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PATHOLOGICAL FINDINGS IN DICEPHALUS DIPUS DIBRACHIUS: IMPLICATIONS FOR MECHANISMS IN TWO PAIRS OF LATERAL CONJOINED TWINS

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INDEXING WORDS

conjoined twins; diprosopus lateralis; anencephaly; myelomeningocele

SYNOPSIS

The anatomical and pathological features of two pairs of dicephalic conjoined twins (case 1 and 2)are described. Both twins showed duplicitas lateralis representing diprosopus dipus dibrachius. There were two complete heads on two necks, one thorax,one abdomen and externally normal two arms and two legs. Case 1 showed dicephalus with anencephaly,two vertebral columns and two spinal cords,which converged from the thoracic region distally. The esophagus, stomachs and partial small intestines were duplicated, which fused at yolk sac(with Meckel's diverticulum). The heart was incompletely fused. The lungs and trachea were doubled. Two spinal cords were fused from the thoracic region caudally and showed myelomeningocele and Arnold-Chiari malformation in case 2. Two larynxes and two thracheas connected with the incompletely fused three lobes of lungs. The conjoined lungs were hypoplastic. The heart was single, showing ventral septal defect, transposition of great arteries,two cuspid aortic valves and preductal aortic coarctation. The duplicated esophagi were conjoined in Y-shape and single stomach, duodenum,intestine and colon were found. There were pairs of kidneys,adrenal glands and ureters and single female genitalia in both cases. These findings indicate that the craniocaudal paleoaxes were separated in the cranial region and converted or fused under the thoracic region like a Y-shape. Further development defects and deformations might be important factors to form malformations in these case.

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INTRODUCTION

Conjoined twinning is a very rare anomaly, reported to occur with a frequency of 1/50000 to 1:100000 births. (5,8) According to Edmonds et al(5) , the crude incidence is 10.25 per million births in the United States. The incidence of diprosopus lateraris variety is not well described, but seemed to be very low. There is a graded series illustrating almost every possible variation from normal single individuals to two normal superficial joined individuals in diprosopus lateralis. When duplication begins in the cranial region, it leads to monocephalus and dicephalus variations according to site of fusion. They show unique malformations of the central nervous system and visceral organs associated with conjoining, developmental defects, and deformations. We conducted pathological studies of two pairs of diprosopus lateraris and discuss the etiology of conjoined twinning.

CASE REPORT

Case 1:

The female twins were born to a 28 year-old, 3 para 2 gravida woman. The second pregnancy was artificially aborted because of a hydatidiform mole at age 25 years. The family history was unremarkable for congenital malformations. There were no possible teratogenic contacts except for antipyretic medication at 8 weeks of gestation. The pregnancy was complicated with polyhydramnios at 27 weeks. The radiological examination revealed that the fetus was conjoined at the cervical level with upper double vertebrae and absence of the skull. The baby was artificially delivered at 27 weeks of gestation, weighing 700 g and died a few minutes after birth. A complete autopsy was performed.

Autopsy findings:

General

The twins were duplicitas lateralis representing diprosopus dipus dibrachius. Both of the fused individuals showed anencephaly with rudimentary skulls, hairlips, median cleft lips and palates and imperforated ani. Two heads fused posteriorly and an area cerebrovasculosa was found. There were one thorax, one abdomen and externally normal two arms and two legs. Radiographically

there were absence of the skull and two vertebral columns. The placenta was single and the single umbilical cord had two arteries and one vein.

Nervous system

Each head showed an area cerebrovasculosa, partly preserved brain stem, one spinal cord and dystrophic hypophyseal gland. The Area cerebrovasculosa contained numerous vessels, meninges, plexus chorioideus, ependymal layer and remnants of cerebral tissue that showed necrosis and degenerative changes without inflammatory reactions. The cerebellum, the midbrain, the thalamus and the pons were degenerated. The medulla oblongata and the spinal cord were preserved with well formed ganglion cells. The ocular apparatus was normal, showing well organized retinal structure. The hypophyseal gland, with defective infundibular connection and posterior lobe, was embedded in the base of the skull.

Respiratory organs

The lungs, trachea, esophagus, larynx, thymus and thyroid were double in the thoracic cage. The adjacent medial thoracic cage was narrowed because of the mediastinal fusion. The doubled tracheas connected with the two pairs of lungs. The lungs were hypoplastic, with thick intraalveolar septa, poor capillary exposure to the potential air spaces, immature mesenchymal cells and cuboidal alveolar lining cells. The lung hypoplasia was most striking in the adjacent reduplicated lungs.

