



Incidental Finding of Cervical Vertebrae Anomaly Yields to an Undiagnosed Case of Crouzon Syndrome

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Abstract

Crouzon syndrome is an autosomal dominant, rare genetic disorder often demonstrating complete penetrance and variable expressivity. It is frequently associated with cervical vertebrae abnormalities which often remain undetected. This article reports the case of an incidental finding of cervical vertebral anomaly of atlanto-occipital assimilation in an 8.5 year old boy who reported with chief complaint of inability to eat food properly, midfacial hypoplasia and class III malocclusion. When investigated thoroughly the case was identified as an undiagnosed case of Crouzon syndrome with Arnold Chiari Type I malformation with syringomyelia and asymmetry of atlanto-occipital joint. The patient's neurological examination revealed early signs of quadriparesis and was immediately taken up for posterior cranial fossa decompression surgery. It becomes extremely imperative for an orthodontist to know the cervical vertebral anatomy and associated anomalies and to seek an appropriate referral, as he may be the first to intercept them. Further investigation are mandatory for any underlying associated disorder, as these findings can be of great importance for patients in whom these anomalies assume clinical significance necessitating early/immediate management or lifestyle changes to prevent or delay aggravation of the pathology.

Keywords: Crouzon syndrome; Cervical anomalies; Arnold chiari malformation; Syringomyelia; Craniosynostosis

Introduction

The lateral cephalogram is an important diagnostic radiograph used in clinical orthodontics and an orthodontist is often the first physician to study the skeletal craniofacial morphology of the patient when they seek orthodontic treatment. However, it is seen that cervical spine anatomy is often overlooked and omitted in the routine lateral cephalometric assessment. It is vital to study the cervical vertebrae anatomy as many cervical abnormalities do not manifest themselves symptomatically until adolescence or young adulthood and an orthodontist may be the first to detect some of these [1].

Assimilation of the atlas to occiput, basilar invagination, os-odontoideum, congenital synostosis, congenital vertebral fusion, increased atlanto-dental interval are few cervical vertebrae anomalies which an orthodontist can diagnose from the lateral cephalogram [2]. These aberrations should be detected at the earliest, corroborated with clinical findings if present, referred to the appropriate specialist for detailed investigation of any underlying pathological condition, which may require immediate/early intervention.

In 1912 French Neurosurgeon Octave Crouzon first described the hereditary syndrome of craniofacial dyostosis in a mother and son [3] characterized by triad of premature craniosynostosis, midface hypoplasia and exophthalmos. Crouzon syndrome (OMIM NO 123500) is the most frequent form of syndromic craniosynostosis with an approximate birth prevalence of 1/25,000 - 1/50,000 [4]. This condition is often associated with cervical abnormalities such as

butterfly vertebrae and fusion of the bodies and the posterior elements. 18% of the cases have cervical fusion of C2-C3/ C5-C6 vertebrae [5,6] and 70% of patients with Crouzon syndrome present with Chiari malformation Type I [7,8].

Arnold Chiari malformation (CM) Type I is a congenital anomaly defined as the descent of the cerebellar tonsil through the foramen magnum into the upper cervical region. Normally the cerebellar tonsils are confined within skull; however, in subjects with CM, the tonsils descend downwards to the level of the first and sometimes the second cervical vertebra. Patients with CM Type I may present with a variety of symptoms and signs such as headaches to severe myelopathy and compromised brain stem [9-11]. In 50-70% of the patients with CM, blockage of cerebrospinal fluid (CSF) leads to the formation of Syringomyelia (Syrinx=a tube; myelia from the Greek=spinal cord) which is a cyst containing fluid (normally CSF) within the substance of the spinal cord. Syringomyelia is characterized with symptoms which include muscle weakness of arms and legs, scoliosis, dissociated sensory loss, urinary incontinence, dysreflexia, male impotence etc [9,10]. It becomes extremely crucial to recognize such clinical signs and symptoms if cervical anomaly is suspected/diagnosed in the lateral cephalogram.

