ARUP LABORATORIES | aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Jonathan R. Genzen, MD, PhD, Chief Medical Officer

PATIENT REPORT

Patient Age/Sex: Female

Specimen Collected: 01-Sep-22 14:00

CMAVM NGS, DelDup **|Received: 01-Sep-22 14:02** **Report/Verified: 01-Sep-22 14:06**

Procedure	Result	Units	Reference Interval
CMAVM Interp	Negative [f1]		
CMAVM Specimen	Whole Blood		

Result Footnote

f1: CMAVM Interp

BACKGROUND INFORMATION: Capillary Malformation-Arteriovenous Malformation (CM-AVM) Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Multifocal, randomly distributed, capillary malformations (CM) of the skin that may be associated with a fast-flow lesion, such as arteriovenous malformations (AVM) or arteriovenous fistula. Fast-flow lesions in the skin, muscle, bone, or central nervous system can cause life-threatening complications such as bleeding, congestive heart failure, or neurological consequences. Type 1 (CM-AVM1) is caused by pathogenic variants in the RASA1 gene; CM-AVM type 2 (CM-AVM2) is caused by pathogenic variants in the EPHB4 gene.

EPIDEMIOLOGY: Prevalence estimated at 1 in 20,000 for CM-AVM1 and 1 in 12,000 for CM-AVM2.

CAUSE: Pathogenic germline variants in the EPHB4 or RASA1 genes.

INHERITANCE: Autosomal dominant. De novo variants account for approximately 33 percent of pathogenic variants in RASA1 and 20 percent in EPHB4. Somatic mosaicism has been reported.

PENETRANCE: 90-99 percent

CLINICAL SENSITIVITY: Not well established but at least 65 percent.

GENES TESTED: EPHB4** (NM_004444), RASA1 (NM_002890)
** - Deletion/duplication detection is not available for this gene.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the RASA1 gene. Capture of all coding exons and exon-intron junctions of the EPHB4 and RASA1 genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity for MLPA is greater than 99 percent. The analytical sensitivity of sequencing is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of CM-AVM syndrome. This test only detects variants within the coding regions and intron-exon boundaries of the EPHB4 and RASA1 genes. Large deletions/duplications in EPHB4 are not assessed. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not

Result Footnote

f1: CMAVM Interp
been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.