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Ectopia Cordis in a 35 Day Old Human Embryo

E. V. ENZMANN, J. C. LULY and S. D. MIROYIANNIS

INTRODUCTION

One of the major, though fortunately rare, abnormalities of human intrauterine development is a condition known as ectopia cordis. It was first described by the Swiss poet, physician and naturalist Haller in 1706.

Arey (1954) briefly characterizes ectopia cordis as an abnormality in which the heart protrudes from the anterior body wall between the widely separated halves of the sternum, and comes to lie exposed on the surface of the chest. Others (cf. De Abbot) have described ectopia cordis as an abnormality in which the heart is malpositioned, high up in the chest, protruding out from the body in the pectoral area, or even displaced into the abdominal cavity.

According to Weese (1818) the cases of ectopia cordis may be classified as follows:

1. Ectopia cordis cum sterni fissura.
2. Ectopia cordis superthoracica.
3. Ectopia cordis subthoracica.

Currently a similar classification given by Townsend, Todd and Rauchfuss (cf. Blatt and Zeldes, 1942) is often used; these authors distinguish the following three types:

- a. Cervical heart, if the organ fails to descend properly into the thoracic cavity and comes to rest in the neck region.
- b. Pectoral heart, associated with sternal abnormalities, especially sternal cleft.
- c. Abdominal heart, where the organ has passed caudad through a defect in the diaphragm.

Scott (1955) has tabulated 152 cases of ectopia cordis; all those cited were human foetuses of premature birth, stillborn children, or infants that died shortly after birth. In a few exceptional cases the afflicted persons reached adulthood. To our knowledge ectopia cordis has not been observed in young human embryos.

The present writers were fortunate in obtaining such an embryo,

estimated to be about 35-37 days old, which showed a typical case of ectopia cordis, associated with numerous other abnormalities.

DESCRIPTION: EXTERNAL FEATURES

The embryo described here came from the collection of human embryos and foetuses of the Still College of Osteopathy and Surgery, Des Moines, and bears the label S-43. It was obtained from a spontaneous abortion and was turned over to us for closer study by the Department of Pathology.

The specimen consisted of an unopened chorion which was loosely attached to a poorly developed placenta, covering about one-third of the surface of the chorion. The edge of the placenta along the terminal sinus was fringed with blood clots. The chorionic vesicle measured about 2 x 1.5 inches. It was nearly devoid of villi, and those present were unbranched. The wall of the chorion was strengthened

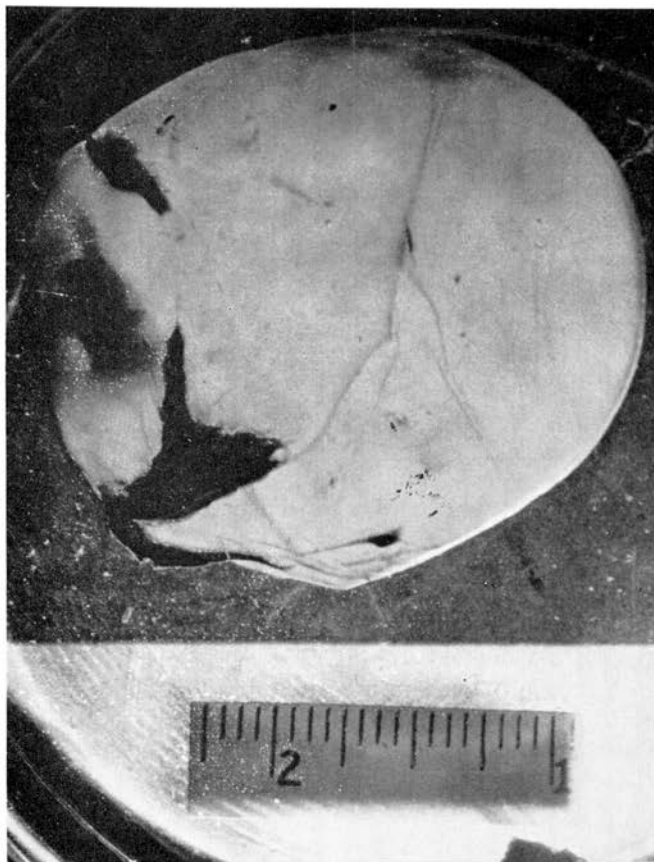


Figure 1. Unopened chorion-annion of the human embryo S-43.

by unusually well developed white fibres, visible as branching strands in Figure 1.

After opening the chorion-amnion an embryo measuring 11 mm (C-R length) was exposed. Estimated from its length the embryo's age was put at 35-37 days.

The body stalk was short and was divided into two branches, the upper one entering the body well below the liver, the more caudal one directed to and entering the area of the bladder; the two branches were of about equal thickness. (The authors are not aware of any other instance of an umbilical cord divided in that fashion. (See Figs. 2 and 3.)

