P2-025

Cushing Syndrome due to an adrenocortical carcinoma in a baby with atypical Beckwith-Wiedemann Syndrome

Tıp Fakültesi

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Background

Beckwith-Wiedemann syndrome (BWS) is a congenital tumor-predisposition syndrome of which around 70% develops because of the methylation defects in the imprinted genes at chromosome 11p15.5. *KCNQ1OT1* hypomethylation is the most common underlying genetic aberration in sporadic BWS, accounting for 50% of the sporadic cases but confers the least tumor risk.

We present a 5 month-old girl with atypical BWS who presented with an excessive weight gain, cushingoid face, arrested growth in height and head circumference since 2 months of age. She was born following an in vitro fertilization (IVF) pregnancy to non-consanguineous parents with negative familial history for malignancies. She had Cushingoid fetures, nevus flammeus between eyebrows, microcephaly, a palpable mass on upper right abdomen and Tanner 2 pubic hair at physical examination **(Figure 1)**. Her biochemical **(Table 1)**, imaging and immunohistochemical studies established the diagnosis of adrenocortical carcinoma (ACC) as a cause of Cushing syndrome **(Figure 2)**. There was no adrenal cortex cytomegaly at histopathological evaluation. Methylation analysis of the imprinted domains at chromosome 11p15.5 revealed hypomethylation at KvDMR (*KCNQ1OT1* gene). Except for a nevus flammeus and adrenocortical carcinoma, she had no features of the BWS. Growth rate of height and head circumference has returned to normal after tumor resection **(Figure 3)**. This case establishes that *KCNQ1OT1* hypomethylation should not only be considered in cases with a clear BWS phenotype but in all pediatric cases of apparently sporadic adrenocortical carcinoma.

