

## Retrospective Study

# Analysis of characteristic features in ultrasound diagnosis of fetal limb body wall complex during 11-13<sup>+6</sup> weeks

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**Specialty type:** Pediatrics**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C, C  
Grade D (Fair): 0  
Grade E (Poor): 0**P-Reviewer:** Guerriero S, Italy;  
Matute JD, United States**Received:** April 14, 2023**Peer-review started:** April 14, 2023**First decision:** April 26, 2023**Revised:** May 3, 2023**Accepted:** May 23, 2023**Article in press:** May 23, 2023**Published online:** July 6, 2023**Cai-Hong Ye**, Department of Ultrasound, Yijishan Hospital Wannan Medical College, Wuhu 241001, Anhui Province, China**Shuo Li**, Department of Ultrasound, Wannan Medical College, Wuhu 241001, Anhui Province, China**Li Ling**, Department of Obstetrics, Wannan Medical College, Wuhu 241001, Anhui Province, China**Corresponding author:** Cai-Hong Ye, Doctor, MM, Associate Chief Physician, Deputy Director, Department of Ultrasound, Yijishan Hospital Wannan Medical College, No. 2 Zhesan West Road, Wuhu 241001, Anhui Province, China. [yhyjsyy@163.com](mailto:yhyjsyy@163.com)

## Abstract

### BACKGROUND

Limb body wall complex (LBWC) is a fatal malformation characterized by major defects in the fetal abdominal or thoracic wall, visceral herniation, significant scoliosis or spina bifida, limb deformities, craniofacial deformities, and umbilical cord abnormalities (short or absent umbilical cord). Early diagnosis of this condition is of great clinical significance for clinical intervention and pregnancy decision-making. With the rapid development of fetal ultrasound medicine, early pregnancy (11-13<sup>+6</sup> wk) standardized prenatal ultrasound examinations have been widely promoted and applied.

### AIM

To explore the value of prenatal ultrasound in the diagnosis of fetal LBWC syndrome during early pregnancy.

### METHODS

The ultrasonographic data and follow-up results of 18 cases of fetal LBWC diagnosed by prenatal ultrasound during early pregnancy (11-13<sup>+6</sup> wk) were retrospectively analyzed, and their ultrasonographic characteristics were analyzed.

### RESULTS

Among the 18 fetuses with limb wall abnormalities, there were spinal dysplasia (18/18, 100%), varying degrees of thoracoschisis and gastroschisis (18/18, 100%), limb dysplasia in 6 cases (6/18, 33%), craniocerebral malformations in 4 cases

(4/18, 22%), thickening of the transparent layer of the neck in 5 cases (5/18, 28%), and umbilical cord abnormalities in 18 cases (18/18, 100%), single umbilical artery in 5 cases.

### CONCLUSION

Prenatal ultrasound in early pregnancy can detect LBWC as early as possible, and correct prenatal evaluation provides important guidance value for pregnancy decision-making and early intervention.

**Key Words:** Early pregnancy; Ultrasonography; Limb body wall complex; Fetus

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**Core Tip:** Limbs-body wall complex (LBWC) is a fatal malformation characterized by severe defects in the abdominal or chest wall of the fetus, resulting in protruding viscera, severe scoliosis or spina bifida, limb deformities, craniofacial malformations, and abnormal umbilical cord (short or absent). Our study focuses on the significance of using prenatal ultrasound in detecting LBWC during early pregnancy, where we also provide a retrospective analysis of ultrasound data and post-abortion consequences of 18 confirmed cases of LBWC. We aim to investigate further and identify the ultrasound characteristics of LBWC in early pregnancy to enhance our knowledge of this condition.

**Citation:** Ye CH, Li S, Ling L. Analysis of characteristic features in ultrasound diagnosis of fetal limb body wall complex during 11-13<sup>+6</sup> weeks. *World J Clin Cases* 2023; 11(19): 4544-4552

**URL:** <https://www.wjgnet.com/2307-8960/full/v11/i19/4544.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v11.i19.4544>

## INTRODUCTION

Limb body wall complex (LBWC) is a fatal malformation characterized by major defects in the fetal abdominal or thoracic wall, visceral herniation, significant scoliosis or spina bifida, limb deformities, craniofacial deformities, and umbilical cord abnormalities (short or absent umbilical cord)[1,2]. Early diagnosis of this condition is of great clinical significance for intervention and pregnancy decision-making. With the rapid development of fetal ultrasound medicine[3,4], early pregnancy (11-13<sup>+6</sup> wk) standardized prenatal ultrasound examinations have been widely promoted and applied. However, there are relatively few reports on early pregnancy ultrasound screening for LBWC. In this study, we retrospectively analyzed the sonographic data and post-abortion results of 18 cases diagnosed with LBWC in early pregnancy to explore the ultrasound features of prenatal diagnosis of LBWC in early pregnancy and enhance the understanding of LBWC.