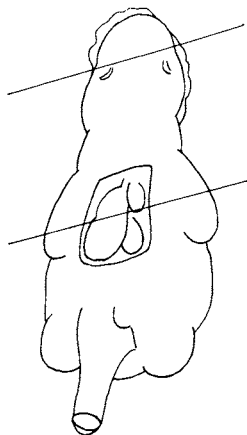


Fig.2

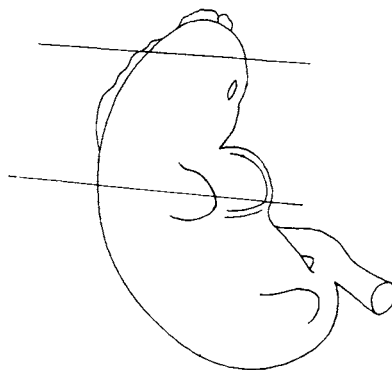


Fig.3

Figure 2. Outline drawing of the same embryo in ventral view showing the ectopia cordis.
Figure 3. Outline drawing of the embryo S-43 in lateral view showing cranioschism and spina bifida.

The fore limbs were in form of large buds, showing as yet no differentiation into upper and lower arm. The hind limbs were present and consisted of smaller buds. The liver swelling was still prominent. The head showed a number of major abnormalities. The eyes were pigmented spots; there was no trace of nasal grooves or mouth opening. The brain was extruded in a cranioschism. The occipital region appeared normal. The neural groove was still open and the spina bifida extended from the region of the cephalic end of the notochord all the way downward. All head flexures were absent.

The four chambered heart was visible through a transparent rectangular area of the anterior body wall. (Fig. 2.)

HISTOLOGICAL FINDINGS

The embryo was sectioned in the planes indicated in Figures 2 and

3. The microscopic examination showed a number of other malformations. At this time it will be sufficient to report only on those which seem to have some connection with the ectopic heart.

Figure 4 shows a cross section of the thorax at the level of the heart. All four chambers are present, the right ventricle being by far the largest. The bulbus cordis is clearly outlined and shows the ridges which would eventually have partitioned the bulb into aorta and pulmonary artery. The myocardium has started to form and some trabeculae carneae are present. The ventricles are connected by a foramen (not visible in the section). There is no indication of heart valves. The heart lumina contain a number of haemocytoblasts and a very small number of hemoglobin holding cells; the latter are macrocytic and hyperchromatic normoblasts of irregular shape. (No such advanced blood cells are present in pig embryos of comparable size and state of differentiation.)

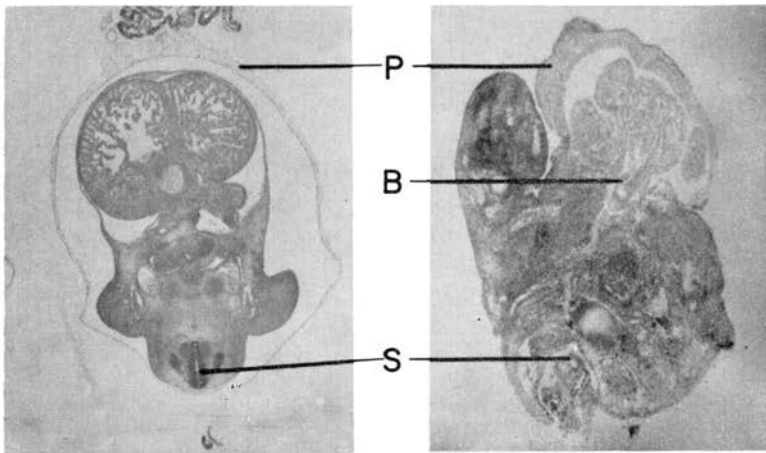


Fig. 5

Fig. 4

Figure 4. Section through the heart of the embryo S-43 showing the abnormal pericardium-body wall (P), the spina bifida (S) and the beginning of the partitioning of the heart bulb (B).

Figure 5. Similar section of a normal pig embryo of a comparable stage of development.

The ectopic heart is protected by a pericardium-body wall of unusual thickness, about five times that of normal, consisting of wide-meshed and transparent mesenchyme. At the junction of this membrane with the "normal" body wall the future skin is lined with a low cuboidal epithelium.

The most startling finding in this section is the extreme stenosis of the dorsal aorta and the cardinal veins. The lumina of these vessels are far smaller than the diameter of a blood cell. In sections above (the one shown in Fig. 4) the vessels are solid strands or completely absent. Some vertebral arteries are present but consist of solid cords.

The spina bifida is extensive. The neuroblasts of the spinal cord show no differentiation and there is no indication of the rudiments of the meninges. Neural crest cells are present and are in the process of migrating ventrad, forming a solid strand on each side of the spinal cord. Dorsal roots and spinal ganglia have failed to form. Scleroderm cells have surrounded the notochord and have moved apart, as in early precartilage.

