ABSTRACT

Aim: Sclerosing stromal tumor is a benign tumor of ovary. We aimed to review the clinical findings and immunohistochemical results of SSTs through the 7 diagnosed cases in our hospital.

Material and Methods: As immunohistochemical, blocks were applied with estrogen receptor, progesterone receptor, inhibin, calretinin, melan-A, CD10, smooth muscle actin, desmin, vimentin, CD34, S-100, C-kit, cytokeratin, cytokeratin7.

Results: Macroscopically, while 5 tumors had a solid appearance, 2 tumors were composed of solid and cystic areas. All the tumors were in shape of ovarian masses with good limits. Microscopically, two types of cells were observed as fusiform fibroblast-like cells and theca-like cells with vacuolised cytoplasm. Immunohistochemical results: vimentin, smooth muscle actin, desmin, progesterone receptor, calretinin, inhibin were positive in all the cases; S-100, cytokeratin, cytokeratin7, estrogen receptor were negative in all the cases; CD-10 was positive in 2 cases; C-kit was positive in 5 cases; melan-A was positive in 4 cases.

Conclusions: The significance of these tumors is that it is necessary to distinguish the histopathology in the frozen section in order to protect the other adnexa because of the characteristics to be observed at early ages (2nd and 3rd decades). Our findings support the conclusion that sclerosing stromal tumors are benign–character tumors that stem from over stroma and are hormonally active tumors because of the detected clinical and immunohistochemical results, although no hormonal effect that could be supported with laboratory tests was observed.

Key words: Sclerosing, Ovary, Immunohistochemistry

RESULTS

Clinical Findings

The ages of the patients varied between 18 and 25 years (mean age- 20 years). Clinically, menstrual irregularities were detected in 2 patients, abdominopelvic pain was detected in 2 patients, and pregnancies were detected in 3 patients. No virilisation was observed. Although SSTs are usually hormonally inactive, most of our cases had occurred together with pregnancies and menstrual irregularities. All the tumours were unilateral. Five tumours were located in the right ovary and 2 tumours were located in the left ovary.

CA125 tumour markers were within normal limits. All the cases were processed with frozen sections, 4 cases were underwent laparoscopic oopherectomies, and the other 3 patients underwent laparotomyal adnexal mass excisions. Patients were followed for a period of 1 to 5 years (mean age–4 years) post-operatively. Clinical findings and surgical procedures have been shown in [Table/Fig-1].

Macroscopic Findings

The sizes of the tumours were between 6 cm and 12 cm (mean size–8.2 cm). All the tumours were observed within good margins.

INTRODUCTION

Sclerosing stromal tumours (SSTs), which were defined by Chalvardjian and Scully [1] in 1973 for the first time, are rare, stromal and benign tumours of ovary. SSTs constitute 6% of the tumours that are derived from the stroma of ovary and more than 80% of such tumours are observed in young adult women in the 2nd and 3rd decades of life [2–5]. Sclerosing stromal tumours are usually hormonally inactive, but it has been reported that some cases are related to pregnancy, androgenic syndromes and endometrial carcinomas. The most frequent presenting complaint is menstrual irregularity and pelvic pain. Macroscopically, they are usually observed as solid and typically unilateral tumours [6–9].

The sharpest histological finding is the pseudo-lobular pattern that is formed by the cellular nodules that are separated from each other by hypocellular, oedematous and collagenous stroma [10]. The hemangiopericytomatosus pattern-like dilated vascular structures are the characteristics of cellular areas, and sometimes, they can be associated with angiomatic lesions [11]. In microscopic examinations, the luteinized theca-like cells with vacuolised cytoplasm and fusiform fibroblast-like cells point out in hypercellular areas.

In this study, 7 SST cases who were aged between 18–25 years, who were diagnosed in our hospital, were examined morphologically, clinically and immunohistochemically (IHC) and were reviewed together with the literature data.

