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Case Report: Ayme-Gripp Syndrome In A 3-Year-Old Male

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Abstract
This report documents the clinical course of Ayushman Pathak, a 3-year-old male with multiple congenital anomalies and developmental delay. His presentation included bilateral congenital cataracts, cleft palate, microcephaly, hypotonia, facial dysmorphism, and global developmental delay. MRI findings revealed Chiari Malformation Type I, periventricular leukomalacia, and encephalomalacia suggestive of prior hemorrhagic injury. Genetic testing confirmed a de novo pathogenic variant in the MAF gene (p.Pro59Leu), consistent with Ayme-Gripp syndrome, diagnosed at 1 year of age. The diagnosis provided a clear explanation for his multi-system involvement. This case highlights the critical role of early genetic screening and multidisciplinary care in managing complex pediatric neurodevelopmental disorders.

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I. Introduction

Ayme-Gripp syndrome is a rare, autosomal dominant disorder caused by mutations in the MAF gene, which encodes a transcription factor involved in eye, ear, and facial development. It is characterized by congenital cataracts, sensorineural hearing loss, developmental delay, intellectual disability, distinctive craniofacial features, and in some cases, growth and neurological abnormalities. Given its rarity, diagnosis is often delayed until genetic testing is performed. This case presents a classic manifestation of Ayme-Gripp syndrome in a 3-year-old male with congenital cataracts, cleft palate, developmental delay, Chiari malformation, and sensorineural hearing loss, confirmed via whole exome sequencing. The case

II. Case Report:

Ayme-Gripp Syndrome in a 3-Year-Old Male underscores the importance of integrating clinical, radiological, and genetic data to ensure accurate diagnosis and guide management in rare neurodevelopmental syndromes. In this case, the diagnosis of Ayme-Gripp syndrome was established at 1 year of age following genetic testing.

Patient Information
Name: Ayushman Pathak
Age: 3 years
Sex: Male
Birth History: Born at 34 weeks of gestation (preterm), CIAB, no NICU admission

Presenting Complaints:
- Poor weight gain
- Failure to thrive
- Global developmental delay
- Facial dysmorphism
- Bilateral congenital cataracts (operated)
- Cleft palate
- Microcephaly, simian crease, overriding toes, sacral dimple

Clinical Findings
Anthropometry:
- Weight: 9.7 kg

- Height: 92 cm
- Head Circumference (OFC): 41.5 cm (Microcephalic)

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- Chest Circumference: 51 cm
- Mid-Upper Arm Circumference (MUAC): 13 cm
- BMI: 11.97 (Underweight)

Neurological status:
- Gross motor delay
- Hypotonia

Facial features:
- Flat face, maxillary prognathism, cleft palate

Ophthalmological:
- Bilateral congenital cataracts, lens aspiration, anterior vitrectomy completed

Audiological:
- Sensorineural hearing loss on recent ear report

Diagnostic Assessment
MRI Brain (28 Jan 2023): Chiari Malformation Type I, periventricular leukomalacia, right temporo-occipital encephalomalacia, microhemorrhages in cerebellar hemispheres.
Chromosomal Microarray: No pathogenic CNVs; region of homozygosity on chromosome 10 (uncertain significance).
Whole Exome Sequencing: Pathogenic heterozygous p.Pro59Leu variant in MAF gene (Ayme-Gripp syndrome).

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Other Investigations: TORCH negative, ECHO normal.
Diagnosis
Confirmed Diagnosis:
Ayme-Gripp syndrome due to de novo MAF gene mutation.
Associated Conditions:
- Chiari Malformation Type I
- Bilateral congenital cataracts
- Profound sensorineural hearing loss detected by BERA test
- Periventricular leukomalacia
- Syndromic developmental delay

Diagnosis was made at 1 year of age based on whole exome sequencing.
Therapeutic Interventions
Surgical: Bilateral cataract extraction with anterior vitrectomy
Supportive: Physiotherapy, occupational therapy, nutritional support
Monitoring: Annual ophthalmologic, hearing, cardiac, and endocrine evaluations
Medical Management: Thyroxin Sodium 50 mcg daily (for hypothyroidism, if clinically indicated)
Follow-up and Outcomes

Case Report: Ayme-Gripp Syndrome in a 3-Year-Old Male At 3 years of age, the child is under regular follow-up with pediatric neurology, genetics, ophthalmology, audiology, and physiotherapy teams. Early intervention services are in place. Prognosis remains guarded, with expected progression of some symptoms, particularly hearing loss and growth issues.

III. Discussion

This case illustrates the importance of integrating clinical, radiological, and genetic data for early diagnosis of rare syndromes. The presentation of Ayme-Gripp syndrome in this patient was complex, with features overlapping other neurodevelopmental conditions. Chiari I malformation and signs of prior cerebral hemorrhage added to neurological morbidity. The diagnosis of a de novo MAF variant underscores the value of WES in idiopathic developmental delay.

IV. Conclusion

This case illustrates the clinical complexity and diagnostic challenges associated with Ayme-Gripp syndrome, a rare genetic disorder. The integration of detailed imaging studies, comprehensive clinical assessments, and molecular diagnostics was key in identifying the underlying etiology in this child with syndromic developmental delay. Early diagnosis allowed for tailored symptomatic management, anticipatory guidance, and appropriate genetic counseling for the family. Regular follow-up with multidisciplinary support has been essential in monitoring and managing his condition. This report emphasizes the need for early referral to genetic services when multiple congenital anomalies are present in pediatric patients. Patient Perspective Parents were counseled on the genetic nature of the condition, prognosis, and the importance of long-term

Case Report: Ayme-Gripp Syndrome in a 3-Year-Old Male multidisciplinary care. They were informed that the variant was de novo, meaning not inherited, and discussed reproductive options for future pregnancies. Informed Consent Consent for reporting and anonymized publication was obtained from the patient's legal guardians.

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Case Report: Ayme-Gripp Syndrome in a 3-Year-Old Male This case report documents Ayushman Pathak, a 3-year-old male with Ayme-Gripp Syndrome. The child presented with bilateral congenital cataracts, cleft palate, microcephaly, hypotonia, and developmental delay. MRI revealed Chiari Malformation Type I, periventricular leukomalacia, and encephalomalacia. Genetic testing confirmed a de novo MAF gene mutation (p.Pro59Leu). This case highlights the diagnostic importance of early genetic evaluation and multidisciplinary care in complex neurodevelopmental disorders.

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MRI Illustration: Chiari I Malformation & Encephalomalacia
Weight-for-Age Growth Chart (3 Years)
BERA Audiogram: Profound Sensorineural Hearing Loss
MAF Gene Mutation Pathway

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