Craniofacial duplication:
one of the rarest malformations in humans

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Abstract
Craniofacial duplication is a twin pregnancy defect; particularly in monozygotic, monochorionic and monoamniotic pregnancies. Of all twin pregnancy complications, the least frequent is a fetus with craniofacial duplication (diprosopus). In this article we report a case with this condition, and we review the literature on this rarest of human malformations.

Key words: twin pregnancy, conjoined twins, diprosopus fetus, craniofacial duplication, neural tube defect, anencephaly

Introduction
Conjoined twins are a very rare biological event. The incidence is estimated to range from 1 in 50 000-200 000 twin pregnancies and 1 in 15 000 000 for disopropus cases. Disopropus twins are a rare variety of symmetric conjoined twining, with less than 40 reported cases in the world. It constitutes a human phenomenon described in several countries, races, and different periods as an aberration of the twin process [1, 2]. Such anomaly constitutes a spectrum which extends from only nasal duplication to complete facial duplication (dicephalus) in just one body and with unaltered limbs.

The most accepted theory is that conjoined twins, including diprosopus are monozygotic twins which originate from embryological disturbance in the separation of the egg during the 2nd week of pregnancy (13-15 days), as a result of the abnormal splitting of the post-implantation blastocyte. Anatomic variations are determined by the degree and the origin point of division. Following we present a case of a disprosopus fetus and review of the literature concerning the proposed theories of its embryogenesis.

Case report
The pregnancy was diagnosed in 37 year old women, gravid 0 with a 28 year old father (in non consanguineous relationship). The family history did not present any malformations or twin pregnancies or any drug ingestion or toxic exposition during pregnancy. At 11th week of pregnancy the ultrasonographic examination indicated cystic hygroma, following polihydramnions and anencephaly 2 weeks later. The pregnancy was terminated due to the diagnosis of fetal malformation incompatible with life. The pathology report confirmed the presence of female conjoined twin, diprosopus with tetraphthalmus, anencephaly, cervicothoracolumbar rachischisis, double nose and one mouth (see Fig. 1 and 2). It presented a normal torso and abdomen, four limbs with discrete acromegaly. External genitalia were feminine, with no alterations and with perforated anus. Bilateral clubfoot was present. The internal examination indicated unique chest and abdominal organs with normal morphology (see Fig. 3).

Materials and methods
Review of the literature was based on the Medline database through PubMed, Ovid, Hinari and Fabumed using following key words: “diprosopus, conjoined” with specificity and sensitivity of 93% and 92% respectively. English and Spanish articles were evaluated with no date restriction. Autopsy as well as the photographic documentation was done with the informed parental consent.

Results
The literature search obtained 50 references including review articles, case reports, pathology findings and diagnosis references. Animal cases were excluded.
Disprosopus fetus is the rarest variant of monozygotic, monoamniotic [7]; 1 in 100 pairs are conjoined twins [8] and less than 1% of all conjoined twins are di-prosopus [5] with a frequency of one case in 15 millions [9]. The first presentation of a di-prosopus comes from image with two heads found in Neolithic sanctuary in Turkey, 6500 BC [3] and the earliest known report has been credited to Ambroise Pare’ (Of Monsters and Prodigies) of the 16th century [10].

Discussion

Disprosopus fetus is the rarest variant of monozygotic, monochorionic and monoamniotic conjoined twin which presents craniofacial duplication of diverse degree (two faces, one head and one trunk); it is associated with high incidence of anomalies in the central nervous system, cardiovascular system, gastrointestinal system and musculo-skeletal system [5].

Twin pregnancies represent 1.16% of all pregnancies (1 in 86 pregnancies) [6]; from which 1% are monocho-

Etiology and pathogenesis

The exact nature of the formation of the conjoined twins is unknown. However many factors have been sug-
gested as predisposing or responsible for the conjoined twins development, such as failure in the rostral neuropore closing, egg aging, maternal age, unspecified chromosomal abnormalities [4] and abnormal placental circulation [1]. In diprosopus twins there is a predominance of females over males (2:1) [1]. As of now there is no reported increased risk of recurrence [5], however some authors suggested environmental and genetic factors as a primary factor in the pathogenesis [1]; others debate the involvement of environmental and chromosomal factors [5].