Herein we present an 8 year old boy who reported to our hospital for orthodontic treatment. Incidental finding of cervical vertebrae anomaly when further investigated led to an undiagnosed case of Crouzon syndrome with Arnold Chiari I malformation and syringomyelia. The patient was immediately taken up for posterior fossa decompression surgery. The purpose of this case report is firstly, to highlight importance of cervical anatomy evaluation on a lateral cephalogram. Secondly to increase the awareness of identification of

cervical vertebral abnormalities and associated clinical signs and symptoms of underlying pathology if present by an orthodontist, which may well be life threatening and requires immediate appropriate referral for further evaluation and medical intervention. Thirdly to highlight the clinical signs and symptoms, morphological and radiological features associated with Crouzon syndrome.

Case Study

An 8 year old boy reported to our dental centre with the chief complaint of difficulty in eating, inability to close his mouth properly and a forwardly placed mandible. The medical history revealed no history of any congenital disorder or any long term hospitalization. There was no relevant family history; the patient's mother had experienced anormal pregnancy and delivery. The patient complained of stiffness in the neck since last 6 months for which no medical treatment was sought. Patient presented with the history of frequent visit to ophthalmologist for recurrent infections in the eyes since last 2 years. Dental history revealed no previous visit to any dental practitioner and early eruption of both maxillary and mandibular permanent teeth at the age of 8.5 years.

Assessment

Extra-oral Assessment

On general examination the patient had short stature and stiff upper body. Extraoral examination (Figure 1) showed frontal bossing, marked facial asymmetry with chin deviated towards the right, hypertelorism, midface hypoplasia and low set ears. Patient had short neck and difficulty in turning his neck on both right and left sides. The patient also had abnormal quality of speech and when questioned, parents noticed the change in the voice since last six months; however, no medical consultation was sought for the same.



Figure 1: Extra-oral photographs demonstrating cephalic and facial asymmetry, hypertelorism, frontal bossing, low set ears and midfacial hypoplasia.

Intra-oral Assessment

Intraoral examination (Figure 2) revealed early eruption of complete permanent dentition in the mandibular arch. Maxillary arch exhibited early eruption of premolars, decreased maxillary transverse dimension with bilateral posterior cross bite and retained upper right primary second molar and upper left primary canine. There was transient bilateral lateral open bite due to early loss of primary dentition.

Patient had negative overjet with class III incisor relationship and non-specific molar and canine relationship bilaterally. Patient also exhibited moderate crowding in the maxillary arch and mild crowding in the mandibular arch. Dental caries was seen in relation to upper right primary second molar and upper left primary canine. Upper right primary second molar also exhibited grade III mobility indicating an early eruption of the succedaneous tooth.



Figure 2: Intraoral photographs of the patient in mixed dentition with anterior cross bite and transient bilateral open bite due to premature loss of primary teeth.

Radiographic Assessment:

Orthopantomogram (Figure 3) revealed early eruption of permanent dentition at the age of 8.5 yrs. In order to determine the cause for premature eruption of permanent dentition patient was referred for hand wrist radiography to ascertain his skeletal age and associated blood investigations. Hand wrist radiography revealed that his bone age coincided with his chronological age (Figure 4).

Blood investigations revealed growth hormone, alkaline phosphatase, IGF1, TSH, Total T3, Total T4 levels within normal limits. Patient's growth velocity chart showed normal growth with his stature and weight between 25th-50th percentiles for his age. The patient was diagnosed with an unexplained rare idiopathic early eruption of permanent dentition at the age of 8.5 yrs.



