Short Discussion

Hallermann–Streiff syndrome: A concealing and expatiative overview

ABSTRACT

The Hallermann–Streiff syndrome is a congenital disorder classified by distinctive craniofacial malformations and significant orodental abnormalities. In spite of rarity, it is vital to know for a dentist because of involvement of multiple congenital abnormalities chiefly affecting the head and the face. Etiology is unknown in most of the cases but may occur as a result of mutations or changes to the genetic material. Early preventive care protocols, detailed oral hygiene instructions, and regular dental visits are essential for patients with this syndrome.

Keywords: Dental abnormalities, dyscephalic syndrome, genetic mutation, orodental abnormalities

INTRODUCTION

Hallermann–Streiff syndrome (HSS) as a rare genetic disorder is known to occur with multiple abnormalities. The signs and symptoms of HSS vary in range and severity among affected individuals.[1] It is a congenital disorder which is distinguished by multiple congenital abnormalities predominantly affecting the head and the face. Around 150 cases have been reported in the literature worldwide. There is no significant sex predilection. The syndrome has been explained as concordant and discordant in monozygotic twins, and an affected female giving birth to two normal children has also been reported.[2]

HISTORY

HSS was first incompletely explained by Aubry in 1893. It was then termed as oculomandibulo-dyscephaly syndrome or Francois Dyscephalic syndrome. Subsequently, HSS had acknowledged this disorder as separate from progeria and mandibulofacial dysostosis and coined the syndrome as HSS in the year of 1948 and 1950, respectively. In 1958, Francois studied 22 published cases and diagnostic criteria for this syndrome were given.[3] These include dyscephalia (scaphocephaly or brachycephaly) and bird face, dental anomalies, proportionate nanism, typical facies (micrognathia, condylar aplasia, and a thin pointed nose), dental anomalies, proportionate dwarfism, hypotrichosis, atrophy of the skin, bilateral microphthalmos, and congenital cataract. Almost all cases of the HSS are sporadic and are typically not associated with chromosomal anomalies.[4,5] Although, Gerinec *et al*.[6] have described the occurrence of this syndrome in two generations with no sex prediction and Schanzlin *et al*.[7] reported a chromosomal defect combined with it.

Richa Wadhawan[1], Himani Lau[2], Mayank Lau[3], Manish Sharma[4], Deepshikha Gogoi[5], Gopal Krishna[6], Dharti Narendra Gajjar[7]

[1]Department of Oral Medicine, Diagnosis and Radiology, Institute of Dental Education and Advance Studies, Gwalior, Madhya Pradesh, India, [2]Department of Conservative Dentistry and Endodontics, Institute of Dental Education and Advance studies, Gwalior, Madhya Pradesh, India, [3]Department of Prosthodontics, Pacific Dental College and Hospital, Udaipur, Rajasthan, India, [4]Sharma Dental Clinic, Morena, Madhya Pradesh, India, [5]Kaveri Dental Clinic, Sonapur, Assam, India, [6]Chahal Aesthetic Clinic, Banglore, Karnataka, India, [7]Ashirwad Dental Clinic, Chikhli, Gujarat, India

Address for correspondence: Dr. Richa Wadhawan, Department of Oral Medicine, Diagnosis and Radiology, Institute of Dental Education and Advance Studies, Gwalior, Madhya Pradesh, India.
E-mail: richawadhawan@gmail.com

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DISCUSSION

HSS is a congenital syndrome associated with oculomandibulofacial abnormalities and potentially difficult airways. It is a rare genetic disorder. Inheritance of the majority of cases of HSS appears to be sporadic.[8,9] Most cases are random, but some have mutations in the GJA1 gene (6q21-q23.2). The most likely hypothesis is that of a single mutant gene (dominant), with most cases representing fresh mutations. Recently, a defect of elastin and abnormal glycoprotein metabolism has been reported. Autosomal dominant and autosomal recessive inheritance has been equally suggested.[10] It is probably due to developmental disorder in the 5th–6th gestational week that results in an asymmetric second branchial arch defect.[11] The use of modern next-generation sequencing-based approaches for gene identification has tremendously improved our understanding of the molecular pathogenesis of the great majority of well-known syndromes, whereas only a few remain to be elucidated. HSS is such a disorder for which the molecular basis is still unknown, although it represents a highly recognizable phenotype. It is primarily described by distinctive malformations of the skull and facial regions such as hypoplastic mandible, microcephaly, and malar hypoplasia. In addition, there is typically an abnormal widening of sutures between certain bones of the skull and delayed closure of fontanelles at the front and back of the cranium.[8,12,13] Degenerative skin changes are also often present and largely limited to the scalp and nose. Due to such changes, the skin in these regions may appear unusually taut and thin, and regional blood vessels may seem unusually pronounced. Reproductive fitness may below, but rare affected individuals have had affected offspring. No significant sex predilection is seen. The facies are sometimes described as 'bird-like' with a beaked nose. Neonatal teeth may be present.[14] Upper air way obstruction may occur due to small nares and glossoptosis (tongue falling backward) secondary to micrognathia, and these may result in cor pulmonale.[15] Severe complications may include early pulmonary infection, respiratory embarrassment, obstructive sleep apnea, anesthetic risk, decreased thoracic compliance, and a marked response of growth hormone to arginine stimulation. No metabolic or chromosomal defect could be demonstrated in this patient. Tracheomalacia is a complication that can cause chronic respiratory insufficiency, causing biventricular cardiac failure and early death.[16] Reports have been evident of ocular features such as districhiasis, ptosis, iris atrophy, and peripapillary choroidal atrophy; cherry-red spot at macula, pale discs, and coloboma at the entrance of the optic nerve have also been reported.[17,18] Dental abnormalities are seen in 50%–80% of the cases. These abnormalities involve malocclusion, open bite, severe caries, enamel hypoplasia, supernumerary and neonatal teeth, hypodontia, oligodontia, or anodontia.[19] The loss of teeth may worsen glossoptosis and can cause other complications. Skeletal abnormalities may include an absence of fusion on the symphysis region. Radiographic examination such as orthopantomogram, lateral cephalogram, and radiographs of long bones is performed to detect bony abnormalities.[20] For further evaluation, the patient should be send for ophthalmological, gynecological, and ear, nose, and throat (ENT) doctor opinion. Evaluation of ophthalmological examination includes bluish sclera, nystagmus, microphthalmos, disorders of refraction and accommodation, sluggish and irregular pupil, glaucoma, and microcornea.[21] Evaluation of absence of axillary and pubic hair and noncommencement of menstrual cycle corresponding with the age is done by a gynecologist. ENT examination is done to evaluate airway passage and glottis closure.[22] Hutchinson–Gilford progeria is due to a *de novo* heterozygous mutation in the lamin A gene (LMNA) on chromosome 1q22 and is distinguished from HSS, as the patient has joint stiffness and repeated nonhealing fractures. Individuals with the disorder typically have normal intelligence, whereas in HSS, intelligence is impaired.[23] The absence of clinodactyly or clitoral enlargement and photosensitivity or deafness will possibly exclude bird-headed dwarf of Seckel and Cockayne syndrome, respectively, though these have in common the bird facies.

