# Knobloch syndrome

Knobloch syndrome (KS) is a rare autosomal recessive disorder associated with multiple ocular and cranial abnormalities. Occult occipital skull defect or encephalocele should raise suspicion of this disease. It is never reported in neurosurgical literature, possibly due to a lack of clinician familiarity, leading to underdiagnosis and inadequate management.

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Four patients originally presented for genetic evaluation of symptomatic structural brain malformations. Whole-genome genotyping, whole-exome sequencing, and confirmatory Sanger sequencing were performed. Using immunohistochemical analysis, Caglayan et al. investigated the protein expression pattern of COL18A1 in the mid-fetal and adult human cerebral cortex and then analyzed the spatial and temporal changes in the expression pattern of COL18A1 during human cortical development using the Human Brain Transcriptome database.

They identified two novel homozygous deleterious frame-shift mutations in the COL18A1 gene. On further investigation of these patients and their families, they found that many exhibited certain characteristics of Knobloch syndrome, including pronounced ocular defects. This data strongly support an important role for COL18A1 in brain development, and this report contributes to an enhanced characterization of the brain malformations that can result from deficiencies of collagen XVIII.

This case series highlights the diagnostic power and clinical utility of whole-exome sequencing technology-allowing clinicians and physician scientists to better understand the pathophysiology and presentations of rare diseases. They suggest that patients who are clinically diagnosed with Knobloch syndrome and/or found to have COL18A1 mutations via genetic screening should be investigated for potential structural brain abnormalities even in the absence of an encephalocele [1)].

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Venkateshappa reported a patient that also had seizures, which is a sporadic presentation of this syndrome.

They report a clinico-radiologic finding of a 7-year-old boy who presented with seizures, cataracts, and an occipital bone defect along with bilateral subependymal heterotopias and polymicrogyria.

This case highlights the importance of consideration of this syndrome in children with a midline occipital bone defect with or without encephalocele and seizures. Early recognition of this presentation is critical for obtaining access to appropriate genetic counseling and subsequent

monitoring and prevention of complications by surgical intervention [2].

# References

[1]
Caglayan AO, Baranoski JF, Aktar F, Han W, Tuysuz B, Guzel A, Guclu B, Kaymakcalan H, Aktekin B, Akgumus GT, Murray PB, Erson-Omay EZ, Caglar C, Bakircioglu M, Sakalar YB, Guzel E, Demir N, Tuncer O, Senturk S, Ekici B, Minja FJ, Šestan N, Yasuno K, Bilguvar K, Caksen H, Gunel M. Brain malformations associated with Knobloch syndrome–review of literature, expanding clinical spectrum, and identification of novel mutations. Pediatr Neurol. 2014 Dec;51(6):806-813.e8. doi: 10.1016/j.pediatrneurol.2014.08.025. Epub 2014 Sep 4. PMID: 25456301; PMCID: PMC5056964.

[2]
Venkateshappa BM, Raju B, Rallo MS, Jumah F, Suresh SC, Gupta G, Nanda A. Knobloch Syndrome, a Rare Cause of Occipital Encephalocele and Seizures: A Case Report. Pediatr Neurosurg. 2021 Mar 31:1-5. doi: 10.1159/000512719. Epub ahead of print. PMID: 33789317.