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**Oculo-auriculo-fronto-nasal syndrome with Duane retraction syndrome and
dysplastic bony structure in the midline of nose**

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Abstract

Oculo-auriculo-fronto-nasal syndrome (OAFNS) is a rare anomaly characterized by features overlapping those of frontonasal dysplasia (FND) and the oculo-auriculo-vertebral spectrum (OAVS)¹. FND features malformation of frontonasal process-derived structures, characterized by anomalies in the central portion of the face. OAVS is characterized by developmental anomalies of the first and second pharyngeal arches. OAFNS is a condition with clinical features of both FND and OAVS.

Here, we present the case of a male with OAFNS who not only exhibited typical OAFNS symptoms but also a dysplastic bony structure that bridged the anterior nasal spine and inferior nasal bones, and unilateral type 3 Duane retraction syndrome (absence of right-eye abduction). Abnormal nasal bones are characteristic of OAFNS; such abnormalities are absent from FND and OAVS. We reduced the dysplastic nasal bony structure via open external rhinoplasty, followed by lateral nasal osteotomy, when he was 16 years of age. The nasal dorsum appeared natural after surgery and he was satisfied with the result.

Introduction

Frontonasal dysplasia (FND) is a complex malformation characterized by abnormalities involving the central portion of the face, especially the eyes, nose, and forehead².

Oculo-auriculo-vertebral spectrum (OAVS) is associated with structural anomalies arising from the embryonic first and second branchial arches, including microtia, preauricular tags, facial asymmetry, mandibular hypoplasia, and epibulbar

lipodermoids³. In addition, vertebral, cardiac, renal, and cerebral abnormalities have been reported⁴. Although the latter features may constitute a different syndrome, Carey

and Yong described a patient with features of both FND and OAVS⁵. Subsequently,

Johnson et al. used the term OAFNS⁶ to describe such cases. Since the first OAFNS patient was described, at least 40 more have been reported⁷. Furthermore, in 2013,

Evans et al. reported that OAFNS patients exhibited nasal ossification abnormalities, whereby bony maxillary structures were absent in those with either FND or OAVS⁷.

Here, we present an OAFNS patient with a dysplastic component of the anterior nasal septum connected to a prominent anterior nasal spine. Also, ocular abduction was

absent on one side; this is characteristic of Duane retraction syndrome (DURS). To date no case of OAFNS accompanied by DURS has been reported.

Patient

The patient was the first-born male of healthy parents, and was delivered full-term at 41 weeks and 1 day of gestation. The pregnancy was free of complications. His mother did not suffer from any disease during pregnancy, did not smoke or drink alcohol, and was not exposed to any environmental risk factors during pregnancy. He first visited our department at 1 month of age. His facial features included a right-sided cleft lip and alveolus, a median cleft alveolus and a median lip notch, a wide nasal bridge and ridge, orbital hypertelorism, facial asymmetry, and bilateral preauricular skin tags (Fig. 1). He showed severe sensorineural hearing loss in the right ear. Renal ultrasound was normal but both chest films and clinical findings revealed pectus excavatum. Ophthalmological examination revealed mild right-eye esotropia in the primary position. We performed an ocular motility examination, which revealed complete absence of abduction and a partial adduction deficiency in the right eye. Right-eye globe retraction and narrowing of the palpebral fissure were also evident. The left eye was normal and we diagnosed

unilateral type 3 DURS. He had no other medical problems and there was no family history of any similar condition.

Results

We first treated the cleft lip and alveolus. The right-sided cleft lip was repaired and the bilateral skin tags were excised at 5 months of age. Secondary bone grafting (SBG) of the right alveolar cleft was performed at 10 years of age, with SBG of the median alveolar cleft performed in the following year. When he was 16 years of age, we planned rhinoplasty to treat the nasal deformity, the wide nasal ridge, and the bifid nasal tip. A preoperative computed tomography (CT) scan of the facial bones revealed a dysplastic bony component of the anterior nasal septum (corresponding to the tip of the nasal bone) connected to a prominent anterior nasal spine (Fig. 2); this formed a dysplastic bony bridge approximately 1 cm in width.

Surgery was performed with an open, external rhinoplastic approach involving reduction of the dysplastic bony structure that bridged the anterior nasal spine and the nasal bones, lateral nasal osteotomy, repositioning of the lateral alar cartilage, and subdermal soft tissue reduction in the lateral nasal wall region to correct the wide flat nasal bridge and ridge. Although alar asymmetry remained, the dorsum appeared natural

after surgery and the patient was very satisfied with the result (Fig. 3).

