IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 3 Ser.17 (March. 2023), PP 26-32
www.iosrjournals.org

Malignant Tumors Of the Suprarenal Gland in Children (About 72 Cases)

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ABSTRACT:
Adrenal malignancies in children are rare. They form a heterogeneous group of lesions dominated by neuroblastomas.
This work is a 5-year retrospective study (2016-2020) of children with adrenal malignancies who are enrolled in the pediatric A surgery department of the Ibn Sina Children's Hospital in Rabat, in collaboration with the pediatric hematology department. Their clinical, biological, radiological and therapeutic characteristics were analyzed, especially the importance of surgery and chemotherapy in the management
of these tumors. 72 patients were diagnosed during this 5-year period. In order of frequency, the adrenal neuroblastoma occupies the first place with 99% of the cases, followed by the adrenal corticosteroid with 1% of the cases. This period was marked by the absence of cases of malignant pheochromocytomas. The average age of our patients is 3 years and 4 months, with male predominance. The diagnosis is suspected on clinical and biological data. The imaging mainly represented by ultrasound and scanner allowed diagnosis in most cases. 66% of our patients have benefited from a surgical treatment with or without chemotherapy. In the majority of cases, it consists of an adrenalectomy. 35% of the cases had a positive outcome, while the rest had relapsed or died or lost sight of.
Key words: *Adrenal neuroblastoma, Adrenocortical carcinoma, malignant pheochromocytoma, child*

Date of Submission: 14-03-2023 Date of Acceptance: 30-03-2023

I. INTRODUCTION:

In children, the adrenal glands can be the site of a number of malignant tumors, located in the adrenal medulla such as neuroblastoma and malignant pheochromocytoma, or in the adrenal cortex cancer, which are quite rare, adrenal cortex cancer being the most frequent.
Imaging based on ultrasound sometimes supplemented by CT scan, anatomopathological examination plays an essential role in confirming the diagnosis and deciding on the therapeutic management.
The anatomical situation of the adrenal gland explains the variety of surgical approaches used for adrenalectomy.
This work reviews 72 cases of malignant adrenal tumors in children taken between January 2016 and December 2020.

II. MATERIAL AND METHODS:

Our work is a retrospective study spanning 5 years between January 2016 and December 2020. This study concerned 72 children followed for malignant tumors of the adrenal gland in the department of pediatric surgery A of the children's hospital Ibn Sina University Hospital in Rabat.

III. RESULTS:

Pathologies	Number of cases	Percentage
Adrenal neuroblastoma	71	98.61%
Adrenocortical cancer	1	1.38%
Malignant pheochromocytoma	0	0%

Table 1: Distribution of patients according to pathology

The average age of our patients is 3 years and 4 months with extremes varying between 3 months and 14 years.

Age	Number of cases	Percentage
Less than 1 year	12	16.66%

1 to 2 years	13	18.05%
2 years to 5 years	39	54.16%
5 to 10 years	5	6.94%
More than 10 years	3	4.16

Table 2: Patient distribution by age

In our series, we found a male predominance with 40 boys (56%) and 32 girls (44%) boys (56%) and 32 girls (44%), a sex ratio of 1.25

Location of the tumor	Number of cases
Left adrenal	34
Right adrenal	37
Bilateral	1

Table 3: Distribution of tumors according to location.

The most frequent mode of discovery in our patients is represented by the abdominal mass in 32% of the patients (23 cases), the other modes are cited below in decreasing order of frequency: Abdominal pain: 21% (15 cases) Abdominal distension: 17% (12 cases) Fever: 8% (6 cases) Bone pain: 7% (5 cases) Arthralgia: 4% (3 cases) Lameness: 4% (3 cases) Exophthalmos: 3% (2 cases) Hypertension: 1% (1 case) Cervical ADP: 1% (1 case) Pubic pilosity 1% (1 case)

