

Familial Williams Syndrome



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INTRODUCTION

Williams Syndrome (WS) is a multisystemic genetic syndrome, which includes characteristic appearance of "elfin face", growth retardation, mild to moderate mental retardation, hypersociality, infantile hypercalcemia, and other endocrine, cardiovascular, urinary and musculoskeletal abnormalities. WS is caused by the hemizygous microdeletion of the long arm of chromosome 7 within the region of 7q11.23. We reported 12-month-old boy with WS presented with infantile hypercalcemia and his mother with WS who was diagnosed during her son's hospital admission.



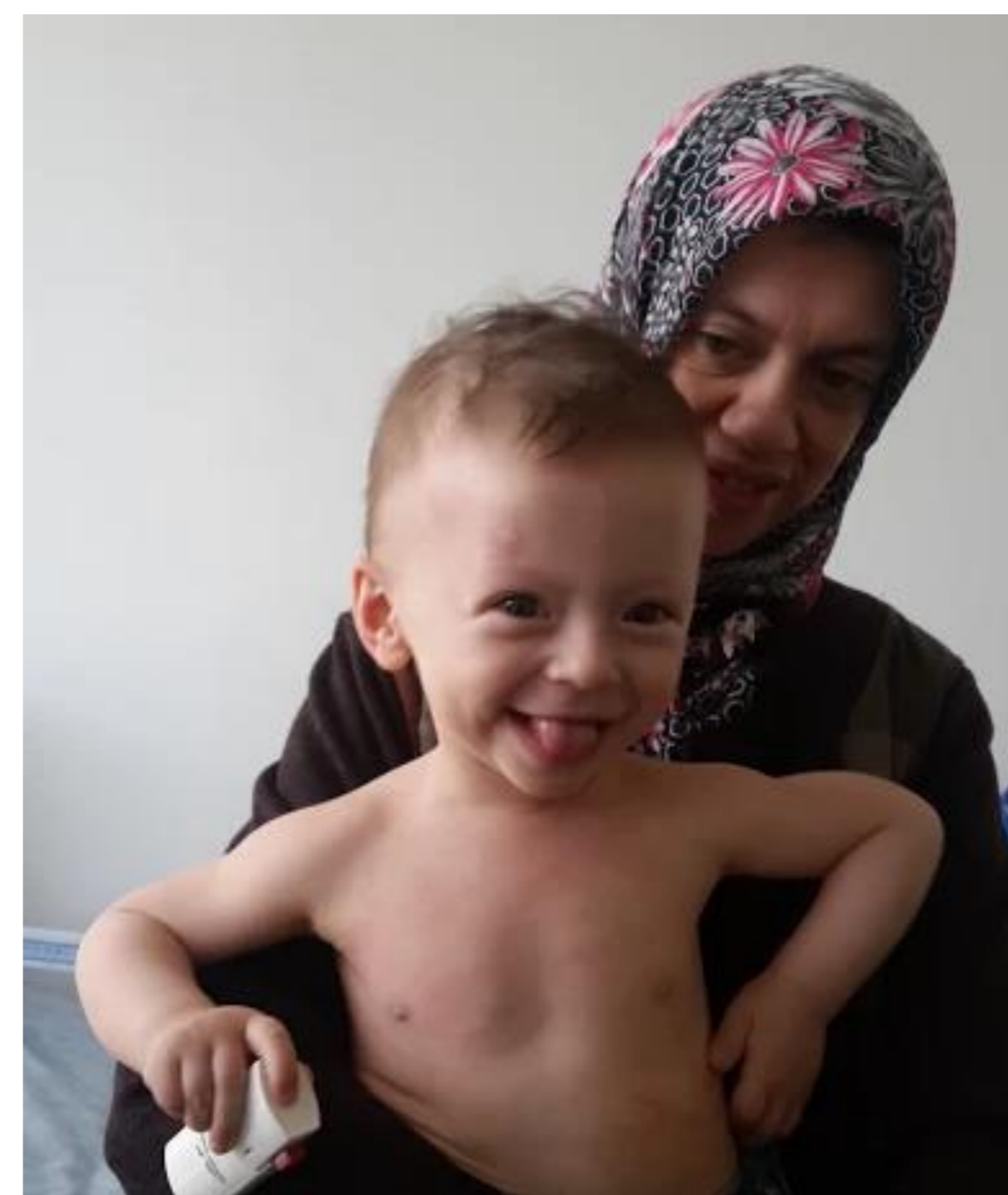
Picture 1: Patient with dismorphic face

CASE REPORT

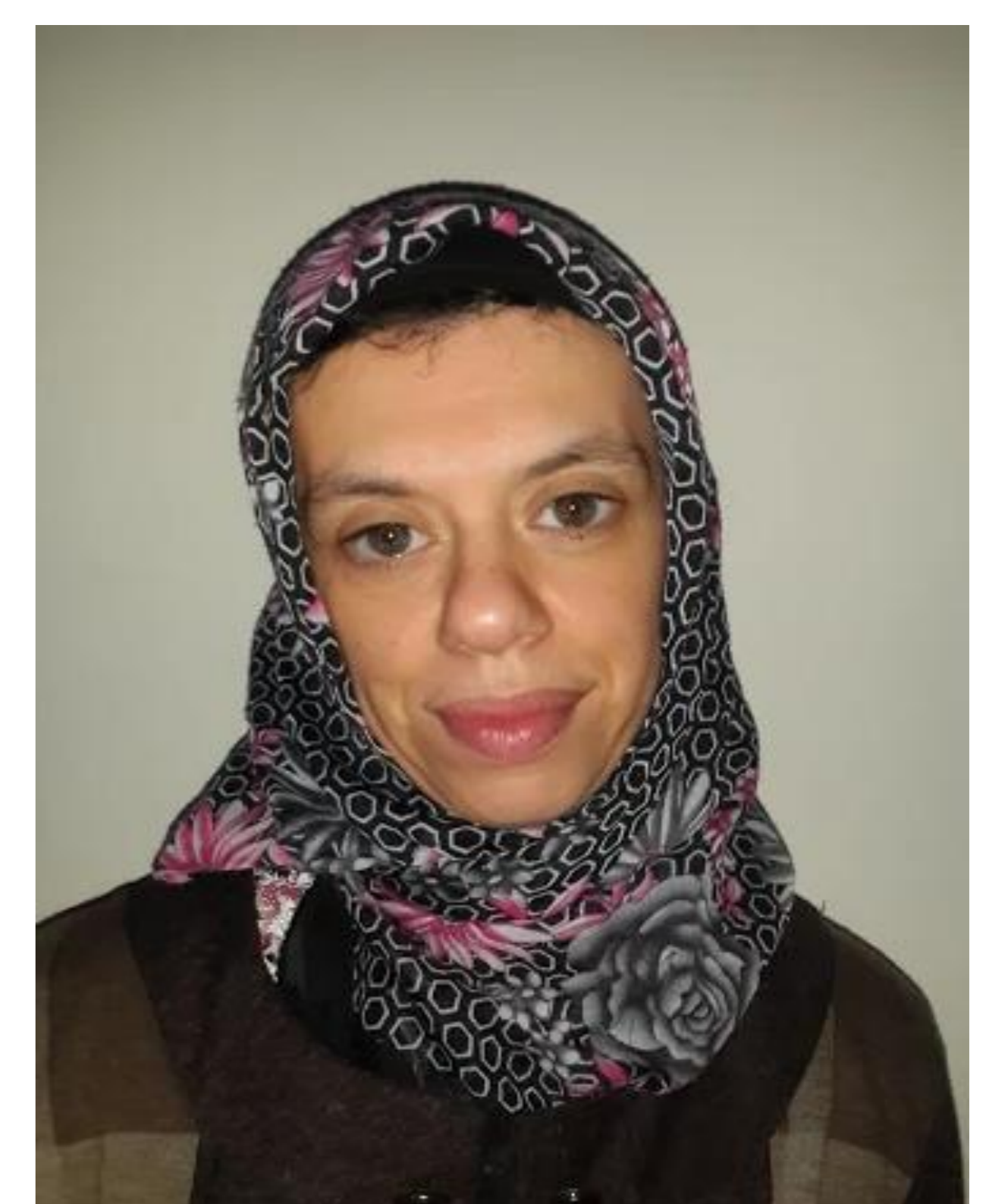
12-month-old boy was admitted with complaints of fever, vomiting, constipation, and fatigue for one week. His weight was 7.5 kg (<3p), his height was 70 cm (75p). Physical examination revealed prominent forehead, sunken nasal bridge, long philtrum, prominent lips, and periorbital puffiness (picture 1). There was 3/6 pulmonary systolic ejection murmur. Laboratory results revealed hypercalcemia (calcium(Ca): 15.8mg/dL). Ca restriction (400 mg/day), intravenous fluid for hydration (2000cc/m²) and intravenous furosemide (1mg/kg/dose) treatment were initiated. Laboratory studies disclosed high spot urine calcium/creatinine ratio (0,72), low PTH serum levels (3>pg/mL), but normal serum phosphate (4,6mg/dL), alkaline phosphatase (62 U/L) and 25-OH vitamin D (48ng/mL). Control serum Ca was measured 15 mg/dL. Third day calcium was detected 20,4mg/dL and due to persistent hypercalcemia, intravenous pamidronate (1 mg/kg) infusion added to treatment. His clinical problems resolved gradually. WS was suspected. Echocardiography revealed peripheral pulmonary stenosis. His mother's facial appearance was similar to her son's with prominent features of elfin face. Genetic analysis of both patient and mother revealed microdeletion of chromosome 7q11.23 which confirmed the diagnosis of Familial WS. Mother's laboratory results and echocardiography were normal. During follow up, mother was observed insufficient in terms of parenting skills and self-care whom psychological evaluation revealed mild mental retardation. 1 week, 1month, 6 months, serum calcium levels was, 10,9mg/dL, 10,6mg/dL, 10,3mg/dL.

