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# Novel case of short stature and co-occurrence of SHOX gene mutation and Fanconi Anemia

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## Background

Fanconi anemia (FA) is a rare congenital disorder caused by mutations in any of over 16 documented genes leading to chromosomal fragility. Patients may present with physical manifestations including short stature or upper limb deformities, hematologic manifestations including progressive pancytopenia, or oncologic manifestations including solid tumors. Short stature (>2 SD below mean) is a common finding in FA and thought to be multifactorial. Both endocrine abnormalities, including impaired spontaneous GH secretion and hypothyroidism, and specific genetic mutations IVS4, have been implicated and are associated with more severe height deficiencies. Of note, a less severe degree of short stature has been documented in FA patients without these abnormalities without a clear underlying cause.

## Case

Patient presented to us at 11.5yrs of age for evaluation of short stature. Was diagnosed with Fanconi anemia at age of 4yrs, and has had history of poor weight gain and need for G-Tube feedings for 6 years. On examination patient was at -3.77 SD for height and -4.03 SD for weight, Tanner stage I, mild mesomelia, absent Madelung deformity, and otherwise normal examination. Biochemical evaluation was performed (Table 1), with low IGF-1 (-1.27SD) and whole gene deletion of SHOX gene. Bone age was delayed by 3 years. Growth hormone was initiated at 0.3mg/kg/week and has been tolerated well. We continue to monitor patient's growth and communicate frequently with hematology group following patient.

## Discussion

We present a novel case study of a 12-year-old male with Fanconi Anemia diagnosed at age 4 and short stature who was later found to have a co-occurring SHOX whole gene deletion. Mutations or deletions of the SHOX gene, located in the pseudodominant region of the X and Y chromosomes, have been implicated as a cause of short stature in patients with idiopathic short stature (ISS), and a cause of short stature and limb abnormalities in patients with Leri-Weill dyschondrosteosis (LWD) and Turner Syndrome. Previous co-occurrence of SHOX gene mutation and Fanconi Anemia has not been documented. Abnormalities in the SHOX gene may be partially responsible for short stature in patients with Fanconi anemia.

## Table 1

| Lab | Result |
|---|---|
| IGF-1 | 65 ng/ml |
| IGF-BP3 | 2 ug/mL |
| TSH | 2.02 UIU/mL |
| Free T4 | 1.2 ng/dL |
| Complete Metabolic Panel | Normal |
| ESR | 25 mm/hr |
| Celiac Screening | negative |

## Main references

1. Petrik et al. 'Endocrine Disorders in Fanconi Anemia: Recommendations for Screening and Treatment'. Journal of Clinical Endocrinology and Metabolism. March, 2015.
2. Wajnrajch et al. 'Evaluation of Growth and Hormonal Status in Patients Referred to the International Fanconi Anemia Registry'. Pediatrics. 107:4. 2001.
3. Giri et al. 'Endocrine Abnormalities in Patients with Fanconi Anemia'. Journal of Clinical Endocrinology and Metabolism. 92(7): 2624-2631.
4. Binder and Rappold. 'SHOX Deficiency Disorders'. Gene Reviews. NCBI Bookshelf. 2015.
5. Rappold et al. Deletions of the Homeobox Gene SHOX (Short Stature Homeobox) are an Important Cause of Growth Failure in Children with Short Stature'. Journal of Clinical Endocrinology and Metabolism. 87(3): 1402-1406. 2002.

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