## MATERIALS AND METHODS

### Study subjects

From March 2015 to October 2022, a total of 35486 pregnant women underwent early pregnancy (11-13<sup>+6</sup> wk) fetal nuchal translucency (NT) ultrasound examination at our hospital. Among them, 18 cases of LBWC were detected and confirmed after induced abortion. The pregnant women's ages ranged from 21 years to 39 years, with an average age of 28 years. The gestational age of the fetuses was calculated based on the menstrual cycle, and all were singleton pregnancies.

### Study methods

GE Voluson E8 and Philips EPIQ7 color Doppler ultrasound diagnostic instruments were used in our study, with a 2-8 MHz two-dimensional convex array probe. In accordance with the requirements of the Chinese "Prenatal Ultrasound Screening Guidelines", pregnant women were informed of the appropriate gestational age, content, purpose, importance, and limitations of early pregnancy prenatal ultrasound screening. In this study, all patients were placed in a supine position, and during the examination, in addition to routine checks for the number of fetuses, fetal heartbeat, placenta, and amniotic fluid, the main growth parameters of the fetus and the spectrum of the venous duct were measured. In cases with multiple pregnancies, chorionicity and amnionicity were determined. The focus was on obtaining the fetal mid-sagittal plane and measuring the crown-rump length and NT thickness on this plane, taking the average of three measurements. The presence or absence of the fetal nasal bone



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**Figure 1** Ultrasound sonographic analysis of limb body wall complex. A: The fetus with the absence of the thoracic and abdominal walls and the contents seen floating within the amniotic fluid; B: The baby postdelivery confirming the evisceration of the heart, liver, stomach, large and small bowel loops; C: Fetal umbilical artery blood flow spectrum, no venous catheter blood flow detected; D: Kyphosis of the thoracolumbar spine.

was also observed.

In addition, the following ultrasound screening planes were included: starting from the fetal head and sequentially examining the skull and brain. The lateral ventricle transverse plane primarily observed the lateral ventricle level cranial halo, cerebral falx, and bilateral choroid plexus in the lateral ventricles. With the abdomen, the umbilical cord abdominal wall entrance transverse plane primarily observed the structure at the umbilical cord abdominal wall entrance. All planes were saved in the workstation. If a defect in the fetal abdominal wall or thoracoabdominal wall was found, it was necessary to carefully observe whether there were abnormal echo masses and the size, shape, and structural echoes of the masses, whether the physiological curvature of the spine had changed, the development of the limbs, and whether there were any abnormalities in the umbilical cord.

## RESULTS

### General information of pregnant women

As shown in **Table 1**, the ages of pregnant women ranged from 21 years to 39 years old, with an average of 27-years-old. Gestational age ranged from 11-13<sup>+6</sup> wk, with an average gestational age of 12<sup>+6</sup> wk. Among the 18 cases, 11 cases of the 18 cases were screened for Down's syndrome in the first trimester and all were found to be low risk.

### Fetal NT measurement

As shown in **Table 2**, all 18 cases of LBWC fetuses were single live fetuses. Among the 11 cases, 5 had increased NT thickness, 2 had cystic hygromas, and 7 were not measurable.

