CENTOGENE
THE RARE DISEASE COMPANY

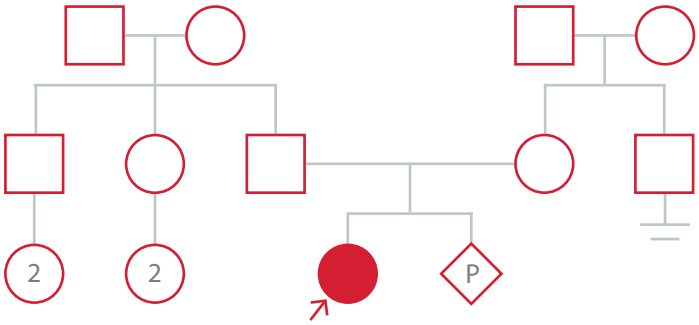
CentoDx®
CASE STUDY

CASE HISTORY

- 7 year old female with normal intelligence
- **Clinical features:**
  - prominent eyes, severe myopia
  - dental caries, molar hypoplasia
  - thin limbs, slender fingers, scoliosis, pectus carinatum, coxa vara, genu valgum and Harrison sulcus
- **Differential diagnosis**:
  - Stickler syndrome and spondyloepiphyseal dysplasia
- **Prior investigations:**
  - X-ray studies – abnormally shaped vertebral bones and epiphyseal & metaphyseal changes
  - CT study of the brain – mild prominence of the subarachnoid space

FAMILY HISTORY

- No family history of disease and no consanguinity
- Mother had an ongoing pregnancy of 13 weeks



TEST ORDERED

Clinical exome sequencing **CentoDx®**

RESULTS

GENE	VARIANT	ZYGOSITY	CLASSIFICATION	INHERITANCE	DISEASE
COL2A1	c.3563G>C p.(Gly1188Ala)	Het.	Pathogenic (Class I)	Autosomal dominant	Type II Collagenopathies (including spondyloepiphyseal dysplasia and Stickler syndrome type I)
FBN1	c.1285C>T p.(Arg429Ter)	Het.	Pathogenic (Class I)	Autosomal dominant	Marfan syndrome and Marfan-like syndrome

Two pathogenic variants detected - one copy each of a c.3563G>C p(Gly1188Ala) pathogenic variant in the COL2A1 gene1 and a c.1285C>T p.(Arg429Ter) pathogenic variant in the FBN1 gene2-4. Both variants have been previously reported as disease-causing in affected individuals.

POST-TESTING RECOMMENDATIONS

- Genetic counseling to discuss the next steps and options
- Parental carrier testing to determine recurrence risk
- Prenatal testing was performed upon request and the fetus was unaffected

CONCLUSION

CentoDx®
- was essential in identifying both diagnoses in the patient, as it is a broad panel covering all known relevant clinical phenotypes
- is a single versatile test to diagnose both the known, suspected phenotypes and unknown, complex phenotypes

Due to the timely and cost-effective diagnosis of the proband accurately using CentoDx®, the physician was able to appropriately counsel this family and provide the necessary care.

REFERENCES

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3. Rommel K et al. (2002) Mutation screening of the fibrillin-1 (FBN1) gene in 76 unrelated patients with Marfan syndrome or Marfanoid features leads to the identification of 11 novel and three previously reported mutations. *Hum Mutat*. 20(5):406–7.
4. Magyar I et al. (2009) Quantitative sequence analysis of FBN1 premature termination codons provides evidence for incomplete NMD in leukocytes. *Hum Mutat*. 30(9):1355–64

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Following GLP and GMP guidelines.

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