METHODS

Seven cases who were aged between 17–25 years with a diagnosis of SST were selected from the files of our hospital between 2001 and 2011. The operational materials of all the cases were examined. The clinical and macroscopic data of the cases were obtained from our archival records and all the archival preparations which were stained with hematoxylin–eosine were reviewed. A block which represented the SST diagnosis best was selected from each case and an immunohistochemical method was performed. The primary antibodies that were used were those for oestrogen receptor (ER), progesterone receptor (PR), inhibin, calretinin, melanA, CD10, smooth muscle actin (SMA), desmin, vimentin, CD34, S-100, C-kit, cytokeratin (CK) and cytokeratin7 (CK7).

Immunoreactive cells were evaluated according to their staining densities and the percentage of positive cells (weak, 1+; moderate, 2+; strong, 3+). A positive control was used for each primary antibody.
A diffuse positivity was detected in all tumours with vimentin. Both SMA and desmin stained strongly in fibroblast-like cells, but no staining was observed in the areas where the theca-like cells were dominant.

Inhibin [Table/Fig-2] and Calretinin [Table/Fig-3] were positive in theca-like vacuolated cells.

While PR was focally positive in all the cases, ER was not positive in any cases.

C-kit was weakly positive in 5 cases, melan-A [Table/Fig-4] was weakly positive in 4 cases and CD–10 was weakly positive in 3 cases in focal areas.

No staining was observed in our cases with CK and CK–7.

The immunohistochemical profile of our cases has been shown in [Table/Fig-5].

**DISCUSSION**

Ovarian neoplasms are rare in adolescents and they are mainly tumours of germ cell origin. SSTs of the ovary are of sex-cord stromal origin, that occur in young women with a mean age of 28 years. This type was defined by Chalvardjian and Scully (1973) for the first time and it is often observed in the 2nd and 3rd decades of life [1]. To the best of our knowledge, although this tumour has been described before in adolescents, only one paediatric case of a bilateral SST (in a 10 year old premenarchal girl) has been described in the clinical literature [12]. An overview on all case reports on SSTs which had been reported between 2003–2013, has been shown in [Table/Fig-6].

Sclerosing stromal tumours are rarely seen together with pregnancies; only 8 pregnant patients have been reported in literature so far. According to the literature, our 3 pregnant patients are the reported 9th, 10th and 11th patients.

Clinically, there was menstrual irregularity in 2 cases and abdominopelvic pain in 2 cases, and 3 cases were pregnant. These findings made us think that these tumours were hormonally active. In the literature, premenarchal, pregnancy women, virilization, cliteromegaly, amenorrhea were presented.

Macroscopically and microscopically, characteristic histopathological findings of the SSTs of ovary were observed in all the cases.

The hormonal activities of these tumours have been presented before. Lam and Geitman [13] proved that these tumours synthesized dehydroepiandrosterone and that when steroidogenesis occurred, it was usually oestrogenic, which caused irregular menses, amenorrhea, and infertility. A precocious puberty in childhood has also been reported. A virilizing SST of the ovary in a young woman with Mc Cune Albright Syndrome was reported in 2012 by Boussaid K et al. [14] and a woman with irregular menstruation was reported by Khanna M et al. [15]. To date, eight cases of virilizing SSTs have been described in the literature and two tumours were diagnosed after clomiphene treatment for infertility in patients whose ovaries had been laparoscopically normal before [16]. Lifschitz–Mercer et al., proved that PR stained positively in SST cells [17]. Kostopoulou E et al., [18] defined that a positivity for ER beta was observed in a significantly larger number of cells than that for ER alpha [19]. In our study, while ER was negative in all the cases,
PR was confirmed to be positive. Although the plasma levels of our cases were not measured, PR positivity on IHC made us think that these tumours could be hormonally active.