DISCUSSION

We diagnosed WS in a hypercalcemic boy and his mother during her sons' inpatient follow up. We suspected WS in mother because of her typical craniofacial appearance and her weakness in daily living and parenting skills. We report autosomal dominant inheritance of WS in this family. The second most affected system is cardiovascular system in WS and the most commonly supravalvular aort stenosis is seen which is followed by pulmonary stenosis. The patient has peripheral pulmonary stenosis while his mother does not have any cardiological abnormalities. Another distinctive feature of the syndrome is overfriendly and emphatic personality (picture 2), which is accompanied by anxiety problems in adolescence and adulthood, disinhibited, distractible, socially isolated, and anxious in adulthood (picture3). D vitamin metabolism abnormalities are the most commonly blamed mechanism of the hypercalcemia. Lately overexpression of transient receptor potential channels (TRPC3) in WS patients' peripheral lymphocytes and intestines was defined. Although biphosphanates has not been approved in pediatric population, there have been five cases whom pamidronate was used in addition to traditional therapy for severe hypercalcemia in WS. To our knowledge, this is the sixth report on pamidronate use in severe hypercalcemia in Williams. We suggest that in addition to abnormalities in Ca absorption, increased bone resorption or increased osteoclastic activity might be component of hypercalcemia mechanism in WS patients. There have been side effects like hypertension, hypocalcemia and fever were reported with biphosphanates. We did not observe any side effects related to pamidronate.



Picture 2: WS infant with cheerful and social character



Picture 3: Mother with silent and introvert character

CONCLUSION

WS is a multi-system disorder that primarily affects connective tissue and the cardiovascular system. Although the syndrome is rarely vertically transmitted, suspected family members should be examined for chromosomal microdeletion. WS patients with infantile hypercalcemia who do not respond to traditional hypercalcemia therapy, pamidronate might be an effective and safe treatment option.

