Evaluation of children with inguinoscrotal ectopic adrenal tissues

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1. Introduction
The adrenal glands originate from 2 different embryologic tissues, the cortex from mesoderm and the medulla from the ectoderm, which are histopathologically different from each other in terms of cell structure, organization, and function. The embryologic development of the medulla and cortex are also different (1). The cortex is formed from the proliferation of mesenchymal cells in the region between the mesentery root of the coelomic epithelium and gonadal draft between the 4th and 5th embryonal weeks. The adrenal medulla is a part of the sympathetic nervous system formed from the crista neuralis with an ectodermal origin. These cells, originating from neural crest cells, then migrate to the primitive cortex structure. Encapsulation of the medulla occurs in the late stages of fetal growth (2–4).

Developmental abnormalities of adrenals consist of ectopic or accessory adrenal tissues and heterotopia. After ectopic adrenal tissue was first identified by Morgagni in the 1700s, several nodules of ectopic adrenal tissue were reported in many sites of the body, such as the kidney, coeliac axis, thorax, liver, lungs, and brain, and in association with the genitalia (1,5–7).

Inguinoscrotal localization of ectopic adrenal tissue is a rare condition. According to published studies, the great majority of adrenal ectopias occur with adrenocortical tissue (8). However, medullary ectopia is extremely unusual. Furthermore, clinical and epidemiologic features of adrenal ectopias in the inguinoscrotal region still need to be detailed. In this study, we retrospectively evaluated 6 cases of inguinoscrotal adrenal ectopias, which were incidentally recognized during surgery.

2. Materials and methods
2.1. Patients
A total of 296 male patients, who had undergone inguinoscrotal surgery between January 2009 and June 2011 in the urology and pediatric surgery clinics of Turgut...
Özal Medical Center and Malatya State Hospital, were included in this study. These patients were diagnosed with hydrocele, undescended testis, inguinal hernia, and atrophic testis. Demographic and clinical data of the patients, such as age and accompanying disorders, were collected. Biochemical and hematologic features of the patients’ blood samples, urine analysis, and serum hormone (adrenocorticotropic hormone (ACTH), testosterone, progesterone, and thyroid-stimulating hormone (TSH)) levels were studied.

2.2. Sample collection
Bright yellow nodules, with an appearance resembling adrenal tissues, were surgically excised and placed in a 10% formalin solution. Data about the nodules, including the localization and nature of the lesions, were recorded. After routine tissue monitoring, the sections obtained were stained with hematoxylin and eosin (H&E) and examined under a light microscope.

3. Results
The mean age of the patients was 4.6 years (ranging between 3 months and 9 years). Ectopic adrenal tissue was detected in 6 (2.02%) of 7 surgically excised tissue samples among 296 patients. Of these 6 cases, 4 patients were diagnosed with undescended testis, and the remaining 2 patients with inguinal hernia and hydrocele. These ectopic adrenal tissues were localized on the spermatic cord (n = 3), epididymis (n = 1), appendix testis (n = 1), and tunica albuginea of the atrophic testis (n = 1). Of the 6 cases, 4 ectopias were located on the left and 2 on the right side, and they were all bright yellow with a soft consistent nodular structure and between 1 and 4 mm in diameter. A photograph of the nodules taken during surgery is shown in Figure 1.

Multiple nodules, up to the spermatic cord, were found in 2 of 6 cases, and single nodules were found in 4 patients. After the histopathologic examination, 5 patients were diagnosed with corticoadrenal ectopia, and 1 patient with cortico-medullary ectopia. Microscopic photographs of cortical cells and cortical and medullary cells are shown in Figures 2 and 3, respectively. In all 6 cases, 3 layers of adrenal cortex (glomerulosa, fasciculata, and reticularis) were histopathologically shown.

The results of the biochemical, hematologic, and hormone analysis of the patients were considered to be within normal ranges. Urine analyses were also included in the patients’ data and are summarized in the Table.

4. Discussion
Morgagni first described ectopic adrenal tissues as yellowish nodules similar to adrenal tissue in 1740 (1). Since then, many studies have been conducted about the localization of ectopic adrenal tissue, and, in the literature, at least 100 cases were detected around the genital region. About 80 of these cases were detected in the genital region of males during childhood (9–11). Ectopic adrenal tissues in the male patients within our study were localized in the genital region, as in the literature. In autopsy studies, ectopic adrenal tissue is observed in the testis of newborns at a rate of 7.5%–15%. These rates may vary between 1% and 9.3% in studies in the pediatric age group. In our study, this rate was 2.02% (n = 6). The lower rate of ectopic nodules in children compared to newborns has been attributed to regression or involution of these tissues. In our study, we found that the nodules were mostly situated on the spermatic cord, which is consistent with previous reports. In addition, we found that the nodules were mostly located on the left side, which is also consistent with previous studies. In conclusion, our study suggests that ectopic adrenal nodules are relatively common in children and may be more frequent on the left side. Further studies are needed to investigate the pathogenesis of these nodules and their clinical significance.
adrenal tissue in adulthood is believed to be due to the atrophy of the remaining tissues. The reason for a lower rate in females could be the differences in type of surgery for underlying disease (11,12).

