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Case report

Bilateral adrenal tumor: A case report and current challenges

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ABSTRACT

Introduction: A bilateral adrenal tumor is a rare case. It differs significantly from unilateral adrenal mass since it is related strongly to genetic and family history. Adrenocortical Carcinoma might cause related hormonal syndromes such as Cushing syndrome, Conn syndrome, and virilization.

Aim: This study aims to report an uncommon presentation of a 15-year-old female with bilateral Adrenal Tumor since an early age with virilization as the main symptoms.

Case presentation: The patient is a 15-year-old girl with female genitalia presentation. She complained of a bulging mass on her right flank with pain four years ago. The mass size grew progressively and initially painless. However, the patient started to feel pain a year ago. Since she was six years old, the mass started to appear on the left flank, and then it also started to appear on the right side. The mass appearance is simultaneous with virilization symptom development, such as the emergence of facial hair, mustache, and sideburns. In 2020, MRI showed a lesion on the right suprarenal with contrast enhancement with 14.5 × 11.5 cm in size, and a 5.6 × 4 cm recurrent left suprarenal lesion. The patient underwent right adrenalectomy resection surgery on January 21st, 2021. The immunohistochemistry examination suggested Adrenocortical Carcinoma.

Conclusion: Adrenocortical Carcinoma is a hormone-secreting tumor that might affect the patient's condition systematically. Neglected cases of adrenal cortical carcinoma might affect secondary sexual organ development in the long term. Thus, an early diagnosis and treatment are paramount for this case.

1. Introduction

The bilateral adrenal tumor is an uncommon case that differs from unilateral adrenal mass due to differences in underlying causes. Genetic is acknowledged as a single factor that plays a key role in bilateral adrenal tumor formation. In one case series study which involves 18 patients with bilateral adrenal tumor, the most common etiology is Pheochromocytoma (6 patients) followed by Primary Lymphoma (4 patients), Nonfunctioning Cortical Adenoma (4 patients), Metastatic Tumors (2 patients), Primary Aldosteronism (1 patient), and Cushing syndrome (1 patient) [1]. Adrenal Tuberculosis and Adrenal Cortical Carcinoma were also reported for causing bilateral adrenal mass in another case report. However, the number of Adrenal Tuberculosis has declined each year [2].

Adrenocortical Carcinoma in pediatric has a poor prognosis [3]. The current knowledge in etiology, presentation, and clinical outcome is still limited. Nowadays, researchers found a strong association between genetic alteration and adrenocortical disorder, especially in GNAS1, PRKAR1A, TP53, and IGF2 genes [4]. Adrenocortical carcinoma primarily affects girls, and it causes virilization symptoms. Adrenocortical Carcinoma is a very rare occurrence in pediatrics. It only occurs for less than 0.2% from pediatric neoplasms and 1.3% from all carcinomas in patients whose age is less than 20 years old [5].

Adrenocortical carcinoma diagnosis could be very challenging [6]. The diagnosis should be based on physical examination, endocrine workup, imaging, and histopathological finding. In physical examination, virilization symptoms such as hypoplasia of mammae and facial hair growth are common in a female pediatric patient [7]. In endocrine workup, clinicians should pay close attention to basal cortisol, ACTH, dehydroepiandrostenedione sulfate, 17-hydroxyprogesterone, testosterone, androstenedione, and estradiol level [8]. Dexamethasone suppression tests and urinary-free cortisol are also recommended as additional tests. Today, there is not yet a single imaging method that could characterize localized Adrenocortical Carcinoma. Experts agreed if a lesion should be categorized as benign if it has ≤10 Hounsfield Unit in unenhanced CT [9]. When we found a lesion with >10 Hounsfield

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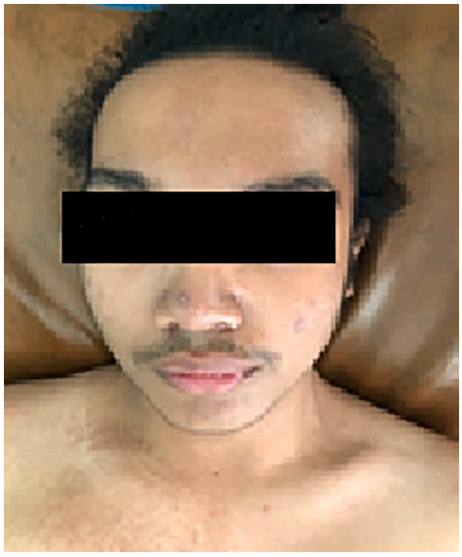

Fig. 1. Physical Examination Finding: Hirsutism.

