

(RESEARCH ARTICLE)



Teratoma induced by amlodipine drug in fetus rats

Dumue Qasim Mohammed ^{1,*}, Ali Naeem Salman ² and Nahla A. Al-Bakri ³

¹ Department of Biology, College of Education for Pure science, Thi-Qar University, Iraq.

² Collage of Education for pure science, Thi-Qar University, Iraq.

³ College of Education for Pure Sciences (Ibn Al-Haitham), University of Baghdad, Iraq.

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Abstract

The current study, performed during the period from February 2021 to June 2022 at the University of Thi- Qar/ College of Education for Pure Sciences, and aimed to follow the changes in external morphological features at different Embryonic developmental stages in pregnant rats treated with different doses of amlodipine. Usage In this study, 18 pregnant rats were randomly divided into three groups, each with six pregnant rats. Each group received different concentrations of amlodipine (0.3, 0.5) in oral doses until the 20th day of gestation, while the control group was injected with 0.9% normal saline.

Teratomas are bizarre tumors derived from embryonic tissue that are normally found only in the gonadal and sacral regions of adults. Primary retroperitoneal teratomas are rare and present challenging management options. In one outcome, a teratoma was found in one of the amlodipine-treated groups. Complete excision of the teratoma mass was performed.

Keywords: Amlodipine; Teratoma; Hypertension; Pregnant rats

1. Introduction

Hypertension is one of the most common chronic diseases with high prevalence, and it is the most important risk factor for cardiovascular and cerebrovascular diseases (1). According to hypertension guidelines, five classes of antihypertensive drugs that include angiotensin in converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), calcium-channel blockers (CCB), diuretics, and beta blockers are suggested for hypertensive therapy (2). Hypertensive disorders of pregnancy affect about 5–10% of pregnancies impacting maternal, fetal, and neonatal outcomes, Hypertensive disorders of pregnancy, an umbrella term that includes preexisting and gestational hypertension, preeclampsia, and eclampsia, complicate up to 10% of pregnancies and represent a significant cause of maternal and perinatal morbidity and mortality (3).

Amlodipine, a basic dihydropyridine derivative, inhibits the calcium influx through 'slow' channels in peripheral vascular and coronary smooth muscle cells, thus producing marked vasodilation in peripheral and coronary vascular beds (4). Short to medium term clinical trials indicate that amlodipine is effective as both an antianginal agent in patients with stable angina pectoris and an antihypertensive agent in patients with mild to moderate hypertension (5).

Teratomas are tumors that are derived from embryonal tissue and composed of somatic cell types from two or more germ layers (ectoderm, mesoderm, or endoderm) (6). A teratoma is a non-seminoma Tous germ cell tumor and is typically located in either the sacrococcygeal region or in the gonads. Most teratomas in this region (retroperitoneal) are secondary to germ cell tumors of the testes or ovaries. Specifically, in male patients, retroperitoneal (7).

* Corresponding author: Dumue Qasim Mohammed

Teratomas are rare congenital neoplasms that develop from more than one and usually all three of the primordial germ cells which differentiate to form ectodermal, mesodermal and endodermal tissue elements. During the fourth week of embryologic development, germ cells originating from the yolk sac migrate in the midline of the fetus along the dorsal mesentery from the urogenital ridge to the developing gonads. Some of the cells do not complete the migration and survive in midline location such as the pineal gland, anterior mediastinum, retroperitoneum and sacrococcygeal area where they differentiate into extragonadal teratomas (8). It's are classified as one of four variants: 1) mature, when they contain adult or differentiated tissue; 2) immature, when they are comprised of predominantly embryonic or undifferentiated tissue; 3) teratoma with malignant transformation; and 4) monoderm, when there is a predominance of tissue arising from one germ cell layer, mature teratomas occur most often in the ovaries and testes (9).

Other terminologies which have been used to describe this tumor include “parasitic teratomas”, because they leech blood from native tissue at their ectopic sites of implantation. This occurs as the tumor, gradually being deprived of their own blood supply, begin to become attached to the adjacent site and forms collateral connection with existing blood vessels (10,11).

Amlodipine it has high interindividual variation in blood pressure control, and polymorphisms of drug metabolism-related genes are one of the influencing factors Clinical drugs–drug interaction studies have shown that amlodipine acts as a substrate of the cytochrome P450 (CYP) 3A subfamily, suggesting that its metabolism may be affected by changes in CYP3A metabolic activity (12). CYP3A is involved in 40%–50% of the oxidative biotransformation of current therapeutic agents (13). Because it is located in the intestinal mucosa and liver tissue, it is associated with drug metabolism ability after oral drug administration.