Cardiovascular organs

The fused heart was single and large. It showed a single atrium and two ventricles with an intact ventricular septum. The thoracic aorta and pulmonary artery of the right twin came from the right sided ventricle and those of the left one were from the left ventricle. A patent ductus arteriosus was found in each and the left pulmonary artery was stenotic. Paired pulmonary veins and single vena cava superior and inferior were joined by the common atrium. The right ventricle had a supra-ventricular crista and a tricuspid-like valve, and the left one had a mitral-like valve. The double thoracic aorta fused beneath the diaphragm, coming into single abdominal aorta.

Intraabdominal organs

The abdominal organs were single except for the stomach, gall bladder and partly duplicated intestine. The duplicated stomachs were conjoined at the duodenum. The intestine was long with duplication in places. The liver was located medially in the abdominal cavity. There were pairs of kidneys, adrenal glands and ureters and single bladder. The bilateral adrenal cortexes showed remarkable atrophy and thinning with a fetal cortex. The kidney showed immature configurations with glomerulogenesis.

Case 2:

The mother was a 27 year-old primipara woman with last menstrual period March 3, 1990, and expected date of confinement December 17,1990. She was diagnosed on ultrasound study at 6 weeks and 5 days of gestation. The mother had no particular family history for congenital anomalies. She had been treated by a herb medicine because of sterility for two years. The pregnancy was uncomplicated by 24 weeks of gestation. At 24 weeks gestation she was transported to Kobe University School of Medicine after having vaginal bleeding. Ultrasonograph examination revealed that the fetus had two heads with hydrocephaly and was conjoined at the cervical vertebrae. The large transverse diameter and cerebral cortex of the left side were 6.7cm,1cm and those of the right were 5.9cm,1cm respectively. The conjoined twins with double heads and single body were detected on MRI. The conjoined twins at the cervical level and the deformity of the vertebrae were found on CT. Laboratory findings were normal except for slight elevation of HPL, 6.4 μg/ml. Stillbirth of a female baby, weighing 1127g occurred at 24 weeks and 6 days of gestation. A complete autopsy was performed.

Autopsy findings:

General

The twins were duplicitas lateralis representing diprosopus dipus dibrachius. Two heads were present on two necks that were fused at the shoulders. There were one thorax, one abdomen and externally normal two arms and two legs. A myelomeningocele was found at the lumbar region. Radiographically there were two complete skulls and two vertebral columns that were conjoined at

the lumbar vertebrae associated with spina bifida. The placenta was single and the single umbilical cord had two arteries and one vein.

Nervous system

In each of the two skulls, there was a well-formed brain, showing one cerebrum, one cerebellum, one brain stem and one spinal cord. The both brains of the fused individuals showed immature configuration and hydrocephaly. The six cortical layers were well-formed in both brains. The cerebellums were hypoplastic. The external and the internal granular layers were thin and sparse and Purkinje cells were remarkably reduced. The dentate nuclei and the nuclei of pons and midbrain were normal. The lower parts of medulla and the upper half of the cervical spinal cord were depressed into the foramen magnum, resulting in the duplication of the cords and cerebellar coning, which corresponded to Arnold-Chiari malformation. The lower half of the cervical cord was almost detached from the upper half. The compressed medulla and upper cervical cord showed neural loss and gliosis with hemorrhage, plexus congestion and inflammatory cell infiltration(Fig. 5)There were two spinal cords adjacent to one another, that were fused from the thoracic region to cauda. In the lumbar region a ruptured myelomeningocele was found.

Respiratory system

In the thoracic cage, two larynxes and two tracheas connected to the three lobes of lungs that were incompletely fused. Although the right lung of the right twin and the left one of the left twin were detected separately, the left one of the right twin and the right one of the left were conjoined vertically. The doubled lungs showed diffuse atelectasis and amnion fluid aspiration with an appropriate morphological development for gestational age, but the conjoined lung was hypoplastic with pseudoglandular features. The thymus was duplicated and well-developed histologically.

Heart

The heart was single. It showed varied malformations, including ventral septal defect, transposition of great arteries, a two-cuspid aortic valves and preductal aortic coarctation. The aorta had two common carotid arteries,which supplied

each head respectively.

Intraabdominal organs

The upper parts of the duplicated esophagus were conjoined at 1.5cm above the esophagocardiac junction. Stomach, duodenum, intestine and colon were single and well-formed female genitalia was found. There were pairs of kidneys, adrenal glands and ureters and single bladder. The kidney showed immature configurations with glomerulogenesis.

