Introduction

Bilateral adrenalectomy is a recognized treatment for a wide range of hormonally active and inactive tumors developing in both adrenal glands as well as different forms of hypercortisolism. However, patients after total bilateral adrenalectomy need lifelong adrenocortical hormone supplementation. Despite apparent sufficient exogenous steroid substitution, chronic dependence on adrenal hormones may impair quality of life. To preserve adrenocortical function and make a patient independent of exogenous corticosteroid replacement therapy, subtotal or partial adrenal resection has been proposed. The operation has been useful and efficient especially in patients with bilateral tumor as phaeochromocytomas common in patients with multiple endocrine neoplasia type 2 (MEN 2) or von Hippel-Lindau disease (VHL), but also in patients with tumors or bilateral adrenal hyperplasia presenting symptoms of hyperaldosteronism or hypercortisolism. We report four patients treated in the Department of Pediatric Surgery in Bydgoszcz between 2004 and 2007 in whom subtotal adrenalectomy was performed. Two children were operated on because of bilateral neuroblastoma. The next two patients with nodular hyperplasia (one of them had symptoms of hypercortisolism) underwent the first stage of surgery, which was a unilateral adrenalectomy. We discuss diagnostic methods, preparations before surgery, mode of subtotal adrenalectomy and postoperative management.

Key words: adrenal-sparing surgery, children, subtotal adrenalectomy

Subtotal adrenalectomy: one- or two-staged surgical procedure in children?

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Abstract

Bilateral adrenalectomy is a recognized treatment for a wide range of hormonally active and inactive tumors developing in both adrenal glands as well as different forms of hypercortisolism. However, patients after total bilateral adrenalectomy need lifelong adrenocortical hormone supplementation. Despite apparent sufficient exogenous steroid substitution, chronic dependence on adrenal hormones may impair quality of life. To preserve adrenocortical function and make a patient independent of exogenous corticosteroid replacement therapy, subtotal or partial adrenal resection has been proposed. The operation has been useful and efficient especially in patients with bilateral tumor as phaeochromocytomas common in patients with multiple endocrine neoplasia type 2 (MEN 2) or von Hippel-Lindau disease (VHL), but also in patients with tumors or bilateral adrenal hyperplasia presenting symptoms of hyperaldosteronism or hypercortisolism. We report four patients treated in the Department of Pediatric Surgery in Bydgoszcz between 2004 and 2007 in whom subtotal adrenalectomy was performed. Two children were operated on because of bilateral neuroblastoma. The next two patients with nodular hyperplasia (one of them had symptoms of hypercortisolism) underwent the first stage of surgery, which was a unilateral adrenalectomy. We discuss diagnostic methods, preparations before surgery, mode of subtotal adrenalectomy and postoperative management.

Key words: adrenal-sparing surgery, children, subtotal adrenalectomy

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therapy, subtotal or partial adrenal resection have been proposed [1, 5]. The method was originally described by DeCourcy in 1934 [4]. He documented patients with severe hypertension who experienced a reduction in blood pressure after bilateral subtotal adrenalectomy [6]. Nearly twenty years later Priestley et al. succinctly documented the initial Mayo Clinic experience with subtotal adrenalectomy for Cushing’s syndrome [11]. Priestley reported on twenty-nine patients, all of whom appeared to have had Cushing’s disease with bilateral adrenocortical hyperplasia and all of whom were treated by total unilateral and contralateral subtotal (90%) adrenal resection, usually as a staged surgical procedure [12].

Preservation of endogenous steroid production is a reasonable strategy. At present progress in adrenal imaging and operative technique allows for a precise diagnosis and exact planning of a range of adrenal resection. Thus subtotal adrenalectomy has become a very attractive technique, which allows to remove a part of adrenal tissue affected by pathological process of different etiology in one or two adrenal glands and may be applicable as a synchronous procedure covering both adrenal glands in one stage or metachronous – in two stages (including patients after unilateral adrenalectomy) [2, 3]. The operation has been useful and efficient especially in patients with bilateral tumor as pheochromocytomas common in patients with multiple endocrine neoplasia type 2 (MEN 2) or von Hippel-Lindau disease (VHL) [9], but also in patients with tumors or bilateral adrenal hyperplasia presenting symptoms of hyperaldosteronism or hypercortisolism [2, 15]. So far, it is not finally clear how to perform the procedure of subtotal adrenalectomy in relation to range of adrenal resection and necessity of vascular supply preservation. The size of the remnants necessary to ensure adequate corticosteroid production after bilateral excision of adrenal tissue has not been determined precisely and little is known about the early postoperative function of the adrenal remnant. After subtotal bilateral adrenalectomy with left of 15% to 30% of adrenal tissue in situ, functional recovery could be observed in all patients [2]. However, subclinical impairment of the adrenocortical function with questionable clinical significance has to be considered in some of the patients, particularly at times of stress. Especially during the early postoperative period, careful monitoring of the patients without exogenous steroid administration is required [2]. Furthermore according to several authors necessity of preservation of the vascular supply to the adrenal cortex is a crucial issue [7, 13], but leaving the adrenal arteries and veins intact in adrenal-sparing surgery is not always possible [7]. However, some reports demonstrate sufficient function after division of the main adrenal vein [3].

