In each cell of our body, we have 23 pairs of chromosomes. We inherit half of our chromosomes from our mother and half from our father. Twenty-two of those pairs are the same between males and females. The last pair of chromosomes is the sex chromosomes. Males have one X and one Y chromosome; females have two X chromosomes.

As the L1CAM gene is located on the X-chromosome, in females, when there is a mutation in one copy of the L1CAM gene on one of the X chromosomes, there is another copy of the gene located on the other X chromosome that can compensate for the mutated copy. No features of L1 syndrome are seen and the female is called a “carrier” of the condition. In males, there is only one copy of the L1CAM gene because there is only one X chromosome. When there is a mutation in this copy of L1CAM, no back-up copy exists and we see features of L1 syndrome.

L1 syndrome can be further broken down into groups of different features that tend to be seen together e.g. X-Linked Hydrocephalus with Stenosis of the Aqueduct of Sylvius (HSAS).

Image Description

5 week-old boy delivered at 38 weeks gestational age via cesarean section secondary to hydrocephalus noted on prenatal ultrasound. He was born with adducted thumbs, macrocephaly (49cm>98th percentile), broad anterior fontanelle, low set ears which are posteriorly rotated, flat nasal bridge and smooth philtrum possibly secondary to the congenital hydrocephalus.

Brain CT suggestive of congenital aqueductal stenosis with massive dilation of the lateral and third ventricles. Ventriculo-peritoneal shunt was placed on Day 1 of life. Brain MRI at 3 weeks of life continues to show macrocephaly with marked supratentorial ventriculomegaly and congenital aqueductal stenosis/occlusion and mild hypertelorism.

The family history is significant with a 20-year-old brother who was noted to have hydrocephalus at around 25 week's gestational age. He also has thumb adduction and had a shunt placement on the
fourth day of life at CHM. He is developmentally delayed and currently in a special needs school.

Patient’s Chromosomal microarray and sequencing of L1CAM gene is positive for *mutation in (c.1453C>T)*, providing confirmation of a diagnosis of a phenotype consistent with L1 syndrome. He has a form of **L1 syndrome called HSAS**(*X-Linked Hydrocephalus with Stenosis of the Aqueduct of Sylvius*). Individuals with HSAS often have severe hydrocephalus, adducted (or clasped) thumbs, spasticity of the muscles and intellectual disability. Management recommendations include placement of a shunt to treat the hydrocephalus and follow up with neurology for any associated seizures or spasticity. Continued monitoring of development is recommended so that affected individuals may reach to their fullest potential.

Genetic Counselling: L1 syndrome is an X-linked disease. Each pregnancy has 50% chance of transmitting the *L1CAM* pathogenic variant female carrier. Sons who carry *L1CAM* pathogenic variant will have disease; daughters who carry the pathogenic variant will be carriers. Affected males do not reproduce. Female relatives should have genetic testing and prenatal testing.

**Images**

![CT Brain Coronal View](image-url)

**Figure 1(A):** CT Brain Coronal View: Congenital aqueductal stenosis with massive dilation of the lateral and third ventricles. Extremely thin cerebral parenchymal mantle remains.
Figure 1(B): CT Brain Axial View: Congenital aqueductal stenosis with massive dilation of the lateral and third ventricles. Extremely thin cerebral parenchymal mantle remains.

Figure 2: MRI of Brain (Post VP Shunt placement): The lateral and third ventricles are markedly enlarged. The aqueduct is markedly stenosed. The fourth ventricle is not enlarged. As a result, there is marked macrocephaly. The cortical mantel is thinned and it is difficult to evaluate for cortical dysplasia. There is almost complete agenesis of Corpus Callosum. Cerebellum unremarkable. Bilateral Medullary Pyramid is not well defined.