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

CentoDx®
RESULTS

<table>
<thead>
<tr>
<th>GENE</th>
<th>VARIANT</th>
<th>ZYGOSITY</th>
<th>CLASSIFICATION</th>
<th>INHERITANCE</th>
<th>DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>COL2A1</td>
<td>c.3563G&gt;C p.(Gly1188Ala)</td>
<td>Het.</td>
<td>Pathogenic (Class I)</td>
<td>Autosomal dominant</td>
<td>Type II Collagenopathies (including spondyloepiphyseal dysplasia and Stickler syndrome type I)</td>
</tr>
<tr>
<td>FBN1</td>
<td>c.1285C&gt;T p.(Arg429Ter)</td>
<td>Het.</td>
<td>Pathogenic (Class I)</td>
<td>Autosomal dominant</td>
<td>Marfan syndrome and Marfan-like syndrome</td>
</tr>
</tbody>
</table>

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

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