The Treatment of Nodular Adrenal Hyperplasia

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NODÜLER ADRENAL HİPERPLAZİNİN TEDAVİSİ

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SUMMARY

Six cases of nodular adrenal hyperplasia (NAH) associated with Cushing's syndrome are reviewed. NAH may be associated with ACTH-dependent, partially-dependent, and independent forms, and is associated with confusing ACTH stimulation, and static and dynamic laboratory tests. Abdominal CT scanning identifies some but not all cases of NAH. Following unilateral adrenalectomy for grossly unilateral NAH, recurrence of Cushing's syndrome is often noted, necessitating subsequent removal of the remaining adrenal gland. It is concluded that in patients with confusing laboratory tests or CT scans suggesting NAH, abdominal exploration and bilateral total adrenalectomy is the treatment of choice

Key words: Cushing's syndrome, nodular adrenal hyper-

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ÖZET

Cushing sendromuna yol açan bir klinik antite olan ve nodiüler adrenal hiperplazi gösteren altı vakayı inceledik. Nodûler adrenal hiperplazi (NAH}, kararlı bir laboratuar bulgusu olmayan, yanıltıcı statik ve dinamik çatışma sonuçları olan, ACTH'a tam bağımlı, kısmen bağımlı ya da tamamen bağımsız olan bir antitedir, Kompüleri-ze tomografi tanıda faydalıdır, ancak tüm vakalarda işe yaramamak ladır. Olandlardan yalnız birinin makroskopik olarak hastalıklı görüldüğü durumlarda tek taraflı adrenalin çıkarılması genellikle nüks ile sonuçlanır. Sonuç olarak, Cushing sendromlu bir hastada kararsız laboratuar bulgulart varsa, CT ile nodûler yapıdan şüpheleniliyorsa NAH düşünülmeli ve bilateral adrenalektomi yapılmalıdır.

Anahtar kelimeler: Cushing lendromu, nodûler adrenal

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Cushing's syndrome was first- described by Harvey Cushing in 1932 (1). The clinical manifestations of Cushing's syndrome result from excessive glucocorticoid secretion (4). Causes of Cushing's syndrome include bilateral adrenal hyperplasia (80% of total cases), and benign adenomas and malignant tumors, together accounting for the remaining 20%.

Bilateral adrenal hyperplasia is further subdivided into diffuse and nodular forms. Nodular adrenal hyperplasis (NAH) accounts for approximately 10-15% of the cases of bilateral adrenal hyperplasia (3). The first clinical cases were described by Mellinger and Smith in 1956 (2). In the early 1960's, NAH became accepted as a distinct clinicopathologic entitiy. NAH has confusing laboratory and radiologic findings (2, 3). It may be seen with ACTH-dependent, partially-dependent, or ACTH-independent forms. Biochemical tests are often not helpful in the preoperative diferentation between diffuse bilateral adrenal hyperplasia, NAH, and adrenal adenomas. Therefore, patients with Cushing's syndrome who cannot be identified as having either bilateral diffuse adrenal hyperplasia or an adrenal adenoma with static and dynamic tests and ACTH levels preoperatively, should have bilateral adrenal exploration. If NAH is found at operation, bilateral total adrenalectomy should be performed. Because of the probability of adrenacortical autonomy, bilateral adrenalectomy rather than hypophysectomy is the treatment of choice.

Between 1972 and 1986, eighty-eight patients with Cushing's syndrome were operated on in the Department of Surgery, Faculty of Medicine, at the

University of Ankara. Six cases of NAH were identified. In this study, the diagnostic features and treatment problems of these six patients are discussed.

MATERIALS AND METHODS

The records of the six patients with NAH presenting between 1972 and 1986 were reviewed. Seven percent of the patients presenting with Cushing's syndrome during this period were found to have NAH (Tablo-I). Table-2 shows the age and sex distribution and duration of disease in the six patients with NAH. Table-Ill illustrates the range of adrenal weights and the histologic classification. Nodules greater than 2 cm in diameter were accepted as macronodular hyperplasia, while glands with microscopic nodules or nodules less than 2 cm in diameter were defined as having micronodular hyperplasia. In this study, no cases of primary adrenocortical nodular dysplasia (in which adjacent areas of adrenal cortex are atrophic) were identified (6). T.

Preoperative low and high dose dexamethasone suppression tests and ACTH stimulation tests were not able to differentiate adrenal adenomas from diffuse or nodular hyperplasia. Abdominal CT scans were performed in all but one case. A diagnosis of NAH was obtained by CT scan in only two of six cases, both with macronodular hyperplasia.

A supraumbilical, transverse transperitoneal incision and exploration were performed in all cases. In five cases, bilateral total adrenalectomy was performed. A 12 year old girl had a left adrenalectomy for a 1.5 cm adenoma, the right adrenal being grossly normal at exploration. However, she presented with recurrent Cushing's syndrome 12 months later, requiring then a right adrenalectomy. Histologic examination revealed NAH.

Table - I

NAH and Other Forms of Cushing's Syndrome

N: 88	
Bilateral diffuse adrenal hyperplasia	**68.1%**
NAH	**6.8%**
Adrenal adenoma	**19.3%**
Adrenal carcinoma	**5.6%**

Table - II

Age distribution :	**12—40 years**
Sex distribution :	**5 female / 1 male**
Duration of disease :	**6 months — 2 years**

Table - HI

Pathology

Micronodular NAH :	**4**
Macronodular NAH :	**2**
Weight of adrenal glands :	**15-26 GM.**

DISCUSSION

In this study, NAH accounted for 6.8% of the total cases of Cushing's syndrome, though previously reported incidences ranging between 10-20% (2, 3). There remains disagreement as to whether NAH is ACTH-dependent or independent (3). However, there are some case reports of recurrence when unilateral adrenalectomy has been performed (3, 5), as occurred in one of our patients. On the other hand, following bilateral adrenalectomy, we have seen no recurrences (2-11 year follow-up).

Because of its low morbidity and mortality, transsphenoidal hyphophysectomy has recently become increasingly popular in the treatment of Cushing's syndrome (4). However, the probability of semiautonomous or autonomous adrenal tissue in NAH makes persistence or recurrence of Cushing's

Table - IV

Laboratory Results in NAH

	Plasma ACTH (ng/ml)	Dexamethasone 4x2 mg for 48 hours 17-OHCS (mg/24 h)	ACTH stim. test (3 day) 17-OHCS (mg/ml)
Normal values :	**10-80**	**< 50% of basal value**	**> 50% of basal value**
Patient 1 :	**18**	**+**	**no response**
Patient 2 :	**60**	**+**	+
Patient 3 :	**120**	**no response**	+
Patient 4 :	**22**	+	**no response**
Patient 5 :	**92**	**no response**	**+**
Patient 6 :	**110**	**no response**	**+**

(+) : Elevation in 17-OHCS levels more than 50% of basal value.

syndrome likely in these cases (7). In our opinion, abdominal CT scanning is mandatory in all patients with Cushing's syndrome, although many cases of micronodular NAH may not be identified by CT scans. Additionally, hyperplasia with confusing laboratory findings may implicate and call attention to NAH preoperatively.

It is therefore our opinion that a patient with Cushing's syndrome with confusing or inconsistent ACTH levels and static and dynamic laboratory tests, or a CT scan suggesting NAH, bilateral total adrenalectomy should be performed. Autotransplantation should not be employed, again because of the possibility of recurrence (Table-IV).

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