DISCUSSION

Conjoined twinning is a rare congenital malformation that occurs in the range of 1:50000 to 1:100000 births. Females predominate in the order of 2 or 3 to one (or 75-95%) (4,5). There are many different types of conjoined twins according to the site of fusion. When embryos begin lateral duplication in the cranial region, the results are monocephalus diprosopus with one head and two faces and dicephalus variants such as those in our cases. In a review by Edmonds et al (5), the frequencies were thoracoomphalopagus (28%), thoracopagus (18%),omphalopagus(10%),parasitic twins(10%), craniopagus(6%), and dicephalus(3.7%). By 1987, fewer than 80 dicephalic twins had been reported. Dicephalic twins are classified into three types; Dicephalus dipus dibrachius, Dicephalus dipus tribrachius, and Dicephalus dipus tetrabrachius. Conjoined twins develop from a single zygote. The mechanism of partial twining is unknown, but there are two hypotheses; 1) the collision theory, which proposed that duplicated embryonic axes fuse prior to tissue differentiation, and 2) the fission theory, which hypothesizes that embryonic tissue divides incompletely and remains fused focally(2,13). The latter is thought to result from an incomplete, delayed fission of the inner cell mass, which is particularly likely to occur from the 13th to 15th day of fertilization(1). Steven et al (11)reported that the eggs of the frog Xenopus laevis, if centrifuged with their animal-vegetal axes inclined 90 to the force vector before first cleavage, formed conjoined twins with one body axis arising from the centripetal side of the egg and one arising from the centrifugal side of egg. McGIRR et al(7) reported a two-headed, two-necked conjoined twin calf

with partial duplication of thoracoabdominal structures and suggested that atypical "hatching" , that is emergence of the blastocyst from the zona pellucida, might cause anomalous twinning. The fusion of twins is likely to be minimal during the earlier period but there is a greater possibility of more extensive fusion occurring during the later period. Three factors such as conjoining, developmental abnormalities and deformations might be necessary to form unique malformations in these cases. It appears that there were two posterior craniocaudal axes (paleoaxes), represented by two vertebral columns in case 1. The paleoaxes diverged completely in the cranial region and converged under the thoracic one Y-shapely. A new anterior midline (neoaxes) was almost parallel to the paleoaxes but converged anteriorly, which expressed a single anterior midline more caudally. This effect was duplication of lungs and upper and lower gastrointestinal tract, gallbladder and no duplication of kidneys, sternum and other components of the anterior body wall. In case 2, the craniocaudal paleoaxes diverged completely in the cranial region and fused under the thoracic region in a Y-shape, which caused the partial twinning involving the development of the notochord as an anteriorly branched structure with retention of the single condition posteriorly. This effect could account for two spinal cords fused at the thoracic region. The anterior midline was probably parallel to the paleoaxes from the prevalence of the findings; the doubled trachea and incompletely fused lungs, the two esophagi fused in a mirror image and complete fusion of external and internal organs under the thoracic area. Ursell and Wigger (12) concluded that duplication of viscera and the number and shape of limbs depend on the amount of separation of vertebral columns. According to Siebert et al(9), the degree of paleoaxial divergence is variable; when two axes are closely approximated, it appears that inductive messages regarding sidedness can be mixed-up or lost entirely, so that structures develop in a variable fashion. Sperber and Machin(10) said "interaction aplasia" describes the phenomenon whereby abnormal induction leads to partial or total suppression of morphogenesis. The most extensive changes appeared in medial structures; two arms two legs, and the respective skeletal muscles, nerves, and blood vessels failed to develop in our two cases.

Anencephaly associated with lateral twinning was reported by Herring and Rowlatt(6). Although the cause of anencephaly in case1 is unknown, the

failure of closing the anterior neuropore resulted in cranial rupture of both twins, which remained as area cerebrovasculosa by secondary degeneration. The cause of the Arnold-Chiari malformation, a maldevelopment of the nervous system found in our case 2, cannot be ascertained precisely, but it seems that incompletely fused spinal cords, associating the failure of the closure of the caudal neuropore might result in the myelomeningocele and Arnold-Chiari malformation secondarily.

The doubled esophagi and stomachs were fused at the upper portion of duodenum and the upper and middle small intestines were partially separated but merged to form a single ileum (with Meckel's diverticulum) distally, which suggested that the site of fusion was the yolk sac (Meckel's diverticulum) and partly the duplication of intestines could be attributed to the refusion secondary to spatial limitations. Currarino(8) reports that vertebral anomalies, lumbosacral meningocele and urogenital tract malformations have been associated with anorectal malformations in many cases. These authors postulated that early abnormal adhesions between the hindgut and the neural tube may cause the notochord to split; this primary split may prevent fusion of vertebrae anteriorly and/or bring the adhesion between endoderm and neural resulting in the fistula formation between them. The partial resorption of the fistula may result in a meningomyelocele or enteric cyst. It is interesting that our case 2 who was associated with sacral myelomeningocele showed no anorectal anomalies but case 1 with anencephaly and intact spinal cords showed an imperforated anus. The pathogenesis of myelomeningocele is unclear, but the abnormal fission of the paleoaxes, following failure of the neuropore closure is a more likely explanation in case 1.