### Ultrasound sonographic analysis of LBWC

As shown in **Table 3**, all fetuses had severe thoracoschisis or gastroschisis (18/18, 100%), either spinal scoliosis and torsion (18/18, 100%). Among them, 6 cases (6/18, 33%) had limb developmental abnormalities, 4 cases (4/18, 22%) had cranial malformations, and 1 case had spina bifida. Umbilical cord abnormalities, such as being too short or absent, were observed in 11 cases (11/18, 61%). Color Doppler examination revealed only one umbilical artery in 5 fetuses. None of the fetuses had detectable facial abnormalities (**Figure 1**). All 18 pregnant women chose to terminate their pregnancies, which was

Table 1 General information of pregnant women

No.	Age	Gestational age in wk	Pregnancy history, G/P/A/L	Embryo transplantation	Down syndrome screening status
1	29	13	G1P0	No	Unchecked
2	28	13 <sup>+6</sup>	G2P0A1	Yes	Unchecked
3	25	13 <sup>+5</sup>	G1P0	No	Low-risk
4	21	12 <sup>+3</sup>	G1P0	No	Low-risk
5	23	12 <sup>+4</sup>	G1P0	No	Low-risk
6	26	12	G2P0A1	No	Low-risk
7	30	11 <sup>+2</sup>	G2P0A1	No	Low-risk
8	29	13	G1P0	No	Low-risk
9	38	11 <sup>+3</sup>	G1P0	Yes	Low-risk
10	25	13 <sup>+2</sup>	G1P0	No	Low-risk
11	28	12 <sup>+6</sup>	G2P0A1	No	Low-risk
12	24	11 <sup>+6</sup>	G1P0	No	Low-risk
13	32	12 <sup>+3</sup>	G2P1L1	No	Low-risk
14	26	12 <sup>+4</sup>	G1P0	No	Unchecked
15	39	13 <sup>+6</sup>	G1P0	Yes	Unchecked
16	31	13 <sup>+5</sup>	G2P0A1	Yes	Unchecked
17	21	13 <sup>+2</sup>	G1P0	No	Low-risk
18	26	13	G1P0	No	Low-risk

G: Gestation; P: Production; A: Abortion; L: Live.

confirmed after induced abortions.

## DISCUSSION

### **Embryonic development mechanism of fetal LBWC**

LBWC is an uncommon, intricate, and fatal multi-malformation syndrome characterized by encephalocele and/or craniofacial clefts, thoracoschisis or gastroschisis, and limb deformities. Other features may include spinal scoliosis, genitourinary abnormalities, and short umbilical cords. The initial diagnostic criteria for LBWC were established by Van Allen *et al*[5] in 1987, and a diagnosis can be confirmed by the presence of two of the following three malformations: any type of limb defect, encephalocele or anencephaly with facial cleft, thoracoschisis or gastroschisis with visceral herniation.

The etiology of LBWC remains uncertain, there are three pathogenic mechanisms that have been discussed by foreign scholars[6-10]. Firstly, abnormal folding of the trilaminar embryonic disc during the first 4 wk of embryonic development. Secondly, early amniotic rupture with amniotic band syndrome. Finally, early embryonic vascular rupture leading to widespread blood flow impairment.

(1) Abnormal folding of the trilaminar embryonic disc during the first 4 wk of embryonic development, which represents the complete failure of folding along the three axes (cranial, caudal, and lateral) of the body. Abnormal longitudinal folding results in thoracoschisis or gastroschisis, while abnormal transverse folding prompts abdominal contents to protrude into an expansive amniotic sac, which inserts peripherally into the placental chorionic plate, resulting in absent or short umbilical cords. As a result of the compression of abdominal viscera, the spine and thoracic cavity cannot develop symmetrically, leading to severe spinal scoliosis and trunk abnormalities. Poor spinal rotation and incomplete pelvic closure may lead to congenital limb deformities[7].

(2) Early amniotic rupture. Early amniotic rupture caused by mechanical pressure or amniotic bands can lead to severe deformities such as spinal malformations, gastroschisis, and extremely short umbilical cords if the rupture occurs at the caudal end, with the lower half of the embryo entering the extraembryonic cavity through the rupture[8]. This mechanism was questioned by Paul *et al*[11], who reported a case of intact LBWC at 10 wk of gestation without rupture of the amniotic cavity.