We report four patients treated in the Department of Pediatric Surgery in Bydgoszcz between 2004 and 2007 in whom subtotal adrenalectomy was performed. Two children were operated on because of bilateral neuroblastoma. The next two patients with nodular hyperplasia (one of them had symptoms of hypercortisolism) undergone the first stage of surgery, which was a unilateral adrenalectomy. The aim of the presentation is to open the discussion whether subtotal adrenalectomy in children supposes to be done as one or two-staged surgical procedure.

**Patients with bilateral neuroblastoma**

The first patient was a 4-month-old boy with an accidentally detected focal lesion of the left adrenal gland. Subsequently done ultrasonography and CT scan showed focal lesions in the both adrenal glands: 2.3 × 1.3 × 2 cm on the left and 9 × 7 mm on the right side (Fig. 1). He underwent bilateral subtotal adrenalectomy as a one stage procedure. A part 1 × 1.5 cm of the left adrenal gland was left. One year after adrenalectomy he doesn’t need any exogenous steroid supplementation.

![Fig. 1. Focal lesions in the both adrenal glands in a 4-month-old boy (case 1)](image)

The second patient was a ten-month-old boy after a right adrenalectomy because of neuroblastoma done at the age of 12 day. At the age of three months a massive dissemination of the neoplasm had occurred with the nodular changes in the left adrenal gland and the metastases to the liver and right testis. After chemotherapy a focal lesion of the left adrenal gland was persistent and the patient underwent subtotal left adrenalectomy at the age of 10 months. An upper-lateral part 1 × 1 cm of the left adrenal gland was left (Fig. 2). One year after surgery the patient demands administration of HCSN and fludrocortisone.

Both patients were examined by an endocrinologist before an operation. In both of them the serum cortisol level, determined in the morning and in the evening were correct. In order to prevent the postoperative adrenal insufficiency on the day before surgery perioperative steroid supplementation was started (HCSN 3 × 2.5 mg orally). Hydrocortisone 4x20 mg intravenously was administered on the day of adrenalectomy. In the postoperative period a regimen of hydrocortiso-
ne was reduced 50% on the fourth day after surgery and gradually doses of HCSN 5 mg-2.5 mg-2.5 mg orally (25 mg/m²) were achieved. Additionally administration of fludrocortisone (0.025 mg three times a day orally) was started from the fourth day after surgery. No complications after operation were observed. None of both patients showed clinical signs of adrenal insufficiency.

**Patients with bilateral adrenal nodular hyperplasia**

The third patient was a seven-year-old girl suffering from Cushing syndrome. Laboratory tests revealed hypercortisolism, increased elimination of androgen metabolites in 24-hour urine collection, suppressed serum ACTH level, no suppression of urinary cortisol excretion in a low-dose and high-dose dexamethasone suppression test, no increase of plasma cortisol levels and low serum ACTH level in corticotropin-releasing hormone stimulation test. NMR imaging showed hyperplasia of both adrenal glands. A pituitary tumor was excluded by MRI pituitary imaging. Radioisotope imaging of the adrenals with the use of labeled iodocholesterol demonstrated a small region of increased uptake in the left adrenal gland. CT scan performed in our department showed bilateral enlargement of both adrenal glands without focal lesions, but the left adrenal gland was definitely larger than the right one (Fig. 3). The patient was qualified for subtotal adrenalectomy with resection of one adrenal gland. To detect a side of adrenal pathology responsible for excessive cortisol secretion before surgery we performed renal vein sampling, but cortisol plasma levels were similar in the test on both sides (10 µg/dl-left vein and 12.7 µg/dl-right vein). Therefore the direct sampling of cortisol concentration was obtained from adrenal veins at the beginning of surgery. The intraoperative sampling suggested the presence of pathology on the left side (cortisol plasma level 21.9 µg/dl in the right adrenal vein and more than 60 µg/dl in the left adrenal vein) and the left adrenalectomy was done. Macroscopically the left adrenal gland was enlarged, with small dark spotted nodules. The clinical data, appearance of the removed adrenal gland and histopathological examination (micronodular hyperplasia of the adrenal cortex) suggest the diagnosis of primary pigmented nodular adrenal dysplasia (PPNAD). The postoperative course was uneventful, normalization of plasma cortisol concentration and physiologic daily rhythm of cortisol secretion were observed directly after surgery. Three weeks after discharge from the hospital the girl presented symptoms of Addisonian crisis (abdominal pain, vomiting, dehydration, hypotonia, high ACTH plasma level) in the course of viral infection. She recovered after administration of hydrocortisone 100 mg/m², but she needed exogenous steroid supplementation initially 14 mg/m² and finally the doses of steroids were gradually diminished to 8 mg/m². Four years after the left adrenalectomy the girl doesn’t need any exogenous steroid therapy and no symptoms of Cushing syndrome are observed. In a control NMR imaging study enlargement of the right adrenal gland was detected.