Figure 3: Orthopantomograph demonstrating early eruption of permanent dentition

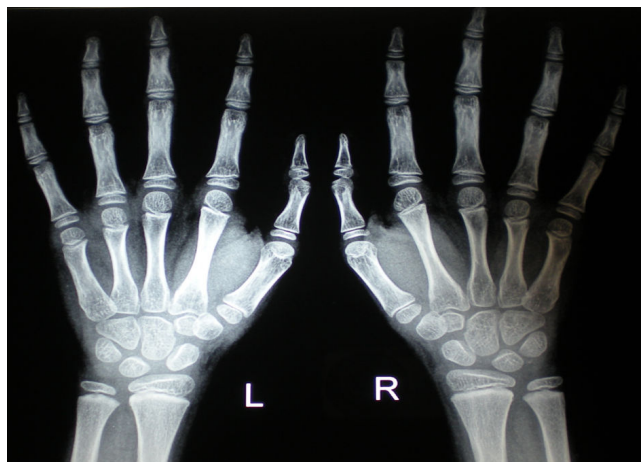


Figure 4: Hand wrist radiograph depicting patient's skeletal age coinciding with his chronological age.

Lateral cephalogram (Figure 5) revealed midface hypoplasia, class III skeletal malocclusion with ANB=-4°C. Patient also exhibited vertical growth pattern with GoGn-SN =35°C. On careful examination cervical vertebral column showed partial atlanto-occipital assimilation and abnormally positioned odontoid process. Collaborating with clinical signs and symptoms of stiffness in the neck since last 6 months the patient was referred to the radiologist for further evaluation and opinion. Cervical extension and flexion radiographs (Figure 6) confirmed asymmetric atlanto-occipital assimilation with the lateral mass on the left partly fused with the occiput. No scoliosis of the cervical spine was seen.

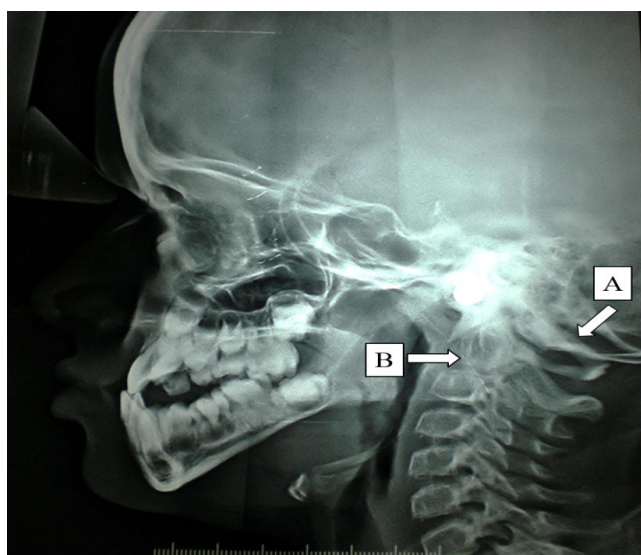


Figure 5: Lateral cephalometric radiograph demonstrating Class III malocclusion with midface hypoplasia, vertical growth pattern, partial asymmetric atlanto-occipital assimilation (A) and abnormally positioned odontoid process (B).

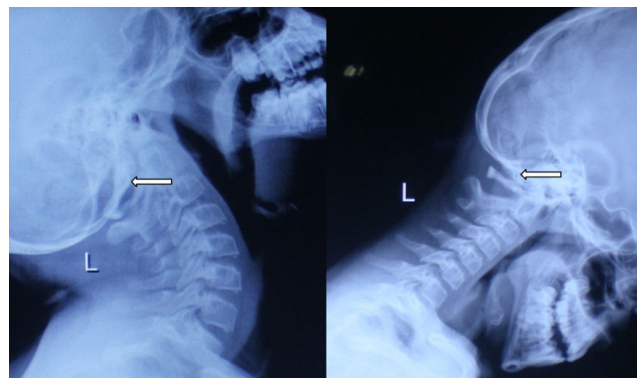


Figure 6: Lateral extension and flexion radiograph of the cervical spine demonstrating asymmetric partial assimilation of the atlas into the occiput.

