**COURSE CHALLANGE-CLINICAL CASE REPORT**

The proband is a female infant born to healthy parents with no known family history of neuromuscular disorders.

During pregnancy, morphological ultrasound showed reduced foetal movements.

Born after 37 weeks and 2 days of gestation, the baby presents with hypotonia, multiple contractures and arthrogryposis (Figure 1).

Serum creatine kinase level is within the normal range. Cardiac function is normal.

Facial muscle weakness is not observed.

A muscle biopsy is performed. Muscle pathology shows myopathic features and rimmed vacuoles (Figure 2). Proband’s DNA is analysed by exome sequencing and the results are analysed using a standard bioinformatic pipeline.

A picture containing application

Description automatically generated

Figure 1: Patient at neonatal age displaying multiple joint contractures in hyperextension involving hands and feet.

LC_1.tif

Figure 2: Muscle biopsy displaying rimmed vacuoles (HE stain)

**ACTIVITY REPORT**

Below is an example of written report that summarizes the genetic findings.

Part 1: Personal info and clinical data

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name** | **Surname** | **Gender** | **Date of birth** | **Sample ID** |
| **XXX** | **XXX** | **F** | **X/X/2022** | **n.a.** |

|  |  |  |
| --- | --- | --- |
| **Test performed** | **Sender** | **Indication for testing** |
| **Exome sequencing** | **Dr.XXX** | **Congenital myopathy** |

Task1: Summarize the observed phenotype using HPO terms (<https://hpo.jax.org/app/>)

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| --- | --- |
| Positive signs | Negative signs |
| Decreased fetal movement HP:0001558 |  |
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Part 2: Variant(s) of interest

Task 2: List the variant(s) of interest in the table below (first raw is an example of the needed info).

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| --- | --- | --- | --- | --- | --- |
| **Gene (symbol)** | **Genomic coordinates (hg19)** | **Annovar Annotation**  **(NM + exon + cDNA annotation + protein annotation)** | **gnomAD frequency** | **Ref\_depth** | **Alt\_depth** |
| COL12A1 | chr6:75843076 | NM\_004370:exon34:c.5727C>T:p.Y1909Y | 0.0006 | 67 | 79 |
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Task 3: Write a brief text commenting each identified variant of interest. The text should contain info about the variant interpretation and classification (do not forget to provide references if available).

Part 3: Conclusion

Task 4: Write a brief text summarizing the study (e.g., are the variants identified compatible with the observed phenotype? Is there a genotype-phenotype correlation? Would you suggest further genetic tests?)

Part 4: Incidental findings

Task 5: List possible incidental findings, if any (see https://www.coriell.org/1/NIGMS/Collections/ACMG-73-Genes)

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| --- | --- | --- | --- | --- | --- |
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