Discussion

FND and OAVS are both well-recognized clinical entities. FND is an etiologically heterogeneous developmental condition featuring malformation of the frontonasal elevation and anomalies of the eyes, forehead, and nose⁸. FND is defined by the presence of two or more of the following symptoms: ocular hypertelorism, a broad nasal root, a midline facial cleft affecting the nose and/or upper lip and palate, cleft alae nasi, a hypoplastic nasal tip, anterior cranium bifidum, and/or a V-shaped frontal hairline⁹. In 1952, Goldenhar described the characteristic features of the condition, which include epibulbar dermoids, pre-auricular skin tags, mandibular asymmetry, and cervical vertebral abnormalities (“Goldenhar syndrome”)¹⁰. Later, Gorlin et al. reported similar cases and suggested use of the term oculo-auriculo-vertebral dysplasia¹¹, which was later changed to OAVS by Cohen¹².

FND has been suggested to reflect arrested migration of olfactory epithelium into the nasal capsule during weeks 4–6 of embryogenesis¹³. OAVS involves structural anomalies that arise from the embryonic first and second branchial arches, the first

pharyngeal pouch, the first branchial cleft, and the primordia of the temporal bone¹³.

Although FND and OAVS are well-recognized as distinct clinical entities, they may be embryologically linked. The medionasal prominence characteristic of FND is derived from the midbrain/forebrain neural crest; the maxillary and mandibular prominence characteristics of OAVS, derived from the first and second branchial arches, arise from the midbrain/hindbrain neural crest⁷. OAFNS is caused by abnormal development of the first and second branchial arches, and by abnormal morphogenesis of the maxillary processes.

Tunc et al. listed 10 symptoms of OAFNS¹⁵. Our case had six of these: microtia, preauricular tags, a notched nasal tip/bifid nose, cleft palate/lip, mandibular hypoplasia, and facial asymmetry. None of the four signs related to eyes/nervous system was recorded in our case: epibulbar dermoid, midbrain lipoma, encephalocele, or vertebral defect. Apart from the 10 major symptoms, Tunc et al. also reported clitoral hypertrophy, premaxillary teeth, and an inguinal hernia, all of which were absent in our case.

Interestingly, our case exhibited complete absence of right-eye abduction; we diagnosed unilateral type 3 DURS. This condition is within the spectrum of congenital ocular

motility disorders, characterized by limitation of horizontal duction in association with globe retraction and consequent narrowing of the palpebral fissure during adduction, caused by dysinnervation of extraocular muscles by branches of the oculomotor nerve¹⁶.

No case report of concurrent OAFNS and DURS has appeared; however, we consider that DURS may co-occur with OAFNS, because DURS is occasionally observed in patients with other genetic diseases including OAVS¹⁷.

In 2013, Evans et al. reported on five OAFNS patients with abnormalities in the anterior nasal spine and nasal bones. The anomalies spanned the spectrum of nasal ossification, ranging from mildly dysplastic nasal bones with prominent anterior nasal spines to severely dysplastic, spoon-shaped flared nasal bones with large nasal spines. Such abnormalities in nasal ossification are not evident on the CT scans of patients with FND and OAVS, suggesting that the spectrum is unique to OAFNS patients⁷. Our case exhibited a dysplastic bony structure in the anterior nasal spine and nasal bones; this was specific to OAFNS. A moderately dysplastic bony structure bridged the anterior nasal spine and nasal bones, confirming our OAFNS diagnosis. The dysplastic structure

affected the appearance of the nasal dorsum, which appeared natural after rhinoplasty involving surgical reduction of the bony structure.

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Figure legends

Figure 1.

Clinical facial features at 5 months of age: (A, B) Cleft lip on the right side, median lip notch, wide nasal bridge and ridge, orbital hypertelorism, and facial asymmetry. (C)

Median and right cleft alveoli.

Figure 2.

(A) The facial appearance prior to rhinoplasty (at age 16 years); the wide nasal bridge and ridge remained evident. (B) Frontal and lateral views of a surface-rendered, low-dose three-dimensional computed tomography (CT) scan of the head and face obtained prior to rhinoplasty; the white region indicates an abnormal anterior nasal spine forming a bridge with the inferior nasal bones.

Figure 3.

(A) The facial appearance after rhinoplasty; the shape of the nasal bridge was improved but the alar asymmetry persisted. (B) Frontal and lateral views of a surface-rendered, low-dose three-dimensional computed tomography (CT) scan of the head and face after rhinoplasty. The abnormal anterior nasal spine bridged with the inferior nasal bones was now sharper.