Male gonadal structures and the adrenal cortex have the same embryological origin, which could explain the similarity of ectopic adrenal tissues with gonadal structures. Ectopic adrenal remains, located away from the original adrenal tissue, consist only of adrenal cortical tissue with no adrenal medulla cells. However, adrenal medulla cells can be found in ectopic adrenal tissues with a more proximal localization. Medulla cells are observed as cellular structures of the capsule of connective tissue, usually with small blood vessels that surround these nodules (13). In the literature, only adrenal cortex was found in ectopic adrenal tissues detected in genital regions, and adrenal medulla cells were not observed (12). Ketata et al. (14) found ectopic adrenal tissue in 1.66% (n = 31) out of 1862 patients who had inguinoscrotal surgery and adrenal medulla was not detected in any of the patients, while all had adrenal cortex. The general opinion is that the observation rate of medullar cells decreases toward zero the more distal the location of ectopic adrenal tissue is (12–14). However, we found that 1 of our 6 patients had adrenal cortex and adrenal medulla together. The case found to contain adrenal medulla was the patient who had an orchietomy because of atrophic testis with intraabdominal localization. Existence of adrenal medulla cells in this case may be due to the intraabdominal location, a position much more proximal than the normal anatomy of the testis.

Because almost all reported cases were found incidentally during surgery, we do not know clearly the characteristics of preoperative biochemical, hormonal, and radiological findings of these patients. Similarly, by reviewing a large series, specific disorders or anomalies were not reported as any significant accompanying disease with ectopic adrenal tissues (12–14). Nevertheless, we did not detect any biochemical, hormonal (ACTH, testosterone, progesterone, and TSH), or hematologic abnormalities suggestive for ectopic adrenal tissue in our patients.

### Table.
Characteristics of the patients with ectopic adrenal tissues.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Accompanying disease</th>
<th>Location</th>
<th>Size (mm)</th>
<th>Number of lesion(s)</th>
<th>Cortex or medulla</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 months</td>
<td>Undescended testis</td>
<td>Left appendix testis</td>
<td>1</td>
<td>1</td>
<td>Cortex</td>
</tr>
<tr>
<td>2</td>
<td>1 year</td>
<td>Undescended testis</td>
<td>Left spermatic cord</td>
<td>1–3</td>
<td>3</td>
<td>Cortex</td>
</tr>
<tr>
<td>3</td>
<td>3 years</td>
<td>Undescended testis</td>
<td>Right spermatic cord</td>
<td>2</td>
<td>1</td>
<td>Cortex</td>
</tr>
<tr>
<td>4</td>
<td>5 years</td>
<td>Undescended testis</td>
<td>Left spermatic cord</td>
<td>1–4</td>
<td>4</td>
<td>Cortex</td>
</tr>
<tr>
<td>5</td>
<td>5 years</td>
<td>Hydrocele</td>
<td>Left epididymis</td>
<td>2</td>
<td>1</td>
<td>Cortex</td>
</tr>
<tr>
<td>6</td>
<td>9 years</td>
<td>Inguinal hernia</td>
<td>Right tunica albuginea</td>
<td>4</td>
<td>1</td>
<td>Cortex-medulla</td>
</tr>
</tbody>
</table>
Surgical interventions are considered according to the patient's clinical symptoms caused by these ectopic tissues. Some authors have reported that ectopic tissues show compensatory functional growth when a total adrenalectomy is performed (15,16). Another clinical aspect is the development of a tumor from the ectopic adrenal remains. Pheochromocytoma, Leydig cell tumors, and adrenal adenomas have been reported to develop from these ectopic tissues, although they are not common (6,17–19).

Suspected nodular structures observed along the spermatic cord or the testis and epididymis during inguinoscrotal surgeries should thus be removed and evaluated pathologically. In our study, the nodular structures were detected microscopically during surgery and definitively diagnosed with a histopathologic investigation. These lesions, incidentally found and easily diagnosed due to their classical histological appearances, were benign. There were no malignant characteristic appearances histopathologically (big mass, infiltration at the margins, atypical and high mitotic activity) with these smoothly encapsulated small lesions. Although no spermatic cord injury has been reported in the literature, the spermatic cord should be carefully dissected during the surgical excision and the spermatic vessels and ductus deferens should not be damaged. No damage occurred during surgical excision on the spermatic cord and ductus deferens in our cases. All of the patients had no problems during the 1-year follow-up.

In conclusion, ectopic adrenal tissue is a rare event during inguinal surgeries. We believe that it may be important for surgeons working in these areas to keep in mind the possibility that yellow millimetric nodules with a soft consistency in the hernia sac, embedded in the cremasteric muscle fibers along the spermatic cord, or around the testis and epididymis, could be ectopic adrenal tissue. They may be excised and histopathologically examined due to malignant transformation.

References