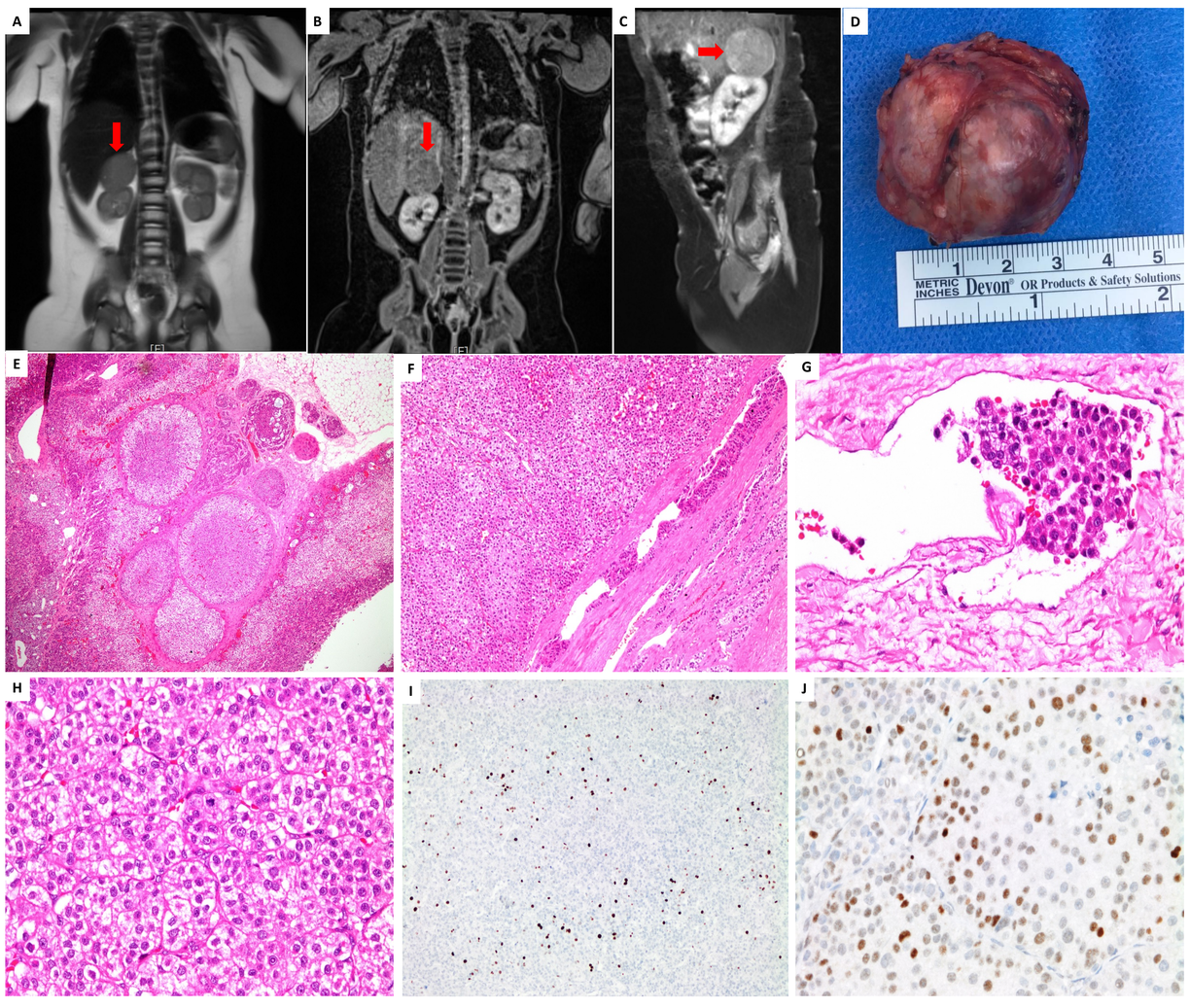

Figure 2. Radiologic and pathological characteristics of the patient. Abdominal MRI identified hypervascular right adrenocortical mass lesion (A=coronal section T2-weighted, B= coronal section T1-weighted, C= lateral view T1-weighted). A 4x3x1.5cm (16 gr) adrenocortical tumor was resected (D). Histopathological evaluation of the lesion revealed a capsulated ACC (E). However, sinusoidal (F) and vascular (G) invasion with atypical mitoses was observed. Tumor showed 25% of Ki proliferation index (I), and an increased expression of p53 (J) in immunohistochemical analysis.

