Septo-optic Dysplasia Complex with Omphalocele, Pre-maxillary Agenesis and Encephalocele

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Abstract Septo-optic dysplasia complex (SODC) is a rare congenital anomaly, characterized with absence of septum pellucidum, optic nerve hypoplasia with or without pituitary dysfunction. Various midline defects are also associated with SODC in addition to its classical findings. We report, for the first time a rare presentation of SODC which is associated with pre-maxillary agenesis along with sphenoidal encephalocele and omphalocele. The case showed resulting median cleft lip and palate along with other multiple congenital defects including hydrocele, inguinal hernia, micropenis and a wide mediastinum.

Keywords Septo-optic dysplasia complex · Corpus callosum agenesis · Encephalocele · Omphalocele · Cleft lip palate · Hydrocele

Introduction

Septo-optic dysplasia (SOD), also named after de Morsier is a disease complex mainly characterised by absence of septum pellucidum and/or pituitary dysfunction [1]. The three basic components of septo-optic-pituitary dysplasia (absence of the septum pellucidum, optic nerve hypoplasia, hypopituitarism) may occur alone or in any combination with wide variety of brain anomalies like agenesis of the corpus callosum, cortical dysplasia, lobar holoprosencephaly or schizencephaly. This association with absence of the septum pellucidum was first described by Reeves [2].

Different degrees of clinical presentations were reported in SOD ranging from otherwise healthy adult patients to

cases resulted in intrauterine death. Its association with pre-maxillary agenesis along with sphenoidal encephalocele is not previously reported. Polizzi et al. [3] proposed the term septo-optic dysplasia complex (SODC) to re-categorize the syndrome as a heterogeneous malformation syndrome encompassing multiple brain, endocrine, and systemic anomalies. The disease complex shows equal prevalence in both sexes with a reported incidence of 1:10,000 births [4, 5]. We report a rare case of SODC with varied clinical presentation and a concise review of SOD is conducted. Along with standard clinical features, this case showed a wide median cleft lip and cleft palate associated with agenesis of pre-maxillary segment, sphenoidal encephalocele and a large omphalocele. The case also showed multiple midline defects other than listed above including hydrocele, inguinal hernia, micro penis and a wide mediastinum. Patient also suffered from recurrent epileptic attacks soon after birth. However no signs of hormonal or growth deficiencies were detected in this case.

Case Report

Full term male baby was born at King Fahd Military Medical Complex Hospital, Dhahran, Saudi Arabia by spontaneous vaginal delivery to consanguineous parents with positive family history of cleft lip and palate running in both families. The paternal and maternal ages was 32 and 26 years respectively. The prima gravid mother did not give any history of licit or illicit drug use during pregnancy. No maternal illness or exposure to any teratogens during pregnancy reported. Baby had a birth weight of 2.28 kg (50th percentile) and head circumference was 32 cm. Apgar score of 6/10 and 8/10 were recorded at 1

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Fig. 1 Photograph showing large omphalocele loose skin fold around micro penis

Fig. 2 Photograph showing hydrocele micro penis with flabby skin foldings

Fig. 3 Photograph showing *left* anophthalmia, wide complete cleft lip palate with agenesis of pre-maxillary segment

and 5 min respectively. He needed oxygen by oxyhood soon after birth.

Initial examination showed multiple congenital abnormalities including an omphalocele, left anophthalmia, hydrocele and wide complete cleft lip palate with agenesis of pre-maxillary segment (Fig. 1).

Further investigations revealed a moderate patent ducts arteriosus (PDA) and atrial septal defect (ASD). The child also showed bilateral hydrocele, micropenis and right sided inguinal hernia (Fig. 2). The right eye was unaffected. Clinical examination of the oro-facial region showed a

Fig. 4 Photograph showing encephalocele presenting as a mass at the roof of the postnasal space

Fig. 5 CT scan showing *left* optic nerve atrophy, and agenesis of corpus callosum with absent septum pellucidum

wide midline complete cleft lip and palate with no pre-maxillary segment (Fig. 3). A bifid flabby soft tissue was noted hanging inward from the columella. No vomerine

Fig. 6 MRI study showing encephalocele, anophthalmia, agenesis of corpus callosum and septal defects

process was detected. Sphenoidal encephalocele was evident on intraoral palpation through the wide cleft (Fig. 4).

An antenatal ultrasound at week 22 detected fairly dilated ventricles and a large omphalocele. Computed tomography (CT) scan and magnetic resonance imaging (MRI) of craniofacial region proved left optic nerve atrophy, anophthalmia, and agenesis of corpus callosum with absent septum pellucidum (Figs. 5, 6). A sphenoidal encephalocele along with lissencephaly was also confirmed. Left eye ball was replaced by a small lobulated cystic space. CT of the facial bone showed midline defect at naso-maxillary region with no evidence of pre-maxillary segment, agenesis of vomerine process was also noted with complete palatine clefting. EEG revealed almost continuous epileptiform discharge from left hemisphere (Fig. 7).

Patient had undergone repair of omphalocele soon after birth and was fed by nasogastric tubing post operatively. Two weeks post operatively patient was managing on room air at the time of discharge from the hospital. Patient had recurrent epileptic attacks and was suffering from recurrent gastric regurgitation of fluids. He was discharged on nebulisations, levetiracetam, topiramate, phenobarbitone, vitamin D3, omeperazole, ranitidine and domperidone.

