ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LXI, N1, 16 SECTIO D 2006

Department of Pediatric Hematology and Oncology, Chair and Department of Clinical Pathology
Medical University of Lublin

JOANNA ZAWITKOWSKA-KLACZYŃSKA, KRZYSZTOF KĄTSKI,
ANNA GAWORCZYK, DANUTA SKOMRA, JERZY R. KOWALCZYK

Adrenocortical carcinoma in a one-year-old girl

Adrenocortical carcinoma is uncommon in childhood. It accounts for approximately 0.3–0.4% of all the solid tumours in children (1). Pediatric adrenocortical carcinoma typically occurs at age less than five years and the majority of affected children are females. Adrenocortical neoplasms can be associated with hemihypertrophy and Beckwith-Wiedemann and Li-Fraumeni syndromes (1). Clinical presentation is mainly related to the endocrine manifestation of the tumour. Virilization alone or coexisting with Cushing's syndrome is the most common symptom at presentation (1). Nonfunctioning adrenocortical carcinoma is less common; it generally occurs in older adults. Local invasion and metastases to lungs, liver, kidney, mesentery, the vena cava, CNS and regional lymph nodes can occur (4). Due to low incidence, there are no established treatment protocol or uniform histological classification. The histologic criteria of Weiss are very helpful, but still adrenal adenoma can be difficult to distinguish from adrenal carcinoma (5). The surgical resection (with or without postoperative chemotherapy) remains the treatment of choice in children with adrenocortical carcinoma (1).

CASE REPORT

A one-year-old girl was admitted to the Pediatric Hematology and Oncology Department at Children's University Hospital in Lublin, in June 2003 because of a tumor located in the abdomen. Five months prior to admission, girl's parents noticed an abnormal hair growth on thighs, and acne on her cheecks. Primary care physician diagnosed this condition as an allergy and prescribed anti-allergic medications, without further investigations of the cause of abnormal hair growth. During the following two months the acne on girl's face aggravated and pubic hair appeared, as well as hair on the child's crura. Excessive perspiration was also noticed. Abdominal ultrasound examination revealed a tumor of the right suprarenal gland, therefore the patient was referred to our institution for further investigation and management. The child remained at general good condition on admission. Physical examination revealed virilization, manifesting as: hypertrophy of labia majora, pubic and crura hair growth, increased muscle mass and acne on the cheeks. Biochemical tests results showed high levels of cortisol (two x norm) and testosterone in the serum (10 x norm), and high levels of 17-kotosteroids in urine (two x norm). The karyotype was a normal female karyotype: 46, XX. The radiographs of the carpal bones demonstrated the accelerated skeletal maturation (estimated at two years). Computed tomography (CT) of the abdomen confirmed the presence of a tumor deriving from the right suprarenal gland (Fig. 1). Chest radiograph and CT scan of the brain were negative for the presence of metastases. Urgent surgical resection of the tumor was undertaken. Histopathologic examination revealed the tumor with predominantly diffuse or solid architectural pattern with some parts arranged in short cords or clusters. Tumor cells appeared irregular and pleomorphic with eosinophilic, compact cytoplasm and pleomorphic, hyperchromatic nuclei. Occasionally the nuclei appeared hyperlobated or multinucleated or contained one or more prominent nucleoli. Nuclear pseudoinclusions could also be found. Mitotic rate was seven

per 50 high-power fields with the presence of atypical forms. Tumor showed vascular proliferation, small foci of necrosis and a few areas of dystrophic calcification. The invasion into the surrounding fat tissue was also present (Fig. 2). The disease was classified as stage III in TNM classification and a postoperative chemotherapy was started. The girl received five courses of CAP: cyclophosphamide (CTX) 500 mg/m i.v. – day one, adriamycin (ADR) 50 mg/m i.v. – day one, cisplatin (CDDP) – 50 mg/m i.v. – day one, in three weeks' intervals. The treatment was well tolerated. The symptoms of virilization receded gradually and were not detectable at three months after completion of treatment. Hormone levels returned to the normal values. The patient is doing well at 17 months after the treatment has been completed (23 months after initial diagnosis).