The fourth patient was a seventeen-year-old boy with congenital adrenal hyperplasia as a result of 21-hydroxylase deficiency (salt-losing form). The boy presented growth retardation and symptoms of precocious puberty. A control ultrasonography revealed presence of a prominent tumor in the left enlarged adrenal gland. Laboratory tests showed cortisol plasma level near upper limit, loss of daily rhythm of cortisol secretion and high plasma concentration of ACTH and androstendion. A CT scan performed after admission of the patient to our department showed presence of a heterogenous nodular formation 48 × 36 × 60 mm with heterogenous
contrast enhancement in the left adrenal gland (Fig. 4). No enlarged lymph nodes in the periaortal space were visible. The patient was referred for surgery and the left adrenal gland with a nodule of 5 cm of diameter in the central part was resected. In the perioperative and postoperative period the patient was given hydrocortisone 240 mg intravenously, the dose was gradually converted to 20 mg orally. Histopathological examination showed nodular hyperplasia of the adrenal cortex, with no neoplastic changes detected. The postoperative course was uneventful. One year after surgery the patient still needs steroid replacement and laboratory tests revealed high plasma ACTH concentration. A control CT scan showed progressing enlargement of the right adrenal gland with macronodular formations.

Fig. 4. Heterogenous nodular formation 48 × 36 × 60 mm with heterogenous contrast enhancement in the left adrenal gland in a patient with CAH (case 4)

Discussion

Surgical strategy in cases with bilateral adrenal involvement in children is still controversial. Preservation of the adrenal gland tissue not only with bilateral changes seems generally rational and desirable, especially in young patients. It allows the correct endogenous hormonal supplementation for the growing organism. However some kind of radical surgical strategy for adrenal pathology should be considered particularly in cases of bilateral changes in the adrenal glands, as it was in our patients with bilateral neuroblastoma (case 1 and 2). One stage subtotal adrenalectomy in such circumstances seems to be possible as the type, localization, size, and biological behavior of primary tumors of the adrenal gland tissue often allow extirpation without having to remove the adrenal gland completely [14]. It may be concluded that subtotal adrenalectomy was an attractive solution in those patients, permitted to preserve endogenous steroid production and avoid risk of life-threatening acute hipoadosteronism.

Subtotal adrenalectomy may be also considered in patients with primary and secondary adrenal hyperplasia of different etiology. Although most data available in the literature recommend complete resection of the adrenal tissue, there are also reports on subtotal adrenalectomy in these cases [8, 10]. In our short series we had finally decided to treat both children with adrenal hyperplasia in the conservative way by unilateral adrenalectomy. The first patient however due to primary pigmented nodular hyperplasia developed after four years an evident hyperplasia of the remaining adrenal gland and there is a real probability that the remaining right adrenal gland should be also subtotally resected in the nearest future. These facts allow to rise the question whether the primary surgery for this disease should be rather conservative or perhaps a little bit more radical and resulted in one-stage bilateral subtotal adrenalectomy.

The second patient with congenital adrenal hyperplasia due to 21-hydroxylase deficiency undergone also unilateral adrenalectomy. At the operation the left adrenal gland with prominent nodular lesion of the cortex was exclusively removed. One year after surgery the patient still needs steroid administration and control tests show high plasma concentration of ACTH. Control CT scan revealed progressing hyperplasia of the remaining adrenal gland, so there is a high probability that the second stage of adrenalectomy will be necessary. Therefore the question arrises how to deal with surgical treatment of adrenal hyperplasia in children and in what way the subtotal adrenalectomy should be performed: in one or in two stages procedure. The history of four presented patients may suggest that similarly to the adults the indications for bilateral subtotal adrenalectomy in children could be broadened.

The literature documents that bilateral subtotal adrenalectomy in adults is feasible, safe and efficient technique. Independence from exogenous steroid therapy can be expected in most patients, making this operation one that should be considered in specific situations [6]. Thorough topographical and hormonal assessment of the adrenal glands before surgery permits to achieve the most efficient results and minimize possibility of postoperative adrenal insufficiency.

References