The medial lungs of both individuals in case 1 and the fused lung in case 2 were hypoplastic,which might be a deformation resulting from the narrower thoracic cage by crowding in utero.

Although the heart anomaly in case 1 is complex, the hemodynamics was symmetric and adequate for both twins during development in utero. It seems that the hearts of individual twins were separate during the earlier period of development. The double hearts were at the phase of development, showing primitive ventricles, conus cordis and truncus arteriosus. The primitive left ventricle of the right twin failed to develop by fusion and the conus cordis

retained original embryological relation with the right ventricle only. The embryonic atrioventricular canal of the left twin, that failed to shift medially and retained its leftward position, divided into right and left atrioventricular ostia connected with the primitive left ventricle. The septum of truncus and heart valves formed later independently with aplasia of the primitive right ventricle. The complicated cardiovascular malformations can not be explained, however, it seems that hemodynamic derangements and disordered intracardiac blood flow might account, in part, for the pathogenesis(3).

Conjoined twins form a wide spectrum, which depends on the nature of splitting of inner cell masses. The orientation and separation of notochord "paleoaxes" seem to affect the sidedness and later organogenesis. Unknown teratogens caused the splitting of the inner cell mass, which led to early bifurcation of embryonic axes and associated maldevelopment and deformations according to crowding in utero might form the unique malformations in these cases.

Fig. 1a: Anterior view of case 1, showing diprosopus dipus dibrachius with anencephaly, single liver and partially duplicated intestine.

Fig. 1b: Posterior view of case 1, showing anencephaly and double vertebrae.

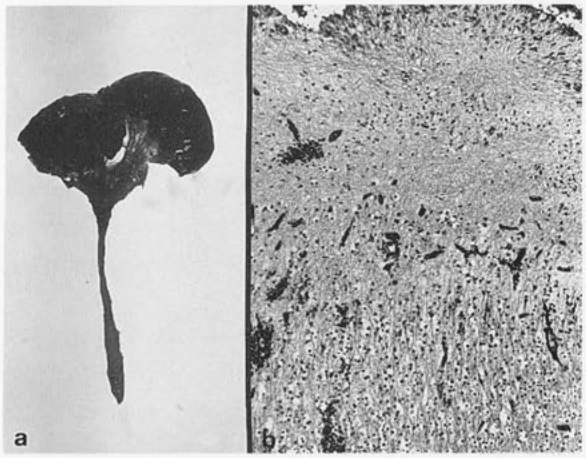

Fig. 2a: Brain and spinal cord of case 1

Fig. 2b: Histological features of the brain of case 1, HE, x 100

Fig. 3a: Anterior view of case 2. Two complete heads, two arms and two legs are seen .

Fig. 3b: Posterior view of case2, showing ruptured lumbosacral myelomeningocele.

Fig. 4: Dorsal view of the spinal cords of case 2, showing Arnold-Chiari malformation. Two spinal cords were fused from the thoracic region to cauda with ruptured myelomeningocele.

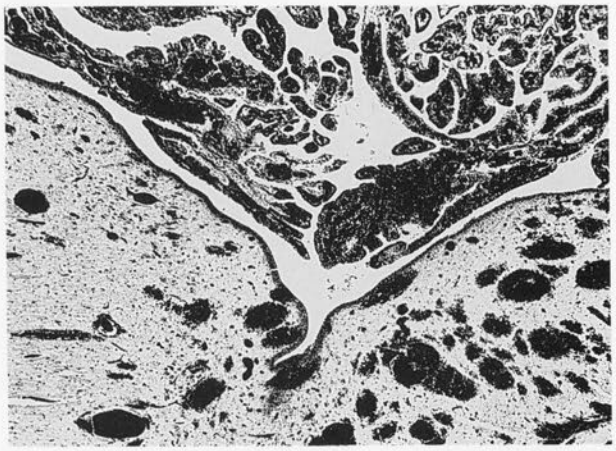

Fig. 5: Compressed medulla oblongata of case 2, showing neural loss and gliosis with hemorrhage, plexus congestion and inflammatory cell infiltration. HE x 360

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