Abdominal ultrasound was performed in all our patients. The dominant ultrasound appearance was that of an echogenic was that of an echogenic and heterogeneous adrenal tissue mass heterogeneous. The presence of characteristic calcifications was found in 30 cases. Regarding the volume of the masses on ultrasound: masses with a diameter exceeding 10cm represent 35% of the cases, those between 6 and 10cm represent 28% of the cases and those 28% of the cases and those smaller than 6cm represent 37% of the cases.
Abdominal CT scan was performed in 91% of patients (65 patients) and showed neuroblastoma in 71% of cases (51 patients), tumor necrosis in 25% of cases (18 patients), endocanal extension in 9% of cases (6 patients), medullary metastasis in 9% of cases (6 patients) (hourglass tumor) and Pepper's syndrome in 1% of cases (1 patient)
Urinary catecholamines were determined in 21 cases (29%), and their metabolites in 32 cases (45%). their metabolites in 32 cases (45%). Dopamine was found to be increased in 10 cases, vanillylmandelic acid (VMA) in 21 cases and homovanillic acid (HVA) in 23 cases. Adrenaline was elevated in only one case while noradrenaline was increased in 3 cases. Normetanephrine was elevated in only one case while Metanephrine returned to normal.
Plasma androgens are measured in our only case of adrenal cortex. The testosterone level came back high while the dehydroepiandrosterone sulphate dehydroepiandrosterone sulfate (SDHEA) returned to normal.
The determination of **plasma cortisol** is performed in our case of adrenal cortex cancer. It came back normal. Lactate dehydrogenase (LDH) was measured in 86% of cases (62 patients), and was found to be elevated in 77% of cases.
Ferritin measurement was performed in 62 patients (86%) and was found to be increased in 60% of cases.
Histopathological study with the MKI index was studied in 95% of cases. The results of the anatomo-pathological examinations of the biopsies and the results of the anatomopathological examinations of the biopsies and the operative parts revealed several histological aspects:

- Neuroblastoma: 94% of cases (68 patients) including:
  - Well differentiated NB: 15.5% (10 cases)
  - Moderately differentiated NB: 14% (9 cases)
  - Undifferentiated NB: 3% (2 cases)
  - Poorly differentiated NB: 65.5% (42 cases)
  - NB in the process of differentiation: 1.5% (1 case)
- Malignant adrenocortical cancer with Weis score 5/9: 1% of cases (1 patient)

Evaluation of tumor extension:

- Skeletal radiographs:
  - Performed in patients with suspected bone metastases (45% of cases), it showed images related to secondary localizations in 27% of cases (19 patients) of cases (19 patients); 42% were in the skull (8 patients), 31% in the pelvis (6 patients) and 26% in the pelvis (6 patients) and 26% in the dorsolumbar spine (5 patients).

- Bone Scintigraphy:
    - In our study, 65% of our patients (47 cases) had a bone scan. It showed secondary bone locations in 39% (28 cases). of the cases (28 cases).
- Marrow extension:
    - Myelograms were performed in 51 patients and showed bone marrow invasion in 29 cases. medullary invasion in 29 cases. Osteomedullary biopsy was performed in 48 patients and showed bone marrow 23 patients showed bone marrow invasion.

- MIBG scintigraphy:
    - It was performed in 42 patients (58%), it revealed neuroblastoma in 21 cases, bone and spinal cord involvement in 12 cases, and normal in 9 patients. returned normal in 9 patients.

Therapeutic management:
Neoadjuvant chemotherapy was indicated in 72% of cases (52cas). The protocol used varied according to the pathology. Excisional surgery was indicated in 66% of our patients (48 cases), 32% of whom received a surgical procedure. 32% of them benefited from an exeresis from the start (23 cases), and 34% were operated on after reduction chemotherapy. 38% of our patients benefited from a postoperative chemotherapy.

- Adrenal Neuroblastoma:
    - Initial chemotherapy:

Initial chemotherapy was administered in 74% of our patients (53 cases). The indication of the protocol used was studied according to age and stage according to the EVANS classification
The number of courses and cycles administered varies depending on the protocol and the response to treatment response.
15 patients were treated with the High Risk Neuroblastoma Morocco (HR-NBL-MA) protocol while 2 patients were treated with the Intermediate-risk Neuroblastoma (IR-NBL) protocol.
15 patients were treated with the alternating CADO-VP16- CISPLATIN, of which 12 received 2 to 4 cycles and 2 patients received 6 cycles to achieve a satisfactory response.
12 patients were treated with the CADO-VP16- CARBOPLATIN and received 2 to 4 cycles. 3 of them received an intensification treatment with Ifosfamide-VP16.
5 patients were treated with CADO alone, and 2 patients in association with CO.
1 patient was treated with CO alone.
1 patient was treated with CO + 2 courses of VP16-CARBOPLATIN.

- Postoperative chemotherapy:

It was necessary in 32 patients.

- Palliative chemotherapy:

The use of palliative chemotherapy using: ENDOXAN per os was indicated in 23 cases (upfront in 11 cases). Intravenous etoposide was indicated in 3 patients.

- Surgery:

Surgery was indicated immediately in 32% of our patients (23 cases) and was complete in 19 patients. cases), it was complete in 19 patients. 36% of the patients (26 cases) were operated on after chemotherapy for tumor reduction tumor reduction chemotherapy, surgery resulted in partial removal of the tumor in 6% (4 patients) and complete removal in 26% (19 patients).
For the remaining 3 patients, the inoperable nature of the tumor was revealed during the during the operation, a simple biopsy was performed. Nephrectomy was necessary in only 1 case.

