may be related to granulosa like cell differantiation.

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