The radiologist recommended a magnetic resonance image (MRI) of the cervical spine. MRI (Figure 7) obtained showed odontoid peg projected posteriorly and superiorly into the posterior cranial fossa leading to severe compression of the medulla which was deformed and compressed against the cerebellar hemispheres. The tonsils were peg like and project 9 mm below the foramen magnum. A short segment syrinx was seen at the level of C4 and C5. The maximal width of the syrinx was 4.4 mm, the cord was expanded and the peripherally placed cord parenchyma thinned. The case was diagnosed as Arnold Chiari Malformation Type I with syringomyelia and asymmetric atlanto-occipital assimilation.

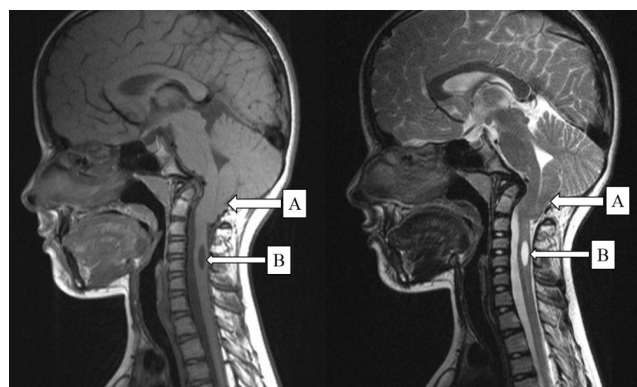


Figure 7: Sagittal T1 and T2 weighted magnetic resonance imaging shows cerebellar tonsil herniation (A) into the foramen magnum (CM Type I) with accompanying syringomyelia (B) between C4 and C5 with the maximum thickness of 4.4 mm.

Discussion

Lateral cephalometric roentgenographic examination of the cervical spine may reveal a pathologic disorder in asymptomatic as well as in symptomatic subjects. During the lateral cephalometric radiographic assessment of the patient; cervical anomaly of atlanto-occipital assimilation was incidentally diagnosed. Preliminary investigations of

this incidental finding steered us to an undiagnosed case of Arnold Chiari malformation Type I with syringomyelia.

Arnold Chiari malformation Type I is generally asymptomatic during childhood and often manifests itself with headaches which are often aggravated by valsalva maneuvers such as yawning, laying, crying, coughing or sneezing. Other symptoms include dizziness, vertigo, nausea, nystagmus, tinnitus, sleep disturbances, dysphagia, impaired coordination, facial pain, dystonia and chronic fatigue, change in voice etc [9-11]. Diagnosis of CM is made through a combination of patient history, neurological examination and an MRI of cervical spine which shows a downward herniation of the cerebellar tonsils greater than 5 mm below the foramen magnum. Patient presented with a history of abnormal change in speech since last 1.5 years however, no medical attention was sought for the same. In the CM patients blockage of cerebrospinal fluid (CSF) generally causes a syrinx to be formed which eventually leads to syringomyelia. Syringomyelia present with a variety of symptoms ranging from neck and arm pain through to fairly severe disability, with muscle weakness and paralysis [9,10]. Syringomyelia was diagnosed in our patient with a syrinx segment at the level of C4 and C5 (Figure 7).

On further physical examination of our patient, attention was drawn towards the patient's facial and cephalic asymmetry, class III skeletal profile, midface deficiency, frontal bossing, shallow orbits, hypertelorism, low set ears, recurrent conjunctivitis and other features resembling craniosynostosis. Further genetic investigations confirmed the diagnosis of Crouzon syndrome. Craniosynostosis involves premature fusion of cranial sutures as early as in utero thereby causing abnormal bone growth and facial deformities. The order and rate of suture fusion determine the degree of deformity and disability. CM Type I has a tendency to accompany syndromic craniosynostosis more commonly than sporadic synostosis [12] and is seen in 70% of patients with Crouzon syndrome [7,8]. The premature fusion of these cerebral sutures especially the lambdoid suture which results in a relatively small posterior fossa has been accepted as the probable etiological cause for the development of CM Type I in patients with syndromic craniosynostosis.