The child had a delayed repair of cleft lip at sixth month. Baby was discharged 2 weeks after surgical correction. An echocardiography at sixth month proved that previously

Fig. 7 EEG showing continuous epileptiform discharge from left hemisphere

detected mild ventricular septal defect and ASD were closed completely.

He was readmitted again at eighth month to ICU care as received in emergency in cardiopulmonary arrest. Even though he was revived after cardiopulmonary resuscitation he developed profound bradycardia towards the end of the day. Chest X-ray done soon after the first arrest showed multiple infiltrates and nasopharyngeal aspirate was positive for respiratory syncytial virus. He went into further cardiopulmonary arrest and was declared dead on second day.

Discussion

Researchers in different case review studies of SOD differ in naming the disease association. Authors agree to accept the term SODC proposed by Polizzi et al. [3] as each case of SOD shows different type of kaleidoscopic association of varied clinical presentations. Garcia-Filion and Borchert noted that some of the cases reported by de Morsier do not have both septal agenesis and a well defined optic nerve hypoplasia [1, 6]. It was also observed by Hoyt et al. that some cases of septo-optic dysplasia had pituitary deficiency; hence, suggested the term “septo-optic pituitary dysplasia” [7]. However the term “septo-optic dysplasia” will be used only for the combination of optic nerve hypoplasia and absent septum pellucidum without hypopituitarism. SOD with other associated findings were grouped as a category “SOD plus” in some reports [8].

The association of fronto-nasal dysplasia was not evident in most case groups; hence, its clinical associations with the syndrome are not well observed [9]. However some cases reports of oculo auriculo vertebral spectrum also showed agenesis of septum pellucidum [10, 11]. Occurrence of any two of the three key components can occur in all combinations even with bilateral optic nerve hypoplasia [11, 12]. A wide variety of other cerebral anomalies, including wide range of focal cortical dysplasias [12], lobar holoprosencephaly [3], basal encephalocele [7], schizencephaly [15], partial absence of the corpus callosum [14], partial absence of the falx cerebri [12], porencephaly [16], hippocampal hypoplasia [12], periventricular leukomalacia [10] and even fusion of the cerebellar hemispheres [17] are also reported.

A wide range of other non craniofacial clinical presentations are also noted in some cases. Most of them can be classified into midline abnormalities. For this reason authors prefer to accept the term SODC coined by Polizzi et al. [3] for such presentations as seen in this case report. Nasomaxillary agenesis, cleft lip palate along with other extra cranial midline defects including cardiac and gastrointestinal defects also can be attributed to explain the

effect of defective neural crest development. Such associations may explain the homeo box gene expression in neural crest cells as potential underlying genetic mechanisms in these diseases [18]. These various intra and extra cranial associations demand the clinician a detailed search for all the possible clinical findings in each case once SODC is suspected.

Endocrine disorders are found in 40 % of the patients with SOD [19]. No pituitary hormonal dysfunction could be noted in this case but an anatomical defect was present at the sella base. Clinical presentation of sphenoidal encephalocele as an intraoral palpable mass at the roof of the postnasal space was an interesting finding in this case (Fig. 1). The presentation of encephalocele was quite different from previously reported cases [20]. Encephalocele, anophthalmia, agenesis of corpus callosum and septal defects were evident in the MRI study. Association of omphalocele and cleft lip palate in SODC was reported earlier by Tanrikulu et al. [21]. Clefting of the lip and palate was associated with absence of naso-maxillary bony segment leaving only a rudimentary pre-maxillary soft tissue. Prominence of vomerine process was also deficient in the anterior region. These findings were not previously reported and explain the peculiar clinical presentation of encephalocele.

Omphalocele in this case was major with a diameter of more than 5 cm necessitating early surgical intervention. Associated cardiac abnormalities ASD, and PDA, were detected immediately after birth. Both conditions resolved taking a normal course. Hence the cardiac findings may or may not be associated with syndrome complex in this case.

Seizures, developmental delay and cerebral palsy are the most frequent neurological associations [19]. Epileptic seizures were observed in 23–39 % of the cases with agenesis of corpus callosum [22]. The EEG in this case confirms the findings (Fig. 7). Forty percentage of SODC patients shows normal pattern of development. The syndrome complex is often diagnosed very late in otherwise normal patients [8]. However cognitive development is compromised in 55 % of the reported cases. In this case weight gain of the infant was progressive. The 8 month old baby was active and playful at times when not in distress. However the cognitive development cannot be assigned at this stage.

Mortality rate reported in SODC is variable since there are wide ranges of clinical presentations. Multiple recurrent respiratory infections may justify the immune-compromise in these patients.

SOD can be caused by mutations in HESX1 and SOX2 [22, 23]. However, currently a genetic diagnosis can only be made in <1 % of the patients. A complete range of genetic study as per hospital protocol did not reveal any significant finding and no specific noticeable etiologic

factors other than the presence of parental consanguinity were seen in our case. Consanguinity is not evident in most of the reported case series [8].

Conclusion

We review and report a rare presentation of SODC associated with midline cleft lip and palate, naso-maxillary hypoplasia, anophthalmia, encephalocele, large omphalocele and other multiple congenital defects. A multidisciplinary team approach is required for all the cases of SODC for defining its various components and early intervention of associated problems.

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