2. Material and methods

2.1. Sample Collection

Female albino rats, ranged in age between 14 to 16 weeks, with an average was of 225 ± 5 gm. The rats were put in the plastic cages breeding with metal lids and Brush the cage with sawdust, environmental conditions controlled at the constant Photoperiod (12 hour day /12 hour night) cycle ventilation, temperature ranged between 20-24 c. Animals were given a sufficient amount of water and food from a local source (Wheat 34% , barley 20% ,corn 25% ,animal protein 10% , powdered milk 10% ,salt 1%) these ingredient were grinded and mixed with some oil and water until they become a paste coherent (14,15,16). And put in the designated place for the food in the cages for animal breeding, two mature females were caged together with one mature male overnight and in the following morning the females were checked for the presence of vaginal plug (17). Date of mating was written on the cages. The day of mating is day zero (D0) of pregnancy and the day after was the first day of pregnancy (18,19,20).

2.2. Isolate of the rat embryos

After 15th days of pregnancy, the pregnant female rats were dissected after being anesthetized with cotton containing diethyl ether and then fixed on the dissection board by the pins and the abdominal cavity was longitudinally cut. The peritoneum was grasped with forceps and cut to expose the abdominal cavity. The uterine horn was removed by grasping the uterus below the oviduct and cutting it free along the mesomerism. Each embryo was separated by cutting between implantation sites along uterine horn. The muscular uterine lining was grasped by sliding forceps between the surrounding muscle layer and enveloped decidua tissue. The muscle layer was ridded and a portion of the decidua exposed then the embryo shelled out by using the tips of forceps. Then embryos were kept in container that contains 10% formalin until the start of the preparation of the histological sections.

2.3. Histological preparation

The paraffine methods prepared according to the method described (21,22, 23,24)

Then the tissue sections were photographed with the by light compound microscope after being equipped with a digital camera containing a film and the photos were taken at magnification force 40X.

3. Results

Results of the current study, which are as follows:

3.1. Control group

At gestation day 15th, is recognizable as a rat and moves actively within uterus, it's sufficiently straightened out that its fore and hind limbs no longer touch, the fingers and toes were already parallel. The eyelids were thickened and have fused over the eyes and pinna cover the auditory meatus, figure 1.

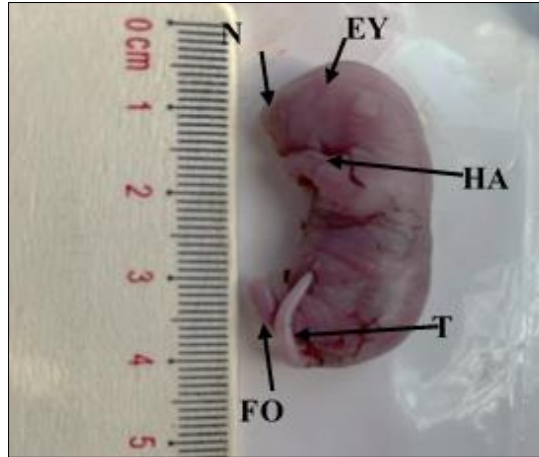


Figure 1 Lateral view of rat embryo at gestation day 15th. (EY) Eye, (FO) Foot (HA)Hand, (N)Nostril, (T)Tail

3.2. Treated group with amlodipine drug (0.5 mg/kg)

The effect of amlodipine drug (0.5 mg/ kg) on external features of rat fetus at 15th day at gestation, Specimen radiograph examination revealed a 9.5 -5.5 cm multilocular, thin-walled fluid-filled cyst (Figure 2). The cyst walls were smooth, gelatinous, and uniform throughout with a regular vascular pattern. Adherent to and within the cyst was a 6.5 4.0 3.0 cm fetiform structure covered with a viscous, sebaceous, keratinaceous-like substance (Figure 2).

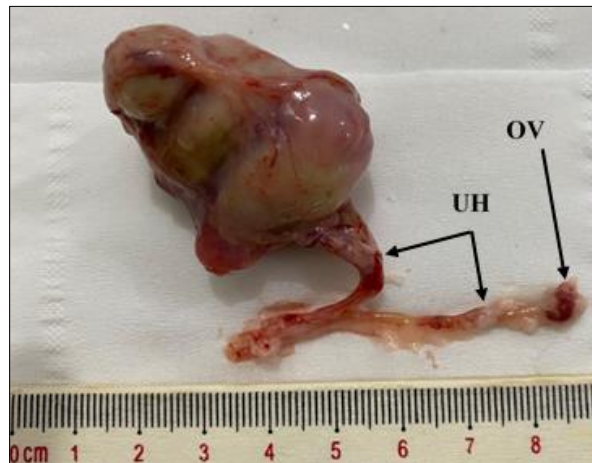


Figure 2 Uterus from pregnant rat at gestation day 15th treated with 0.5 mg /kg amlodipine, mass with solid and cystic components, (OV) Ovary, (UH) Uterus Horns