Cockayne syndrome, with approximately 80% have mutations in the ERCC6 (excision repair cross-complementation group 6) gene.[24] Wiedemann–Rautenstrauch syndrome is an extremely rare genetic disorder and is inherited as an autosomal recessive genetic trait. It has been suggested that the syndrome might be caused by biallelic variants in POLR3A and is characterized by neonatal progeroid appearance, prenatal and postnatal growth deficiency, and subcutaneous lipoatrophy. Most infants and children with this syndrome have unusually thin arms and legs, abnormally large hands and feet, progressive neurological and neuromuscular abnormalities, varying degrees of intellectual disability, and psychomotor retardation. Head appears large in contrast to microcephaly in HSS.[25] Among children who present with microcephaly and bilateral congenital cataracts with small eyes, one should also consider MICRO syndrome, a rare autosomal recessive disorder characterized by microcephaly, microphthalmia, microcornea, congenital cataracts, optic atrophy, corpus callosum hypoplasia, severe intellectual disability, spastic diplegia, and hypogonadism. This disorder is caused by a mutation in the RAB3GAP2 gene on chromosome 1q41; the

RAB3GAP1 gene on 2q21.3; the RAB18 gene on 10p12.1; or the TBC1D20 gene on 20p13.[26]

TREATMENT

The treatment for HSS depends on the specific signs and symptoms present in each affected individual. Early disease management for infants may include monitoring of breathing, consideration of tracheostomy, and various measures to improve feeding and ensure sufficient intake of nutrients. Furthermore, early surgical removal of cataracts may be recommended to help to preserve vision. Tracheomalacia should be considered in a patient with HSS who presents with an unusual cry, stridor, choking, or apnea.[27] At an appropriate age, surgical reconstruction of certain craniofacial malformations (particularly the mandibular and nasal region) should be done. For some affected infants and children with heart defects, medical treatment and/or surgical intervention may be recommended. Some affected individuals may have a risk of anesthetic complications since endotracheal intubation and laryngoscopy may be difficult due to upper airway obstruction. Intubation may be required for the delivery of oxygen or anesthetic gases during surgery, and laryngoscope acts as an aid in helping to identify the vocal cords and is used before intubation. An endotracheal tube is then passed through the oral cavity down the throat and into the windpipe. The greatest anesthetic challenge lies in the maintenance of an appropriate airway due to upper airway deformities which make mask ventilation, laryngeal exposure, and tracheal intubation difficult. Nasal lipofilling has been used to treat the atrophy of the nasal skin, resulting in improvement in nasal skin color and texture.[28] The dental problems need thorough treatment with an interdisciplinary approach. Early preventive care protocols, detailed oral hygiene instructions, counseling of the parents, and regular dental visits are necessary for patients with this syndrome. Patients should be recommended oral prophylaxis, extraction of grossly carious and mobile teeth, and root canal treatment in all the existing teeth followed by abutment preparations for overlay dentures. Medical treatment in such patients is not mandatory after patients reach adulthood, though some ophthalmologic problems may need. To avoid unfavorable sequelae and facilitate future nutritional intake, every possible effort should be made to preserve these prematurely erupted deciduous teeth until the eruption of successor permanent teeth can be confirmed. Also, because individuals with HSS are predisposed to developing severe dental caries so ensuring and maintaining good oral hygiene is essential. It may be difficult to perform root canal treatment and other therapies to preserve a tooth with underdeveloped roots, and therefore, these patients need appropriate, frequent pediatric dental evaluations.[29]

CONCLUSION

Despite being a rare syndrome, this syndrome has to be included in differential diagnosis of other syndromes. An interdisciplinary approach has to be undertaken for the benefit of the patient. In this review, we summarize the current knowledge on the phenotypic traits and present innovative future strategies for gene identification.

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Conflicts of interest

There are no conflicts of interest.

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