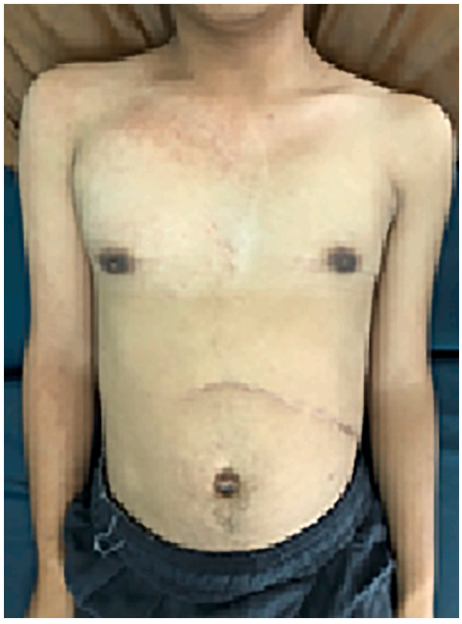

Fig. 2. Physical Examination Finding: Hypoplasia of Mammae.

Unit, we could use contrast media washout to differentiate benign and malignant lesions. An absolute washout <50% suggests a malignant adrenal lesion. Besides CT-Scan, clinicians also can utilize Magnetic Resonance Imaging to diagnose Adrenocortical Carcinoma. The primary finding that we could found is the presence of isointense to hypointense signal on T1-weighted images, a hyperintense signal on T2-weighted images, and a heterogeneous signal drop on chemical shift [10]..

There are several current choices of therapy for adrenocortical carcinoma. However, only complete surgical resection is acknowledged as the only effective and potentially curative treatment. Surgical resection can be whether exclusive adrenalectomy or extensive surgery, including nephrectomy, partial hepatectomy, or intracanal thrombus, depending on the disease severity. Open Adrenalectomy resection offers several benefits for the surgeon because it gives the surgeon a wider surgical field [11,12]. However, minimally invasive surgery is the most frequent way to conduct adrenalectomy resection. Chemotherapy could be used to reduce tumor size before surgery and prevent tumor recurrences. The most common agent used for chemotherapy in adrenocortical carcinoma is mitotane. However, it has a low response rate, and there are several reports stated that it could cause hepatotoxicity, fatal adrenal insufficiency, growth failure, and neuropsychiatric symptoms [5]. Other agents such as fluorouracil and doxorubicin are not recommended for adrenocortical treatment because of their ineffectiveness. One study reported that patients treated with those agents were relapsed two to five months after medication withdrawal. Before the operation, the patient should be administered an empiric stress dose of glucocorticoid, primarily when mitotane is used because mitotane can suppress cortisol synthesis. This case report discussed the resection of Adrenocortical Carcinoma which performed on a15-year-old girl at RSUP Haji Adam Malik Medan. This case report was made according to the SCARE guideline [13].

2. Case report

Fifteen-year-old girls came to our hospital with a painful mass in the right flank region, which appeared approximately five years before being admitted to the hospital. She came to our hospital because the family feels dissatisfied with the result of the treatment in the previous hospital. The mass size was getting bigger size its appearance. The patient also complained of growing beard, mustache, and other facial hair since she was six years old (Fig. 1). At the age of ten, her voice grew deeper, and the muscle of her extremities keeps getting bigger. In 2013, when she was 8 years old, she underwent a left mass resection surgery in Penang, Malaysia. It was concluded as Left Gynandroblastoma. Based on the history taking, the family history was remarkable. From our physical examination, we could see virilization symptoms, bilateral hypoplastic mammae, and post-operative scar in the flank region (Fig. 2). We continued the examination with MRI, and it showed a suprarenal lesion sized 14.5 × 11.5 cm with contrast enhancement and a recurrent left mass lesion with 5.6 × 4 cm in size (Fig. 3). Following the MRI examination, we conducted an ultrasound evaluation. From the ultrasound examination, it illustrated a right ovarium with 0,83 × 0,55 × 0,55 cm in size and left ovarium sized 0,72 × 0,42 × 0,55 cm. Ultrasound evaluation showed that both of the ovaria were normal and a hypoplastic uterus (Fig. 4). Laboratory workup result suggests an Adrenocortical Carcinoma due to both testosterone and DHEA-S elevation (Fig. 5). Normal ovarian ultrasonographic evaluation and the laboratory workup strongly suggested that gynandroblastoma was highly unlikely. Then we performed a Right Open Adrenalectomy with Laparotomy Approach. This surgery was led by Yacobda Sigumonrong M.D. and assisted by Ben Mantiri, M.D. The surgery took two and half hours. After that, we conducted a histopathology workup, and the result was Adenocarcinoma Cortical Adrenal. The patient was discharged after five days post-operation without any history of in-hospital complication.