Saitoh et al., [19], Shaw et al., and Kawauchi et al., [6] have defined the smooth muscle cells in SSTs before. Shaw et al., [20] emphasized that SSTs stemmed from the perifollicular myoid stromal cells that were normally present in the theca externa. The IHC and ultrastructural results of the study of Santini et al., [21] proved that the smooth muscle differentiation was a component of the specialised gonadal stromal tissue. In our study, SMA and desmin were found to be as positive in fibroblast-like cells on IHC in all the cases. These findings

<table>
<thead>
<tr>
<th>Article</th>
<th>Patient Age</th>
<th>Side</th>
<th>Clinic</th>
<th>CA-125</th>
<th>Tumor size (cm)</th>
<th>Gross apperance</th>
<th>Immunohistochemical staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Fefferman NR et al., 2003</td>
<td>10</td>
<td>L</td>
<td>Pain, vague, voiding</td>
<td>N</td>
<td>13 x 10</td>
<td>Solid, multilocule</td>
<td></td>
</tr>
<tr>
<td>(2) Peng HH et al., 2003</td>
<td>24</td>
<td>L</td>
<td>Irregular menstruation</td>
<td>N</td>
<td>6x5</td>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>(3) Kim JY et al., 2003 (3 cases)</td>
<td>16</td>
<td>L</td>
<td>Vaginal bleeding, menorrhagia</td>
<td>N</td>
<td>6x5</td>
<td>Solid, SMA(+), Vimentin (+), PG(+), Cystic</td>
<td></td>
</tr>
<tr>
<td>(4) Kuscu E et al., 2003</td>
<td>34</td>
<td>R</td>
<td>Hirsutism, oligomenorrhea</td>
<td>N</td>
<td>Solid</td>
<td>SMA(+), CK(-), Keratin(-), S100(-), desmin(-)</td>
<td></td>
</tr>
<tr>
<td>(5) Yerli H et al., 2003</td>
<td>34</td>
<td>L</td>
<td>Amenorrhea hirsutism</td>
<td>N</td>
<td>12,5x10</td>
<td>Solid, Actin focally (+), CK(-), S100 (-), Desmin (-)</td>
<td></td>
</tr>
<tr>
<td>(6) Deval B et al., 2003</td>
<td>29</td>
<td>R</td>
<td>Pregnancy, pelvic pain, dysuria</td>
<td>N</td>
<td>4,5x4</td>
<td>Solid, cystic, hemorrhagic</td>
<td></td>
</tr>
<tr>
<td>(7) Calabrese M et al.</td>
<td>30</td>
<td>R</td>
<td>Pregnancy, pelvic pain, dysuria</td>
<td>N</td>
<td>14</td>
<td>Cyst</td>
<td></td>
</tr>
<tr>
<td>(8) Buturkci K et al., 2004</td>
<td>14</td>
<td>L</td>
<td>Pain, vague, voiding</td>
<td>N</td>
<td>Solid, calified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(9) Gurbuz A. et al., 2004</td>
<td>21</td>
<td>L</td>
<td>Irregularly menstruation</td>
<td>N</td>
<td>6x5</td>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>(10) Bouraouis et al., 2003 (3cases)</td>
<td>15</td>
<td>L</td>
<td>Irregularly menstruation</td>
<td>N</td>
<td>4,5x4</td>
<td>Solid, cystic, hemorrhagic</td>
<td></td>
</tr>
<tr>
<td>(11) Polopkivski S et al., 2005</td>
<td>26</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>44x33</td>
<td>Multicystic, solid, necrosis</td>
<td></td>
</tr>
<tr>
<td>(12) Koreczynski J et al., 2005</td>
<td>30</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>23x8</td>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>(13) Teulauch F et al.</td>
<td>18</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, cystic, SMA (+)</td>
<td></td>
</tr>
<tr>
<td>(14) Chang W et al., 2006</td>
<td>11</td>
<td>B</td>
<td>Pelvic pain</td>
<td>N</td>
<td>Left 8,5x6; right 17x12</td>
<td>Solid, cystic, SMA (+)</td>
<td></td>
</tr>
<tr>
<td>(15) Pai R et al., 2005 (4 cases)</td>
<td>Mean 22</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>23x8</td>
<td>Solid-cystic (2)</td>
<td></td>
</tr>
<tr>
<td>(16) Akylildiz EU et al., 2004 (3 cases)</td>
<td>23</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>Right 13</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(17) Charfi Darghouth L et al., 2007</td>
<td>15</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>44x33</td>
<td>Multicystic, solid, necrosis</td>
<td></td>
</tr>
<tr>
<td>(18) Kravanoo G et al., 2008</td>
<td>26</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>23x8</td>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>(19) Ergeni MH et al., 2008</td>
<td>11</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, cystic, SMA (+)</td>
<td></td>
</tr>
<tr>
<td>(20) Chang YW et al., 2009</td>
<td>12</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(21) Youm HS et al., 2009</td>
<td>71</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(22) Wada H et al., 2009</td>
<td>52</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(23) He Y et al., 2010</td>
<td>4</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(24) Amorim-Costa C et al., 2010</td>
<td>11</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(25) Park SM et al., 2011</td>
<td>11</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(26) Bank T et al., 2012 (3 cases)</td>
<td>19</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(27) Chung CP, et al., 2012</td>
<td>59</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(28) Khanna M et al., 2012</td>
<td>32</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
<tr>
<td>(29) Boussaid K et al., 2013</td>
<td>24</td>
<td>L</td>
<td>Pelvic pain</td>
<td>N</td>
<td>8,5x6</td>
<td>Solid, calcification</td>
<td></td>
</tr>
</tbody>
</table>