The trachea is short but distinctly bifurcated. Sections cephalad to the one shown here present the pharynx, the arytenoid swellings and the entrance of the trachea.

DISCUSSION

Nearly all the papers dealing with ectopia cordis mention the fact that usually a number of other abnormalities are associated with an extruded heart. These abnormalities may be classified into three groups:

1. Those which are believed to be directly connected with the ectopia cordis from a development standpoint. These defects include failures of the sternal bands to meet in the midline of the body, leaving a gap, through which the heart may protrude (Greig, 1926). Other abnormalities in this group are the absence of the manubrium, the xyphoid process, malformation of the mediastinum, an open pericardium, defects in the diaphragm and anterior body wall below the diaphragm (Major, 1953). There may be abnormalities in the size and shape of the great vessels, such as stenoses, duplications or atresia. The protruding heart may or may not be covered with skin (Cutler and Wiles, 1925).
2. Malformations of the heart itself and of the coronary vessels. These include such conditions as persistence of the left sinus horn, defective interventricular septum, teratology of Fallot, oddities in the coronary vessels and arrested development of the heart, resulting in bi- or trilobular heart.
3. Abnormalities which cannot be said to be directly connected with the ectopic condition, though may be due to the same primary cause. Such defects occur usually at distant locations, and include club foot, hare lip, cleft palate, spina bifida, anencephaly, hernias of various kinds (George, 1945).

Several interesting theories have been put forward to explain the genesis of ectopic heart formation. The most widely quoted (Cosgrove and St. George, 1924) assumes that developmental defects of neighboring structures produce the ectopia. This includes failure of normal descent of the heart and diaphragm from the cervical region to the thoracic cavity, improper formation of the mediastinum.

defective development of the rudiments of the sternum, etc. This would explain the case reported by Greig (1926) where the abortive heart was found attached to the hard palate. The heart develops in close relation to the mandibles, which may explain such associated abnormalities as cleft palate, hare lip, etc. (Greig, 1926).

Pectoral hearts are usually explained as the consequence of faulty formation of the sternum or of its parts (Scott; and others). Defects in the diaphragm, or failure of the pericardio-peritoneal canal to close may lead to an abdominal heart (Scott, 1955).

George (1945) refers to a theory which assumes that increased blood pressure is responsible for the ectopia.

Pathological ova (Sintgen, 1933) and defective germ plasm (Major, 1953) have also been considered as causes.

The present writers assume a theory of phenotypic teratogenesis based on what some embryologists refer to as "critical periods" during development. These critical periods coincide with periods of speeded-up growth and differentiation of structures. Many kinds of factors acting during critical periods are capable of producing abnormalities, such as mechanical influences, radiation, infection, etc. In the case reported by Sintgen (1933) the abort-producing drug taken by the mother during the early weeks of pregnancy may have indirectly caused the abnormality of her baby.

The immediate cause of the malformation of our embryo seems to be starvation during the critical period. The placenta was so poorly developed that transfer across it may not have been possible. The atresia of the aorta, cardinals and the other great vessels seems to bear out this assumption. The appearance of hyperchromatic normoblasts seems to be an adaptation to a diminished gas exchange. In case of embryo S-43 it can be stated definitely that the ectopia of the heart was not caused by a failure of the sternal anlagen to meet in the midline. The sternal rudiments appear much later than the heart; it seems more logical to assume that the ectopic heart interferes with the normal formation of the sternum, hence a cleft sternum is caused by an ectopic heart, not the other way around. The theory of teratogenesis by certain factors acting during critical periods is well supported by experiments reported some time ago by Enzmann (1951). Various abnormalities were produced in imagos of *Drosophila* by exposing their larvae to x-ray, neutron bombardment, or ultraviolet light. It was found that in each case those organs showed gross abnormalities, whose imaginal discs passed the critical period during the time of exposure. The condition of the imaginal discs was checked histologically in larvae of the same age as those in which aberrations were produced.

As an interesting corollary to the theory of critical periods the following possibilities should be considered. During embryonic development sometimes more than one structure passes a critical period simultaneously. Any harmful agent acting at such a time may then affect more than one organ; the result will be a complex of associated defects. In fruit flies, for instance, one often finds deformed antennae associated with eye defects. The imaginal discs of eyes and antennae form an associated structure and differentiate at the same time. It is therefore not surprising to find that ectopia cordis in humans is nearly always a part of a complex of defects. The organs which show malformation have their critical periods close together in the developmental time schedule.

Summary and Abstract

A case of ectopia cordis in a 35 day human embryo is reported. Associated abnormalities included cranioschism, spina bifida, branched umbilical cord, malformation of the placenta and stenosis of the aorta and other great vessels. It was concluded that in this case the cause of the defects was starvation of the embryo during the critical periods of development of the affected structures due to malformation of the placenta.

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