3. Discussion

The case in this study is unique and very rare. There are several points that we could discuss what happened with this patient. First of all, this disease may be neglected. From the patient's history, we could see that the patient started to feel a growing mass on his body since she was six years old. The first resection surgery trial was when she was eight years old. It was left adrenalectomy. The histopathological finding was a Gynandroblastoma. It makes sense since the patient showed an apparent virilization symptom. However, the virilization symptoms continue until the patient grows into puberty seven years after her first surgery. Furthermore, the mass in her right flank region was growing over time, and after resected seven years later, the histopathological conclusion was adrenal cortical carcinoma.

Negligence is one of the main factors on why the virilization symptom could go this far. Secondly, Gynandroblastoma is a hormone-secreting tumor that could cause virilization syndrome. However, the

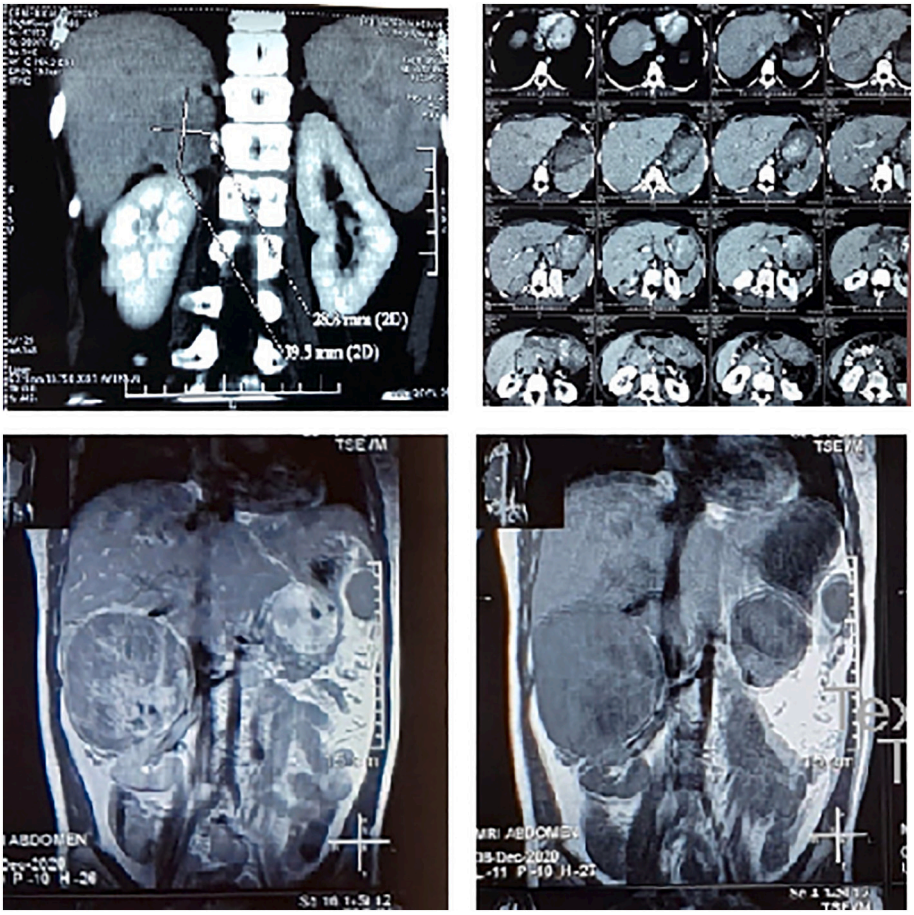

Fig. 3. MRI Evaluation.

symptoms should decline after resection of the tumor. Nevertheless, that is not the case in this patient. In addition, the histopathological finding on the right adrenalectomy was adrenal cortical carcinoma. There are two possibilities in this case. The first one is that Gynandroblastoma and adrenal cortical carcinoma both existed in the first place and cause a synergistic effect to amplify the patient virilization symptom [14]. The other possibility is that the first histopathological finding could be a mistake, and both tumors could be adrenocortical carcinoma. Bilateral adrenal cortical carcinoma is a rare case, but it is not unheard of before. However, two primary tumors in one patient (Gynandroblastoma and adrenocortical carcinoma) are sporadic. Thus, the second theory is more make sense in terms of prevalence and epidemiological study. Likewise, bilateral adrenal cortical carcinoma is reported to be able to cause severe virilization syndrome as well—furthermore, ultrasound evaluation showed a normal ovarium making a diagnosis of Gynandroblastoma highly unlikely. Lastly, the laboratory result suggested Adrenal Cortical Carcinoma instead of Gynandroblastoma. Both the testosterone and DHEA-S were elevated in this case, whereas in Gynandroblastoma, the DHEA-S should not be elevated. This finding is also proven by the latest immunohistochemistry investigation conducted in Haji Adam Malik Hospital. The result was adrenocortical carcinoma. Thus, re-investigation on the first histopathological examination (2013) is paramount in this case.