Factors mentioned above are similar to the ones, which affect monozygotic twin pregnancy [13]. The hypothesis suggests that decrease of oxidation process affects the fetal environment just before gastrulation [14] leading to embryonic disturbance and abnormal splitting of embryo between 15-25 day post-implantation [15]. Recently some authors have postulated that conjoined twins result from two independent notochords which were initially destined to become separate twins, but which were too close to develop independently [17]. Conjoined twins can be classified with respect to the notochord. The orientation of axes determinates the degree of coalescence [16]; most cases have two well formed independent notochords, therefore there is relatively low interference in development of each twin, giving as result cranio-cranial, caudo-caudal, and ventro-ventral conjoined twins. Minority of twins have notochords very close to each other, disposed side by side, parallel (described above) which results in the development of two bodies with different degree of duplication. These types are the dicephalus (two heads) and diprosopus (two faces) [18]. The classification is became more complex since the case presented by Kastenbaum et al. in which parallel orientation of notochords was not “side by side”, that lead to anterior union, face to face presenting less symmetrical morphology and different pathogeny [19]. Therefore some cases are not easily classified.

**Associations**

The variety of diprosopus presents a high incidence of neural tube defects suggesting the possibility of a common mechanism or a relationship among these two events [20]. The neural tube defects association, especially anencephaly in the diprosopus in not fortuitous, in fact two thirds of the disprosopus, are anencephalic [19]; this frequency seems to be related to the failure of the rostral neuropore closing [21]. Monozygotic twins are in general 1.67 times more likely to be anencephalic than dizygotic twins or singletons [20]. The cardiac malformations include VSD, an overriding aorta, dextrocardia and hypoplastic ascending and descending aorta and an aortic arch also are congenital anomalies commonly associated and the output of four large vessels of the ventricles is reported [22]. The esophagus, stomach, and intestines can be duplicated and Meckel’s diverticulum can be present [5]. The defects in the other organs include diaphragmatic hernia, spine fusion, spine duplication, holoprosencephaly, cheilognathopalatoschisis and gastroschisis [4, 5]. Alterations of skull vault have also been noted [23].

**Differential diagnosis**

Conjoined twins are classified according to the fusion place, symmetry and degree of duplication. The most common type of conjoined twins is thoracopagus whereas the least frequent type is diprosopus [24]. The differential diagnosis should include teratoma, acardiac fetus and *fetus in fetu*. Teratomas can be differentiated from *parasite twin fetus and fetus in fetu* by the lack of notochord, vertebral axis and disorganized growth of a tumor [25]. Spencer et al. (2001), proposed the following criteria to differentiate acardiac fetus from teratoma: 1) acardiac twin is inside amniotic sac, 2) it is covered by normal skin, 3) has recognizable anatomical parts and 4) is attached to the placenta by an umbilical cord along with ipsilateral anastomosis [26]. Acardiac fetus frequently shows well developed spine, ribs and irregular bone structure correspondent to the skull base. Pelvis bones as well as parts of the legs’ bones can be present. The number of organ alterations decrease in craniocaudal direction [17, 28]. The concept *fetus in fetu or parasite fetus* applies to a fetal anomaly in which a small, imperfectly formed twin (usually with vertebral segment or/and internal organs) incapable of independent existence, is contained within the body of normal twin.

**Prognosis**

Complete duplication is associated with poor prognosis for the infant; however treatment options of the duplicated parts in case of partial diprosopus have been variably successful [29]. Development depends on related malformations of the neurologic, cardiac and respiratory systems [30] but even without these malformations the outcome is poor due to the high rate of neural tube defects associated with this anomaly.

**Conclusion**

The disprosopus twin is a complication of multiple monozygotic pregnancies. It is very rare anomaly among
conjoined twins and one of the rarest in among human beings.

References


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