- Radiotherapy: +Radiation therapy was indicated in 8 patients.

- Adrenocortical cancer:

Our patient underwent complete excision followed by four courses of chemotherapy following the VP16-CARBO protocol.

Evolution-Pronosis:
The evolution of our patients treated for malignant tumors of the adrenal gland was marked by a complete remission in 35% of the cases (25 patients), a death in 19% of the cases (13 patients) 19% of the cases (13 patients), a relapse in 18% of the cases (13 patients), while 28% of cases were lost to follow-up (20 patients).

IV. DISCUSSION:

Malignant adrenal tumors are rare with an incidence of 0.2-0.3 new cases per 1 million children per year (1). Neuroblastoma is the most frequent extra-cranial solid tumor in children, presenting in children,

accounting for 6 to 10% of all childhood cancers (2). The incidence of malignant pheochromocytoma is approximately 0.02 cases per million per year, it represents less than 10% of pheochromocytomas
pediatric pheochromocytomas (3). In our series, adrenal neuroblastoma is the most common tumor, representing 98% of all adrenal malignancies, equivalent to 71 cases over a period of 5 years.
The median age of onset of neuroblastoma is 2 years of age. In one third of cases, the tumor occurred in children under 1 year of age and in 96% of cases before the age of 10 (4). In our series, the average age was 3 years and 4 months with a male predominance.
The average age of onset of pheochromocytoma in children is between 10 and 13 years with a male predominance. (5)
The sex ratio of adrenocortical cancer varies with age at diagnosis of the disease. (6) Our patient with adrenocortical cancer is 1 year old.
The clinical signs of malignant adrenal tumors are characterized by a clinical polymorphism explained by the variety of the size, the location and the degree of evolution of the tumor (metastasis). Abdominal pain or an abdominal mass are the clinical signs in half of the cases. in half of the cases, in the other half the suggestive signs are caused by hormones by the hormones produced by the tumor.
The biological diagnosis of neuroblastoma and pheochromocytoma is based on the determination of catecholamines and their metabolites. (7) If adrenocortical tumor is suspected, the hormonal workup should include the following blood tests: testosterone, cortisol, dehydroepiandrosterone sulfate (SDHEA), 17-hydroxyprogesterone, androstenedione, plasma renin activity, aldosterone, corticosterone and deoxycorticosterone. (8)
Today, imaging of the adrenal glands in children is based on a combination of combination of ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). Intravenous ureterography and arteriography are no longer used for exploration, whereas they were reference techniques 20 years ago.
Only in children is labelled MIBG scintigraphy of interest. It is a tracer that concentrates on adrenal tissues except for the normal adrenal gland. It allows to identify neuroblastomas, pheochromocytomas and to visualize their metastatic extensions or their extra-adrenal localizations. (9)
Postoperative anatomopathological represents the examination of certainty for the diagnosis of diagnosis of adrenal tumors in children.
Peripheral neuroblastic tumors are classified into 4 categories according to the INPC (The International Neuroblastoma International Neuroblastoma Pathology Classification) known as Shimada:

- Neuroblastoma with poor stroma, is subdivided into 3 groups:
    - Undifferentiated neuroblastoma
    - Poorly differentiated neuroblastoma
    - Differentiating neuroblastoma
- Mixed ganglioneuroblastoma: is a transitional form between ganglioneuroma and neuroblastoma
- Nodular ganglioneuroblastoma
- Ganglioneuroma (10,11)

The main prognostic factors are age at diagnosis, histological group INPC (International histological group INPC (International Neuroblastoma Pathology Classification), the stage of tumor extension stage according to the INSS (International Neuroblastoma Staging System) or Staging System (INSS) or the International Neuroblastoma Risk Group (INRG) and certain genomic changes. On the one hand, these changes are expressed by the extension of N-Myc, which is a poor prognostic factor. (12)
No predictive criteria for the malignancy of a pheochromocytoma have been found at present, but there are markers of malignancy risk, including: clinical signs, weight and size of the pheochromocytoma, and on histology: Ki67 index (antigen expressed during cell division and detected in immunohistochemistry) greater than 4%, non-labeling of the pS100 protein and the existence of tumor necrosis [13].
The management of adrenal tumors in children is based primarily on surgery, chemotherapy surgery, chemotherapy, radiotherapy and some other drugs.

- Medical preparation for surgery: Concerns pheocromocytoma by managing the cardiovascular effects of catecholamine hypersecretion and the hypercorticism of adrenal cortex tumor. (14)
- Surgery:
    - The approaches:
        - Adrenalectomy by laparotomy: (15,16)
            - Anterior approaches: are the most practical in children:
                - Incision:
                    - Median approach: Through a vertical, median incision from the xiphoid the xiphoid appendix to below the umbilicus, the creation and repair of this This incision is quick to create and repair.