Crouzon syndrome is an autosomal dominant, rare genetic disorder which may demonstrate complete/incomplete penetrance and variable expressivity [13]. It may be transmitted as an autosomal dominant genetic condition or can express as a mutation with complete/incomplete penetrance and variable expressivity. It makes up approx. 4.8% of all the cases of craniosynostosis making it the most common syndrome associated with craniosynostosis [14,15]. The disease is characterized by premature synostosis of cranial sutures which begins in the first year of life. Once the sutures become closed, growth potential to those sutures is restricted. The clinical picture may vary greatly from mild to severe midfacial and orbital anomalies; which include abnormal head shape, mandibular prognathism, midfacial hypoplasia, shallow orbits, bilateral ocular proptosis, divergent strabismus, hypertelorism, conjunctivitis or exposure keratoconjunctivitis, optical atrophy and a non-explained loss of visual accuracy [5,6]. Upper airway obstruction can lead to acute respiratory distress and increased intracranial pressure can lead to optic atrophy which may produce blindness if the condition is left unmanaged. Intraoral manifestations include V shaped maxillary arch with dento-alveolar crowding. Occasional cleft palate, bifid uvula, oligodontia, macrodontia, and pegshaped teeth have also been reported [16]. Class III malocclusion due to maxillary hypoplasia is seen in 75% of patients

with Crouzon syndrome [17]. Hydrocephaly and mental retardation may also develop due to premature closure of cranial sutures.

Crouzon syndrome is caused by mutation in the fibroblast growth factor receptor 2 (*FGFR2*) gene at the chromosomal locus 10q 25.3q 26 and more than 30 different mutations within the gene have been documented in separate families [18]. Five autosomal dominant craniosynostosis syndromes (Apert, Crouzon, Pfeiffer, Jackso-Weiss and Crouzon syndrome with acanthosis nigricans) result from mutations in *FGFR* genes [19]. Cervical vertebrae abnormalities associated with Crouzon include butterfly vertebrae and fusion of the bodies and the posterior elements. Cervical fusion are present in 18% of the cases with C2-C3 and C5-C6 being equally affected [5,6].

The current case is a unique example of Crouzon syndrome with rare idiopathic early eruption of permanent dentition. Despite presence of clinical features of cranial and facial asymmetry, frontal bossing, hypertelorism, recurrent eye infections, restricted neck movements and abnormal changes in speech, the patient and his family never attempted to seek professional medical help. It was only when the patient reported to seek orthodontic treatment for midface deficiency and the incidental finding of cervical vertebrae anomaly was diagnosed and investigated that a diagnosis of Crouzon syndrome with Chiari Malformation I and syringomyelia was established. The patient's neurological examination revealed early signs of quadriplegia and was immediately operated for foramen magnum decompression. It has been shown that both craniosynostosis and CM Type I with craniosynostosis are diagnosed at an early childhood [20]. However, our patient remained undiagnosed till the age of 8.5 years. It is assumed that the syndrome would have not been diagnosed had the incidental finding of atlanto-occipital assimilation not been identified and investigated or until the onset of severe symptoms with aggravated pathology.

Summary

The cervical spine in the lateral cephalogram is often overlooked and omitted in orthodontic cephalometric tracings. Many cervical abnormalities do not manifest themselves symptomatically until adolescence or young adulthood and the orthodontist may be the first person to detect some of these. It becomes imperative for an orthodontist to have a sound knowledge of cervical anatomy to diagnose some of these defects which not only influences the orthodontic treatment plan but also can have serious implications on the quality of the life of an individual. Progressively degenerative defects, if discerned early, may help in mitigating of the severity of their consequences.

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