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Hallermann Streiff Syndrome: A Rare Disorder

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Abstract **:** Hallermann streif syndrome (HaSS) a rare genetic disorder effecting 1 in every 1000 people globally. The rareness is a matter of concern due to its unavailability of immediate cure & yet more information on its etiology is required. The reported cases are the only source of information relied upon. The syndrome identified with many malformations observed at various regions in skin, hair, dental, facial & skull as Fontanelles, microcephaly, malarhypoplasia, micrognathia & retrognathia. Here we discuss about the syndrome discovery, clinical finding's along with reference case studies.

Keywords: Hallermann streiff syndrome, malformations, case studies.

INTRODUCTION :

Hallermann streiff syndrome (HaSS) was first discovered in 1893 by Aubry and was first explained completely by Hallerman in 1948 and then by streiff in 1950. Francois ruled out seven signs as a diagnosis criteria for HHS after extensive analysis of twelve cases. Its known by several names such as HSS, Francois dyscephaly syndrome, Hallermann Streiff Francois syndrome, oculomandibulo-facial syndrome, oculomandibulo-dyscephaly with hypotrichosis.

As varied symptoms and signs observed from case to case, all observations are noted and further investigated to develop a proper etiology of this rare disorder.

Table 1: HHS diagnosis criteria's seven signs with observed percentage effected

S.No	Sign's	% effected
1.	Dental abnormalities	(80-85)
2.	Short Stature	(45-68)
3.	Bird face/dyscephaly	(89-90)
4.	Atrophy of nose region	(68-70)
5.	specially Hypotrichosis	(80-82)
6.	Congenital Cataract	(81-90)
7.	Bilateral microphthalmia	(78-83)

Expected Life span: Approximately 47 years.

ETIOLOGY : The etiology of HHS is indistinct as most cases are sporadic (i.e., cause is unclear) or by genetic mutations, by two scientists schanzlin and pugliese found a defect in chromosome related to this syndrome. Gerinec described this syndrome in two generations

1. Autosomal recessive

2.Autosomal dominant inheritance patterns followed with denovo mutations.This syndrome is gender neutral and is result of dominant gene.

Francois described certain changes like alteration of elastin in connective tissues and hypothesized a minor and significant disturbance in glycoproteins metabolism.

So, the possible cause for HaSS includes:

- An asymmetric second bronchial arch defect during 5-6 week of gestation
- Paternal age
- Infections to mother during pregnancy.
- Exposure of toxins during pregnancy.

TABLE 2: clinical findings in various regions of Hallermann Streif Syndrome

Face	Ocular	Dental	Other	Head
• Micrognathia • Retrognathia Beak shape nose • Atrophy of skin • Hypotrichosis	• Congenital bilateral cataract. • Bilateral microphthalmia leads to blepharoptosis. • Nystagmus • Blue sclera • Glaucoma Palpebral fissures strabismus	• Malocclusion • Hypodontia • Anodontia Enamel hypoplasia Eruption of teeth before or after birth	• Premature birth • Low birth weight Growth deficiency	• Brachycephaly • Parietal or frontal bossing Microcephaly • Malar hypoplasia Delayed closing of fontanelles

The facial changes of nose, jaws can cause respiratory problems in children observed like:

a. Obstruction of upper airway due to small nostrils
b. Difficulty in swallowing and early respiratory infections due to micrognathia
c. Tracheomaladia is also reported in few cases
d. Heart failure due to tracheomalacia is also seen in some reports

Treatment:

1. Tracheostomy - to maintain effective airway and proper nutrient intake
2. Cataract removal in severe cases to preserve vision
3. Regular follow-ups followed by surgical intervention of nystagmus, entropion & ptosis to avoid amblyopia and prevent vision loss
4. Dental evaluation for good dental health
5. Various craniofacial surficial reconstructions for facial abnormalities
6. For anesthetic complications during surgery laryngoscope is used during intubation **Others:**
7. Early intervention
8. Genetic counseling
9. Nutritional counselling
10. Symptomatic treatment.

Now let's observe few reported cases with the following:

Case study report 1: (Peter robotta,et,al,2011)
Age: 9 years
Gender: male
Complaints: general mobility and progressing loss of teeth
Observations:
1.Bilateral cataract
2.spare hair
3.stature short
4.beak shape nose
5.dental abnormalities.
On examination:
1.small mouth opening.
2.development of definition was not as the boy's age.
Lab investigation: The radiograph showed permanent definition and underdeveloped roots
Treatment: dental prosthetics and symptomatic treatment.

Case study report 2(Nicholson AD,et,al,1995)
Age: 3 days old
Gender: female
Complaints: presented with
1.white spot in eyes
2.sparse eyebrow and eye lashes
3.shallow anterior chamber
4. respiratory tract Infections

General examination:
1.Beak nose
2.Short stature
3.Natal teeth
4. Atrophy of skin
Assessment:
1.Mother was given counseling
2.Immediate preventive care program and dietary hygiene instruction were given
Treatment:
1. For Dental malformations, Dental procedures with dental notion 51,61,74,and 84th teeth were done .
2. Since the child had repeated RT infections, lensectomy was done for left eye at 10 weeks.

Case study report 3: (Kirzioglu, et,al, 2009)
Age: 4 years old
Gender: female
Complaints: Dental deformities
History: Sleep Apnea and recurrent lower respiratory infections
Family history:
1.Consanguineous marriage of parents.
2.Father had Loss of hearing due to meningitis.
3.Mother had taken
4.Ampicillin-Sulbactam Treatment for tooth infection in first trimester.
Observation:
1.physical growth is retarded
2.Sparse hair on head eyelashes and eyebrow
3. Brachycephalic skull.
4.Blue sclera
5.Congenital cataract
6.Beak shaped nose
7.Small mouth opening.
Assessment:
1.Mother was given counseling.
2.Immediate preventive care program, dietary and hygiene instructions were given
TREATMENT:
1.For dental malformations, Dental procedures with dental notation 51, 61, 74 and 84 th teeth were done .

IN a recent study published they concluded that Hallermann-Streiff syndrome in a consnguineous family is possibily brought on by a novel biallelic frameshift in the TRPM7 gene.

Case study report 4: (Behjat Ul Mudassir,et,al,2023)
Age : 10yr 6 months
Gender: male
Complaints : patient was presented with all the 7 possible signs and symptoms of hallerman steriff syndrome

1. Severe intellectual disability
2. Cognitive impairment
3. Bilateral cataract
4. Microcephaly
5. Short stature
6. Pinched nose
7. Dental deformities

History : 1. Family history of neurodevelopmental disorder
2.Consanguineous marriage of parents

Assessment: Genomic study of the patient was done using whole exome sequencing. By using several in silico methods, such as SIFT, FATHMM mutation assessor, and Franklin genoxx software, the loss of function mutation was categorized as detrimental and pathogenic. After that, the HOPE protein modeling program was used to carry out the expression analysis. The TRPM7 gene experienced a unique glutamine frameshift at position 877, leading to protein truncation and loss of function, which prevents TRPM7 protein from carrying out typical biological functions throughout the early stages of brain development.

CONCLUSION: With many rare disorders around the world reported till date. Hallerman streiff syndrome reported cases till date are barely reaching 200 and still counting on the observation of the reported cases.
There is a need to understand the patient & their family both psychologically and morally for making them to take up treatment plan by effective patient councelling and also be aware of the disorder updated.

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