**Table/Fig-6**: Overview of all case reports on SST between 2003–2013
supported the findings which were seen in the literature. The IHC markers in the sex–cord–stromal tumours, such as inhibin, calretinin, melan–A, WT–1, CD99 and mullerian inhibiting substance, were studied for making the differential diagnosis of SST [22-23]. According to the results of these studies, a correlation was observed between the calretinin and inhibin expressions and the luteinization level of tumour [24].

In the sex–cord stellar tumours of ovary, calretinin is a more sensitive, but a less specific marker than inhibit [22]. McCluggage and Maxwell [23] observed calretinin positivity in only one tumour. Komnoss et al., [25] observed inhibit positivity in 4 of 11 cases. In our study, calretinin and inhibit were detected as positive in luteinized, theca–like cells with vacuolized cytoplasm in all the cases.

Jungbluth et al., [26] detected melan–A expression in normal gonadal sex–cord and stromal cells and in the cells that produced steroid hormone in adrenal cortex. These researchers detected melan–A positivity in 4 Leydig–cell tumours and 3 Sertoli–Leydig–cell tumours [27]. So, they emphasized that melan–A immunoreactivity could be used as a determinant in the differential diagnosis of the tumours that produced steroid hormones. Stewart et al., [28] proved that melan–A was a moderately sensitive and a specific marker that showed the sex-stromal differentiation. In the study of Stewart et al., [28], they detected strong positivities in the hilus cells in normal ovaries, and focal positivities in the tubular cells of the rete ovaries in 2 cases. So, they thought that melan–A reactivity could probably be existent in normal and hyperplastic cortical stromal cells. In our study, melan–A ranged perivascularly, similar to the inhibit staining, in 4 cases.

CD10 is a marker that is used in detection of endometrial stromal tumours. Oliva et al., [29] reviewed the CD10 expression in full stromal and sex–cord stromal tumours of ovary in 101 cases, and they observed that the frequency and density of CD10 staining in these tumours were much lower than those of the endometrial stromal tumours. They pointed out that among these tumours of ovary, steroid-cell tumours more often showed CD10 positivity as compared to the others. In 3 of our cases, CD10 was observed to be positive in the luteinized cells with vacuolized cytoplasm.

While no staining was observed in any case with CK, CK7 and S–100, it should be remembered that a CK negativity can be checked for distinguishing the signet ring–like cells in the histopathology of SSTs, which are diagnosed as per Krukenberg diagnosis. The significance of these tumours is that it is necessary to distinguish the histopathology in frozen sections, in order to protect the other adnexa, because of the characteristics which are observed at early ages.

Our findings support the conclusion that SSTs are benign tumours that stem from stroma and that they are hormonally active tumours [21]. Our findings support the conclusion that SSTs are benign tumours [21].

REFERENCES


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