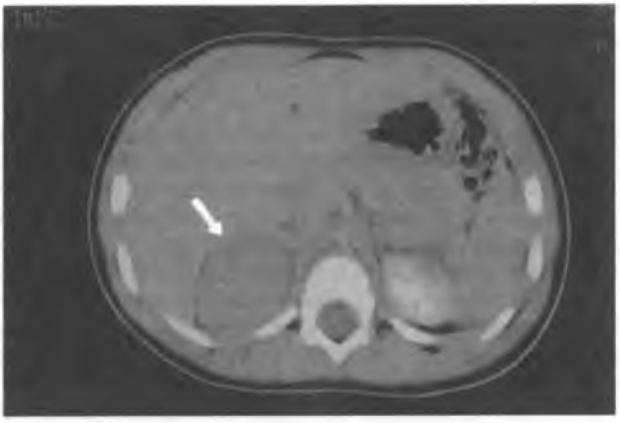

Fig. 1. CT scan revealing a tumour of the right suprarenal gland

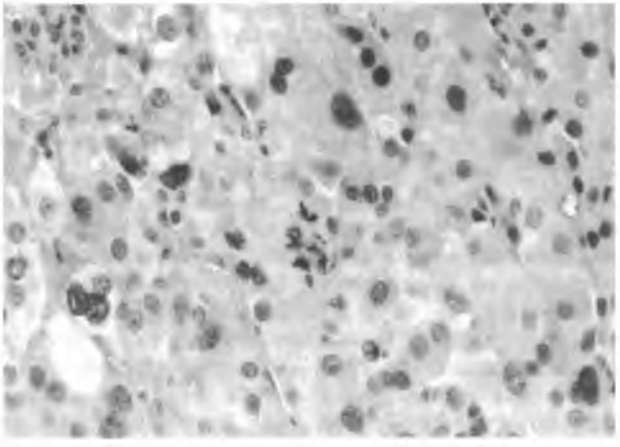

Fig. 2. Adrenal cortical carcinoma. The tumor has nesting pattern of irregular pleomorphic cells. Atypical mitotic figure is present. H+E. Magn. 400x

DISCUSSION

Clinical presentation of adrenal tumors is mainly related to its endocrine manifestations. Virilization alone or with Cushing's syndrome is the most common symptom at presentation in

children (1). Therefore it is crucial that the endocrine manifestations of these tumors be urgently evaluated and recognized. However, symptoms in a child with functioning adrenocortical tumor may be indistinguishable from those of patients with adrenal hyperplasia or precocious puberty (1). Ultrasound examination is a highly effective tool in the initial detection of the primary tumor. Other cross-sectional imaging studies, including CT which is considered the most valuable technique for examining the adrenal glands, add their value in the assessment of the primary tumor size as well as they allow for the detection of metastases – the basic prognostic factor (1). Despite wide availability of ultrasonography, our patient was referred for the abdominal examination at the late stage, after the disease had progressed. Primary care physicians should be aware that neoplasms of the adrenal cortex may affect their pediatric patients. Therefore they should be included in a differential diagnosis of signs and symptoms of endocrine abnormalities. Early diagnosis of adrenocortical carcinoma is essential for successful treatment, since the therapeutic options are limited. The mainstay of therapy remains surgerical resection of a tumor with chemotherapy indicated for patients with metastases or persistent elevated hormone levels following surgery. Due to the tumor's aggresiveness and its poor sensitivity to radiotherapy and chemotherapy, the effectiveness of both as sole methods of treatment is questioned. Mitotan (p-DDD) is the only drug of proved efficacy, acting through selective cytolysis of adrenocortical cancer cells. However, treatment with p-DDD results in many adverse effects and its use in children is limited (2). Many other drugs, including cisplatin, cyclophosphamide, adriamycin, etoposide and vincristine, were tested in small groups of patients (3).

Due to histopathological examination, which revealed the presence of cancer cells in the lumen and in the arterial wall the child underwent postoperative course of chemotherapy. CAP regimen was chosen, because it combined the most of the potentially effective drugs. During the course of treatment, the general state of the patient was good and no serious side-effects were observed. At present, the child is followed up on out-patient basis and in good condition with no signs of the disease.

REFERENCES

1. Argons G.A. et al.: Adrenocortical neoplasms in children: radiologic-pathologic correlation. Radiographics, 19, 4, 989, 1999.
2. Berruti A. et al.: Mitotane associated with etoposide, doxorubicin and cisplatin in the treatment of advanced adrenocortical carcinoma. Italian Group for the Study of Adrenal Cancer. Cancer, 83, 10, 2194, 1998.
3. Bonacci R. et al.: Cytoxic therapy with etoposide and cisplatin in advanced adrenocortical carcinoma. Br. J. Cancer, 78, 4, 546, 1998.
4. Piniella A.M., Siatkowski R.M.: Adrenal cortical carcinoma to the brain in a child. J. Neuroophthamol., 20, 1, 35, 2000.
5. Wajchenberg B.L. et al.: Adrenocortical carcinoma: clinical and laboratory observation. Cancer, 88, 4, 711, 2000.

SUMMARY

Adrenocortical carcinoma is uncommon in childhood. The surgery is the treatment of choice in children with adrenocortical carcinoma, however the studies on the effectiveness of chemotherapeutic agents are carried out. A one-year-old girl was admitted to the Department in June 2003 because of a tumor localised in the abdomen. Physical examination revealed virilization. Biochemical tests results showed high levels of cortisol and testosterone in the serum, and high levels of 17-ketosteroids in urine. Computed tomography of the abdomen confirmed the presence of a tumor deriving from the right suprarenal gland. Histopathologic examination revealed adreno-

cortical carcinoma. Urgent surgical resection of the tumor was undertaken. The girl received five courses of CAP. The patient remains well at 17 months after completion of treatment.

Rak kory nadnerczy u rocznej dziewczynki

Rak kory nadnercza jest rzadkim nowotworem wieku dziecięcego. Leczeniem z wyboru jest zabieg operacyjny, jednak prowadzone są badania nad skutecznością chemioterapii. Dziewczynka w wieku jednego roku była przyjęta do Kliniki w czerwcu 2003 r. z powodu guza zlokalizowanego w jamie brzusznej. W badaniu fizykalnym stwierdzono cechy wirylizacji, a w badaniach biochemicznych wysoki poziom kortyzolu i testosteronu w surowicy krwi oraz wysoki poziom 17-ketosterydów w moczu. Wykonano pilnie zabieg operacyjny. Dziewczynka otrzymała pięć cykli CAP. Pacjentka pozostaje w remisji 17 miesięcy od zakończenia leczenia.