- Subcostal approach: Through a transverse abdominal incision with an inferior concavity that can involve a single sub-costal region, or a bi-sub-costal incision rib from one tip of the 11th rib to the other in case of bilateral adrenalectomy, or both.

- Antero-lateral lumbar puncture:
  - Incision: It starts at the level of the external border of the paravertebral muscles above the 11th rib and follows this path, extending a few centimeters beyond the lower end of the rib. centimeters beyond the lower end of the rib.
- Posterior lumbotomy:
  - This approach was proposed by YOUNG in 1936 and offers direct access to the adrenal gland. Two types of incision can be made: The first incision The first incision is a posterior lumbar vertical incision described by YOUNG. It starts at the top 3 fingerbreadths (5 cm) above the line of the spinous veins, at the level of the 11th or 12th rib, and ends at the or 12th rib to end below on the iliac crest (8 cm from the midline). the midline). The second incision, called the field hockey stick incision, proposed by MAYOR, is identical in its upper part to that of YOUNG, but in its lower part it follows the lower part, it follows the path of the 12th rib.

- Adrenalectomy by video endoscopy: (17,18)
  - The indications for laparoscopic adrenalectomy are still very controversial, and most controversial, and most authors limit its indications to a priori benign tumors of less than benign tumors of less than 6 cm.
    - Transperitoneal route in supine position
    - Transperitoneal route in lateral decubitus
    - Retroperitoneal route

- Pheocrmocytoma:
  - Complete excision is the surgical principle in the malignant form as in the benign form of pheochromocytoma. However, in malignant pheochromocytoma, it will be retained only if all the metastases are resectable in a healthy margin. However, surgery alone is rarely curative (19).
  - In case of metastatic or unresectable pheochromocytoma, surgical debulking for symptomatic purposes may be discussed, although it does not improve the outcome. surgical debulking for symptomatic purposes can be discussed, although it does not improve survival (the level of scientific evidence for these rare cases is very low). (20)
  - In locally advanced malignant pheochromocytoma without metastases, the subcostal approach is preferred. Routine lymph node dissection has become controversial and can no longer be recommended in recommended in current practice (20).

- Adrenalocortical cancer:
  - The cornerstone of treatment is surgical excision, the quality of which generally affects the generally affects the prognosis. It must be performed by a well experienced surgical team. experienced surgical team. Removal is usually performed by laparotomy, via a homolateral subcostal incision through a transperitoneal approach (21, 22). In our study, we chose for our patient the anterior approach with transverse incision above the right umbilicus, muscle section.
- Neuroblastoma:
  - The possibility of macroscopically complete excision of the primary tumor clearly depends on its extension to tumor clearly depends on its extension to the surrounding organs (23).
  - The presence of microscopic residues for these tumors has no effect on survival, which is close to 100%, this may be due to the fact that the residual tumor will become a "regressing tumor" or a "maturing tumor" (24, 25)
- Chemotherapy:
  - Malignant pheochromocytoma: Chemotherapy and radiation therapy have been used, but their value is questionable (26)

- Adrenal cortex cancer: In children, various retrospective series or reported clinical trials indicate that adrenocortical cancer may be chemosensitive. The combinations used are generally based on those used in adults [27].
- Adrenal Neuroblastoma:
- Neuroblastoma is a chemosensitive tumor, which makes chemotherapy an important element in the treatment. (28)

- Radiotherapy:
  - Adrenal Neuroblastoma:
    - Neuroblastoma is a radiosensitive tumor. However, its place in the current treatment remains to be defined. Radiotherapy has been used for a long time to improve the prognosis of prognosis of localized forms, but the current chemotherapy, which has become more has become more efficient has limited its indications. (29)
  - Adrenal cortex cancer: For a long time, adrenocortical cancer was considered a low radiation-sensitive tumor. (30)

V. CONCLUSION:

Adrenal tumors in children, dominated by neuroblastoma, are most often malignant and rare. Neuroblastomas usually present as an abdominal mass, while adrenal cortical and pheochromocytomas are while adrenocortical and pheochromocytomas present as endocrine dysfunction.

Surgery plays a central role in the treatment of neuroblastoma and varies according to the mode of presentation of this heterogeneous disease. The goal of surgery is clear: "remove the primary tumor as completely as possible macroscopically", but the "cost" of the resection must be proportionate to the risk factors.

Early diagnosis and total resection are the best possible management of pheochromocytoma. for pheochromocytoma. Surgery should be performed by a team of team of anesthesiologists and surgeons experienced in the removal of this tumor.

In adrenocortical disease, complete resection of the tumor is the most effective initial treatment for small most effective initial treatment for small tumors, otherwise administration of mitotane can be discussed

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