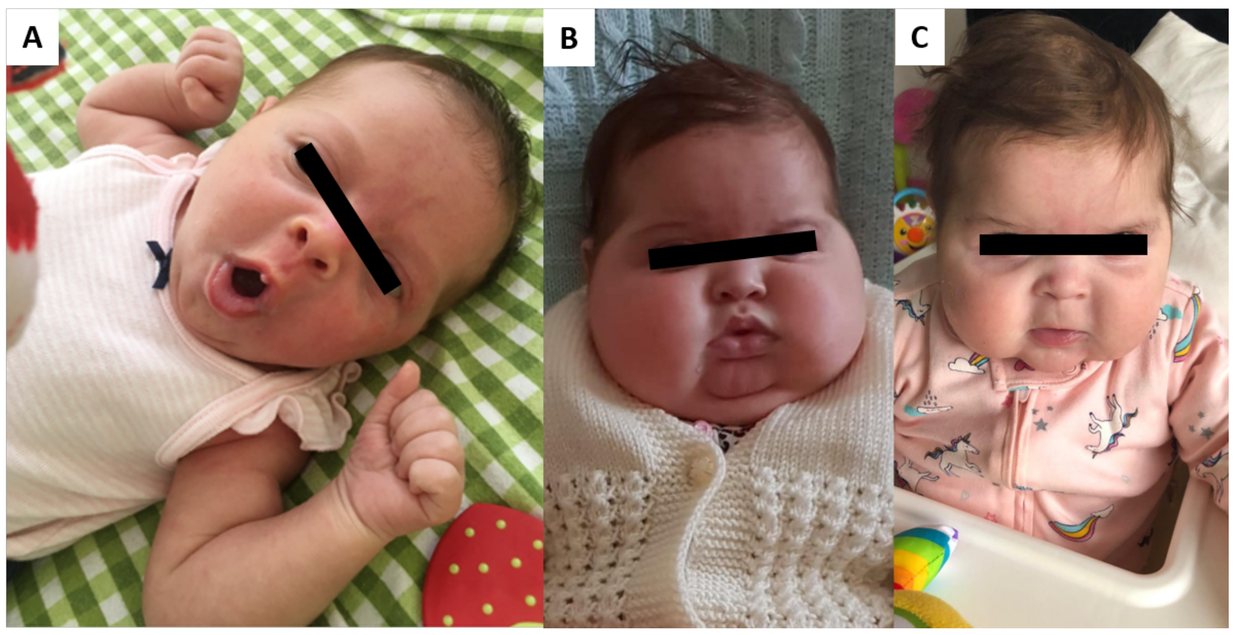

Figure 1. Evolution (A and B) and resolution (C) of Cushingoid appearance of the patient A: pre-operative at one-month; B: pre-operative at 6 months of age; C: 1.5 month after resection of adrenocortical tumor which cured her Cushings syndrome

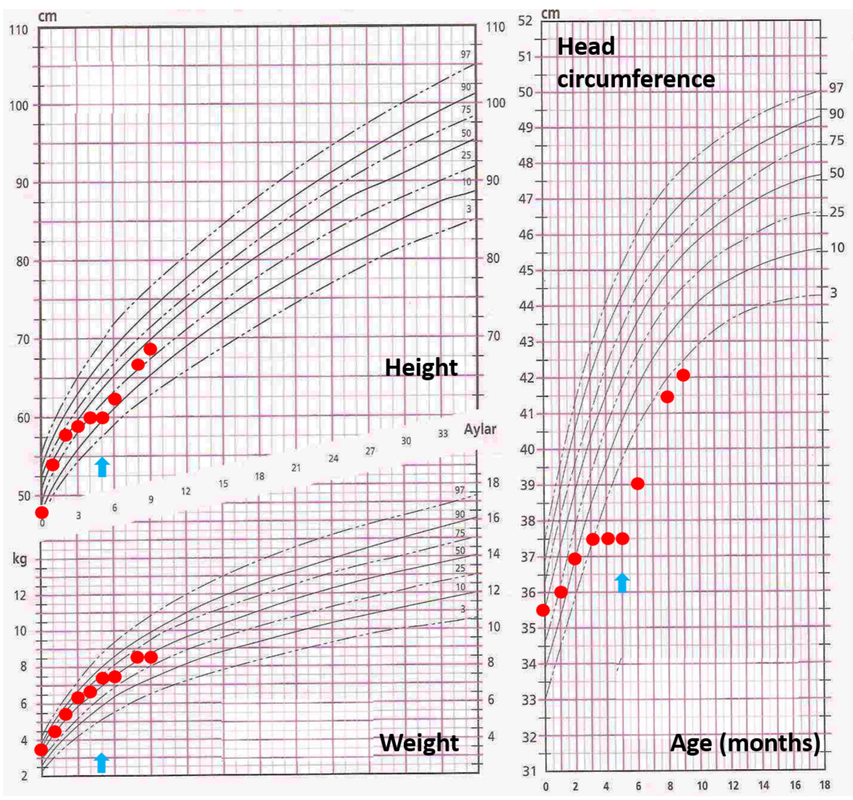

Figure 3. Slowing of growth and head circumference before surgery and restoration after cure. Blue arrow shows the time of operation.

Table 1. Laboratory measurements of the patient with Cushing syndrome due to ACC

Measurement	Value
Fasting blood sugar (mg/dL)	76
Serum Na/K (mEq/L)	139/ 5.3
ACTH (pg/mL)	<5
EAM cortisol (mcg/dL)	16.1
DHEAS (mcg/dL)	503
T. testosterone (ng/dL)	149
Serum cortisol after 8 mg overnight dxm sup test	16.9

Learning points

- Beckwith-Wiedemann syndrome should always be considered in children with adrenocortical carcinoma. BWS does not always present with classical features. However, patients with BWS clinical score ≥2 merit genetic testing for investigation and diagnosis of BWS*. This is critically important for long-term management of patients with BWS.
- *KCNQ1OT1* hypomethylation should be considered in all pediatric cases of apparently sporadic adrenocortical carcinoma.