In addition, the patient's condition is exceptionally well except for virilization symptoms and pain on her flank. Adrenocortical carcinoma is a highly progressive tumor and can metastasize to another organ. The patient's general condition makes malignancy diagnosis questionable. Furthermore, the patient did not receive any cytostatic medication. Mitotane was not used in this patient, considering her young age. We believed that adrenocortical carcinoma should be classified further based on its genetic profile since it can be caused by genetic alteration in several site such as GNAS1, PRKAR1A, TP53, and IGF2. In our hypothesis, a difference in number or type of the defected gene would result in different clinical presentation, symptom, and severity even though it may look similar in general. A further genetic investigation would be beneficial to understand the behavior of adrenocortical carcinoma in this patient.

4. Conclusion

In summary, bilateral adrenocortical carcinoma is a scarce case and could cause a very debilitating problem to the patient. Therefore, we should not neglect patients with this disorder and closely monitor them for a specific period. In addition, early diagnosis and intervention might produce a better result for the patient in the long run. We felt an urgency to classify Adrenocortical Carcinoma further because it might be essential in determining prognosis and therapy. We also think there should be research regarding chemotherapy for Adrenocortical Carcinoma. Further research related to this topic would be a key stepping stone in understanding Adrenocortical Carcinoma more comprehensively.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available on demand.

Declaration of competing interest

The authors declare that they have no competing interests.

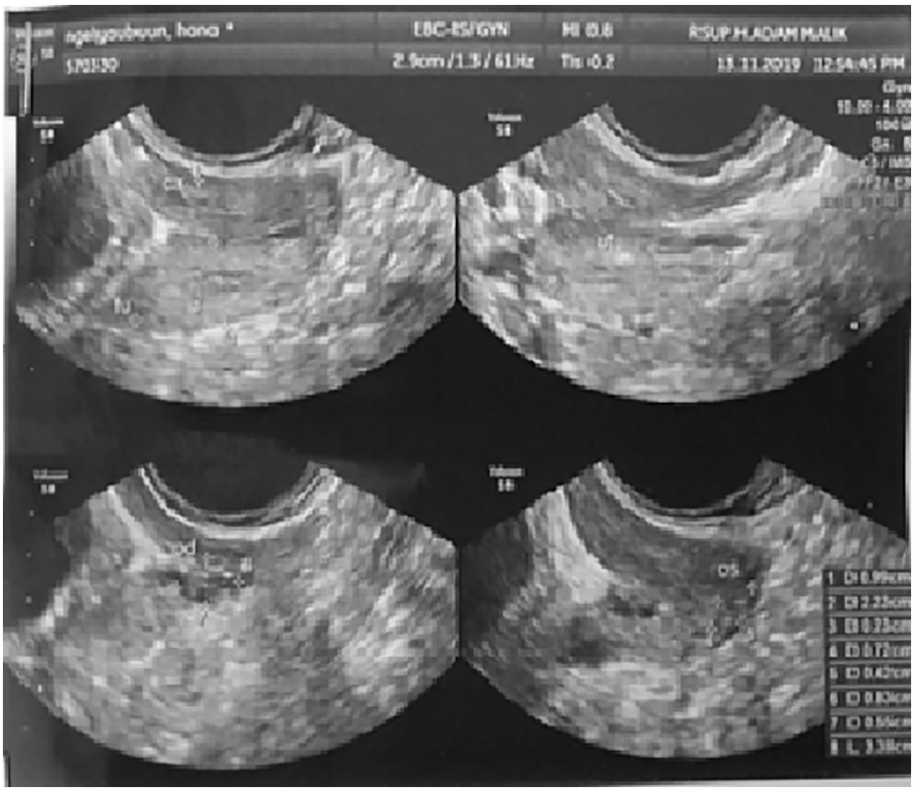

Fig. 4. Ultrasound Evaluation.

Parameter	Nilai	Nilai Normal	Satuan
Fungsi Hormon			
Testoterone	> 13,5	3 – 10.6	ng/mL
17-OH	4.5	3.7 – 19.4	ng/mL
DHEA-S	> 3000	8.6 – 169.8	ug/dL

Fig. 5. Hormonal Evaluation Result.

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Ethical approval

This case report has been exempted from ethical approval by Universitas Indonesia Ethical Committee.

Consent

The patient and her parents have given their consent in order for us to publish this case.

Author contribution

BJM carried out the data collection, analyzing the data and drafted the manuscript. YS participated in the design of the study and helped to draft the manuscript. All authors have read and approved the manuscript.

Registration of research studies

Not applicable.

Guarantor

Ben Julian Mantiri, M.D.

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