Anencephaly Does Not Cause Structural Alterations in the Fetal Penis

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ABSTRACT

Introduction. Anencephaly is the most severe neural tube defect in human fetuses. There is an increasing need for tissue replacement in chronic diseases and reconstructive surgeries. Fetal tissues have been used as a substitute for native organs.

Aim. The aim of this article was to compare the structure and morphology of the corpora cavernosa (CC) and spongiosum (SP) of penises from anencephalic and normal human fetuses.

Main Outcome Measures. The main outcome measures of this study were the proposition of a new model for biological studies and tissue transplantation.

Methods. We studied 11 penises from normal human fetuses, aged 14–23 weeks postconception (WPC), and five penises from anencephalic fetuses, aged 18–22 WPC. The organs were removed and processed by routine histological and immunolabeling techniques. Analysis of connective tissue (Cot), smooth muscle (SMC), and elastic fiber (EF) were performed in sections. Data were expressed as area density (Ad) using digital processing and software. Means were statistically compared using the unpaired *t*-test and linear regression was performed. Statistical significance was considered if $P < 0.05$.

Results. The intracavernosal septum was present in all samples. We did not observe differences in the Ad of Cot and SMC in the penises of anencephalic fetuses when compared with normal ones. The simple linear regression suggested that during human development, there is a gradual increase in Cot ($R^2 = +0.45$) and a decrease of SMC ($R^2 = -0.62$) in the CC in both groups studied. Elastin was observed only in fetuses from 20th WPC.

Conclusions. There was no difference in the structure of the CC and corpus SP of anencephalic fetuses compared with normal ones. Elastin was documented from 20th WPC, which suggests the maintenance of erectile function. Histochemistry and immunolabeling suggested that penile shaft development is maintained and unaltered in anencephalic fetuses. Further studies should be performed to analyze anencephalic fetuses as a potential tissue-donating group and a model for biological studies. **de Carvalho JPM, Costa WS, Sampaio FJB, and Favorito LA. Anencephaly does not cause structural alterations in the fetal penis. J Sex Med 2012;9:735–742.**

Key Words. Penis; Erectile Tissue; Neural Tube Defects; Human Fetuses; Corpora Cavernosa Structure

Introduction

Neural tube defects (NTDs) are one of the most common congenital malformations of the central nervous system, with an average prevalence at birth of 1 per 1,000 [1]. Anencephaly is the most severe fetal NTD, resulting from failure of the neural tube to close at the base of the skull between the third and fourth weeks postconception (WPC), leaving the skull bones that usually surround the head unformed. Therefore, the brain lacks part of the cerebrum, and the remaining brain tissue is often exposed to injury from the amniotic fluid [2].

Anencephaly invariably is lethal, but some anencephalic infants are born alive with a rudimentary brain. The absence of a functional brain makes the anencephalic incapable of consciousness or feeling pain, but the brainstem reflexes can cause actions like breathing and such newborns

occasionally respond to sound and touch. Anencephalic newborns are not viable or tractable and the survival is measured in hours or days [3].

The pathogenesis of anencephaly is still controversial. Both failure of closure of the neural tube and reopening after closure have been hypothesized as responsible for this problem. Several studies have suggested that anencephaly arises from exencephaly, in which the cerebral tissue is not covered by the meninges, so that the cranium and skin is progressively destroyed within the uterus by the amniotic fluid [4].

Despite ethical conflicts, the literature shows some reports about the use of anencephalic fetuses' organs for transplantation [5–8]. The organ structure of anencephalic fetuses is almost unknown. Recently, the structures of anencephalic fetal kidneys [9] and bladder [10] have been studied.

The use of tissue engineering using penile shaft tissue from anencephalic fetuses would be potentially beneficial in developing countries where penile cancer incidence and need for treatment are increasing [11], as well as in cases of pelvic trauma [12]. Cadaveric penises from adults have been used to test new pharmacological drugs [13]. Use of penises from anencephalic fetuses opens new possibilities for the study of the histology and anatomy of a particular group not yet exposed to external environment disorders.

In addition to providing important information for experiments on the pathophysiology of penile disorders, data on the penile extracellular matrix might also be beneficial for investigations of techniques for surgical reconstruction of the penis, especially when using different tissues.

Aim

The morphology of the penis in anencephalic fetuses is unknown. The intent of the present work is to compare the structure and morphology of the corpora cavernosa (CC) and corpus spongiosum (SP) from anencephalic and normal human fetuses in order to propose a new model for biological studies and tissue transplantation.

Methods

The present work was approved by the institutional review committee and by the parents. It was carried out in accordance with the ethical standards of the institutional committee on human experimentation.

We studied 16 penises obtained from 11 normal human fetuses and five penises from anencephalic human fetuses that died of causes unrelated to the genitourinary tract. The gestational age of the fetuses was determined in WPC, according to the foot-length criterion. At present, the foot-length criterion is considered the most acceptable parameter to calculate gestational age [14–17]. The fetuses were also evaluated regarding crown-rump length and body weight immediately before dissection, and all measurements were taken by the same observer.

After the measurements, the fetuses were carefully dissected with the aid of a stereoscopic lens with ×16/25 magnification. The fetal penis was carefully removed, together with the kidneys, ureters, bladder, and prostate.

The penis was separated from the other structures and fixed in 10% buffered formalin and routinely processed for paraffin embedding, and 5 μm thick sections were obtained at 200-μm intervals. Smooth muscle cells (SMCs), connective tissue (Cot), and elastic system fibers were studied by histochemical and immunolabeling methods.

Cross sections were stained with hematoxylin-eosin to assess the integrity of the tissue. We performed the following staining: Masson's trichrome, in order to quantify Cot and smooth muscle, and Weigert's resorcin fuchsin with previous oxidation in order to observe elastic system fibers. Cot, SMCs, and elastic system fibers were quantified by a digital method [18]. Five sections per specimen were stained, and five fields of each section were selected. All selected fields were photographed with an Olympus DP70 camera (Olympus BIOSCOPS, Center Valley, PA, USA) coupled to an Olympus BX51 microscope (Olympus BIOSCOPS, Center Valley, PA, USA). The images were processed and saved with the Image Pro software (Mediacybernetic, Bethesda, MD, USA). The tissue was quantified using the Image J software (National Institute Health, Bethesda, MD, USA) to determine the area density (Ad) of each component [18] (Figure 1).

Immunolabeling was performed to confirm the results. For SMCs, Monoclonal Alfa Actin Antibody 08–0106 (Zymed Laboratories, San Francisco, CA, USA) was used. To confirm the results for elastic fibers (EFs), Monoclonal Elastin Antibody ab 9519 (Abcam Laboratories, Cambridge, MA, USA) was used. Means were statistically compared using the unpaired *t*-test, and linear regression was performed when applicable. Statistical relevance was accepted if $P < 0.05$.