PTEN Hamartoma Tumor Syndrome (Overlap of Cowden Syndrome and Bannayan-Riley-Ruvalcaba Syndrome): Case Report

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INTRODUCTION

PTEN Hamartoma Tumor Syndrome (PHTS) is a rare disease with dominant inheritance characterized by benign (hamartoma) and malignant tumors (breast, endometrium, thyroid). These include Cowden syndrome (CS), Bannayan -Riley-Ruvalcaba Syndrome (BRRS) and Proteus-like Synome. Mutations in the tumor suppressor gene *phosphatase and tensin homologue (PTEN)* gene are responsible for the etiology. CS entails increased risks for malignancies of a number of organs (particularly breast, thyroid and endometrium) and benign overgrowth of a number of tissues (skin, colon, thyroid, etc.). BRRS is a rare pediatric disorder that was initially felt to be distinct from CS. The most common clinical features include macrocephaly, hamartomatous intestinal polyps, lipomas and pigmented macules on the penis.

OBJECTIVE

We present an 11-year-old male who was followed-up for follicular thyroid carcinoma, and was diagnosed with PHTS due to accompanying macrocephalus, arteriovenous malformation (hemangioma), hyperpigmented macules on the glans penis and papules on the skin.

CASE

An 11-year-old male was followed-up in our clinic due to follicular thyroid carcinoma.

Medical History:

- He was investigated due to **macrocephaly** in the antenatal period but the etiology could not be determined.
- At the age of 7 years, fine needle aspiration biopsy (FNAB) of a 14x10 mm nodule on the right thyroid lobe showed normal histology. Because of the increase in the nodule diameter (35x20 mm) in the 6-month follow-up, FNAB was repeated which revealed follicular neoplasia. Hemilobectomy was performed. Histopathological examination was consistent with **follicular thyroid carcinoma.**
- At the age of 9 years, MRI revealed a mass lesion in the thigh (14x6.5cm). The mass removed surgically and pathology was reported as **arterio-venous malformation (hemangioma**).

Physical Examination:

- Weight: 39 kg (-0.39 SDS),
- Height: 151 cm (0.35 SDS),
- Head circumference: 60 cm **(3.74 SDS),**
- Autism findings were not present and mental development was normal.
- Pubertal stage was Tanner 3
- Papules on face, mass lesion (vascular anomaly) of approximately 10x7 cm on the left hip, **hyperpigmented macules on the glans penis** were observed.
- Neurological examination, EEG, and cranial MRI did not reveal any brain abnormalities.
- The patient had no hyperextensibility or muscle weakness.

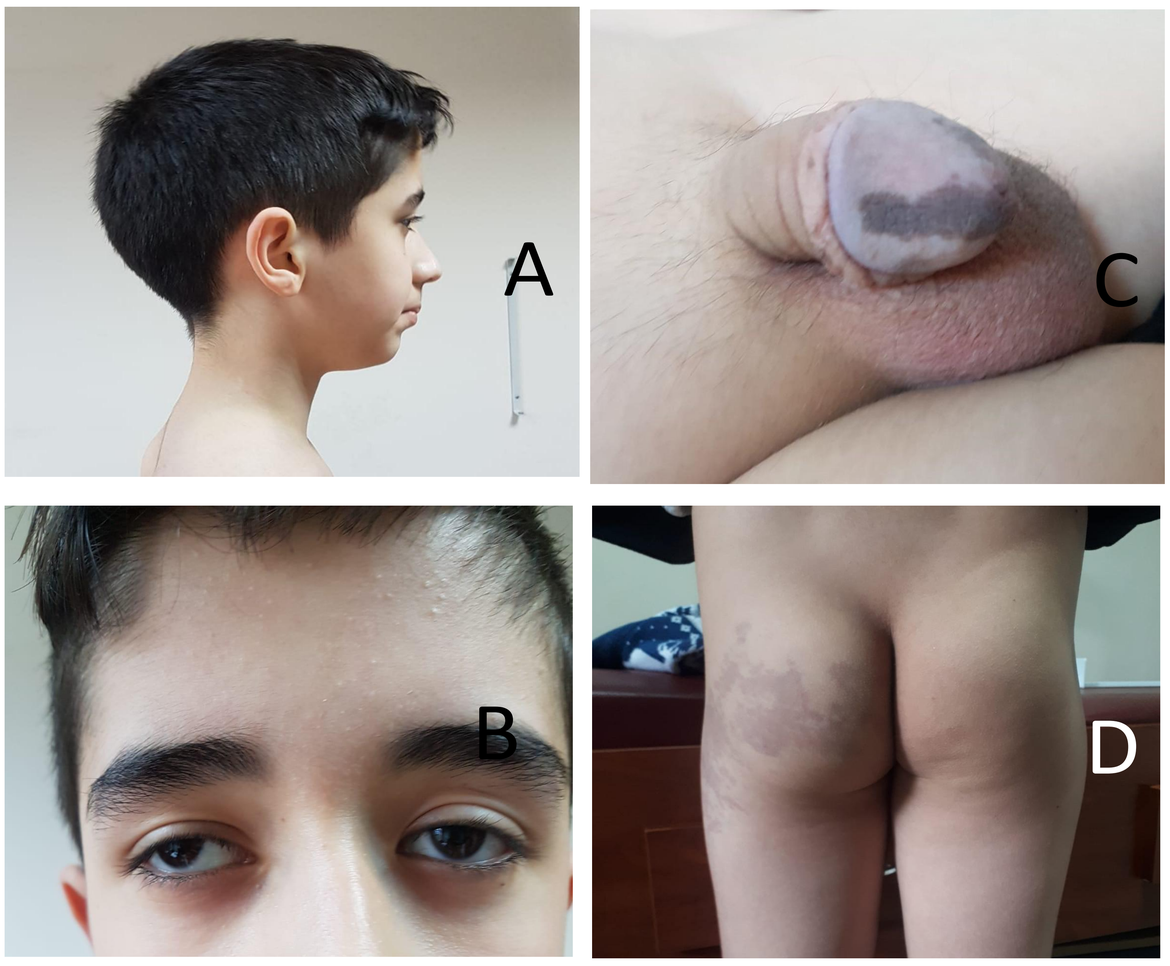

Figure 1. Macrocephaly (A), Papullomatous papules (B), Macules on penis (C), Hemangiomas (D)

Radiological Findings:

- Spine radiography revealed **dextroscoliosis**.
- High circulated and smooth boundiaried multiple nodules in left thyroid lobe (The largest one's dimension is 18*9 mm).
- EMG study did not show abnormal sign
- Small **intestinal polips in** upper gastrointestinal sistem endoscopy and colonoscopy.

PTEN Molecular Analysis:

- Molecular analysis showed c.388C>T heterozygous pathogenic variant in the *PTEN* gene.

CONCLUSION

Because of the early age at diagnosis and macular lesion in the penis, the patient was concordant to BRRS syndrome; and was overlapped with CS because of thyroid malignancy. PHTS is rare and its subtypes may not be differentiated. In this report, the 11-year-old patient whose clinical findings were concordant both with CS and BRRS, was pointed out. PHTS requires multidisciplinary monitoring and approach in terms of endocrine and non-endocrine pathologies.