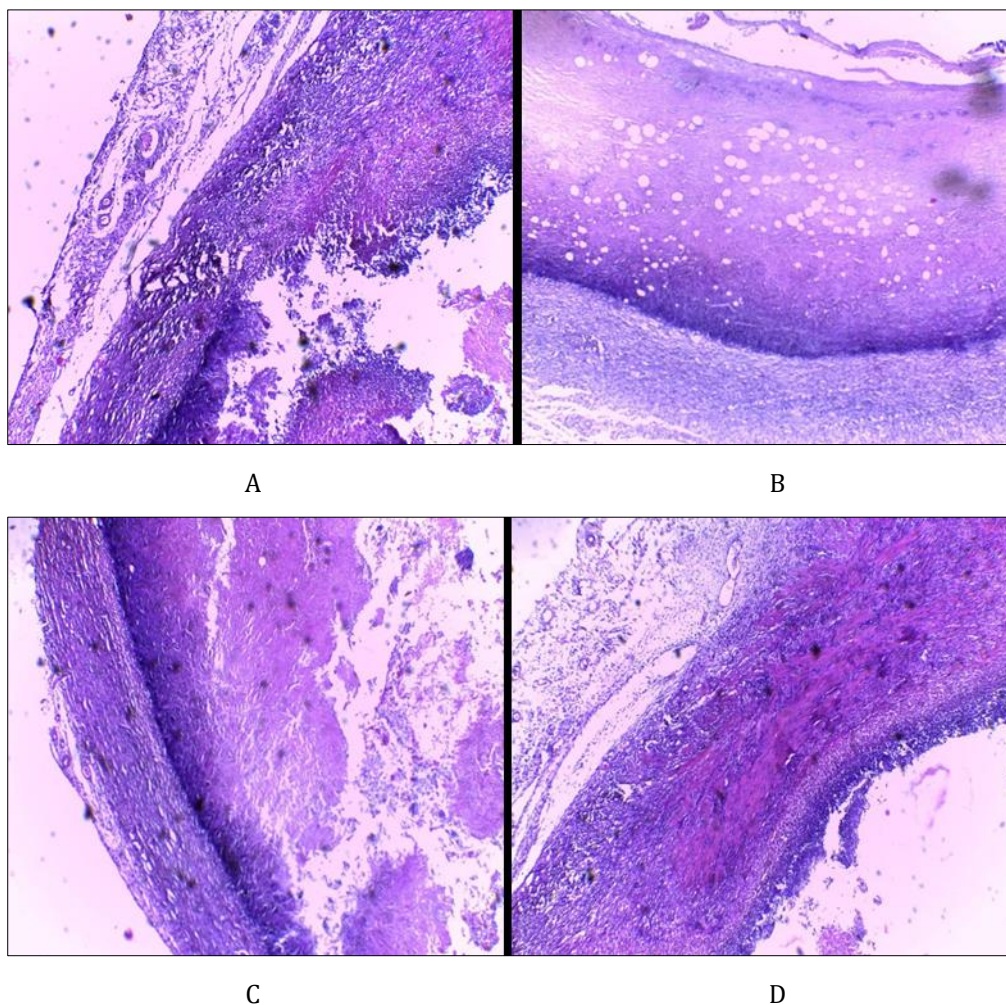


Figure 3 Histological section of teratoma, (H&E) (40x)

4. Discussion

Teratomas are bizarre neoplasms derived from embryonic tissues that are typically found only in the gonadal and sacrococcygeal regions of adults, Teratomas can be predominantly cystic or completely solid in appearance, Retroperitoneal mature cystic teratomas are characterized by a bimodal peak in incidence, occurring in the first 6 months of life and in early adulthood, diagnosis is made with help of radiological findings and can be confirmed after resection and histopathological examination. Surgery remains the mainstay of treatment. A definitive diagnosis is made following resection and histologic evaluation. Although teratoma is a benign tumor, its biological potential is unpredictable and it should be resected completely because it may grow and become unresectable, this study agrees with (15) Okulu et al (2015).

5. Conclusion

The results of this study showed that high doses of amlodipine caused teratoma formation. The incidence of immature teratoma is higher in adult, and its caused is unknown. Diagnosis requires a combination of clinical, radiological and laboratory findings. This article provides new information about the effect and interaction of drugs used in the treatment of pressure on pregnant women, as well as provides information about the use of appropriate and effective drug dose in the treatment of blood pressure.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

This article has been subject to ethical standards.

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