Table 2 Fetal nuchal translucency measurement result

No.	NT	Nasal bone visible	Ductus venosus
1	2.0	Yes	Visible, no reverse a-wave
2	Unmeasurable	No	Invisible
3	Unmeasurable	No	Visible, no reverse a-wave
4	Unmeasurable	Yes	Invisible
5	Unmeasurable	No	Invisible
6	2.3	Yes	Visible, no reverse a-wave
7	3.8	Yes	Invisible
8	Unmeasurable	No	Visible, no reverse a-wave
9	Unmeasurable	Yes	Invisible
10	1.3	Yes	Visible, no reverse a-wave
11	1.8	Yes	Invisible
12	3.4	Yes	Visible, no reverse a-wave
13	1.1	Yes	Visible, no reverse a-wave
14	4.7	Yes	Visible, no reverse a-wave
15	2.8	Yes	Visible, no reverse a-wave
16	Unmeasurable	No	Invisible
17	3.6	Yes	Visible, no reverse a-wave
18	2.4	Yes	Visible, no reverse a-wave

NT: Nuchal translucency.

And (3) early embryonic vascular rupture or developmental abnormality. Some studies[10] suggest that vascular rupture during early pregnancy (at 4-6 wk of gestation) leads to the interruption of normal blood supply to the developing embryo, resulting in ischemia, hypoxia, hemorrhagic necrosis, and abnormal development of the embryonic disc, which in turn affects the closure of the abdominal wall and extraembryonic cavity.

Arshad believes that the pathogenesis of LBWC is more inclined towards the theory of early embryonic abnormal folding[12], with the malformations associated with LBWC depending on the degree of abnormal folding of the embryonic disc. On the other hand, Sahinoglu *et al*[13] and others believe that due to the complexity of LBWC malformations, all of the above pathogenic mechanisms are possible, leading to different subgroups.

### **LBWC classification**

There are many literature reports and controversies about the classification of LBWC, and most studies currently divide it into two types based on the characteristic abnormalities of LBWC[13-16]. Type I is based on craniofacial defects, while Type II is based on thoracoschisis or gastroschisis. However, Sahinoglu *et al*[13] proposed a new phenotypic classification, dividing it into three types, Type I still refers to craniofacial defects, while Type II refers to gastroschisis located above the umbilicus and large chest-abdominal wall defects. Type III pertains to defects located below the umbilicus, while the chest wall remains intact. This article primarily concentrates on thoracoschisis and gastroschisis, which aligns with the research conducted by Akinmoladun *et al*[17].

### **Ultrasonographic features of LBWC in early pregnancy**

At present, early pregnancy ultrasound examination is considered the safest and most reliable imaging technique for screening severe fetal structural malformations. Owing to the relatively large extraembryonic coelom in early pregnancy, it becomes straightforward to distinctly display the extent of thoracoschisis or gastroschisis as well as the protrusion of organs in the thoracoabdominal cavity into the extraembryonic coelom, making the diagnosis relatively easy. With the widespread popularity of early pregnancy (11-13<sup>+</sup> wk) prenatal ultrasound examinations, many severe fetal structural malformations have been detected. Some scholars believe that the most characteristic ultrasonographic clue for LBWC in early pregnancy is spinal curvature[18]. The basis for ultrasound diagnosis of LBWC may be when the fetus has a large abdominal or chest-abdominal wall defect, herniation of the viscera, short or

Table 3 Ultrasound sonographic analysis of limb body wall complex

No.	Ultrasonic anomaly					
	Body wall defect and bulge	Spine	Limbs	Brain	Umbilical cord	Others
1	Gastroschisis (bulge is liver)	Torsion	Both feet varus	-	Short	
2	Gastroschisis (bulge is liver)	Torsion	-	-	Undetectable	Cloacal malformation
3	Thoracoschisis and Gastroschisis (bulge are heart, liver, intestinal tube)	Twist into angles	-	Brain herniation	Short	
4	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Twisted arrangement irregularity	-	Encephalocele	Undetectable	Fetal cystic hygroma
5	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Torsion	Miss left upper limb	Meningoencephalocele	Undetectable	
6	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Curved, middle and lower segments not shown	-		Short	
7	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Twist into angles	Miss one upper limb		Undetectable	
8	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Abnormal bending, abnormal alignment			Short	Fetal cystic hygroma
9	Gastroschisis (bulge is liver)	Torsion		Meningoencephalocele	Undetectable	
10	Gastroschisis (bulge are liver, gastric vesicle and intestinal tube)	Lordotic bending		-	Short	Single umbilical artery
11	Thoracoschisis and gastroschisis (bulge are heart, liver, intestinal tube and gastric vesicle)	Lordotic bending		-	Undetectable	
12	Gastroschisis (bulge are liver, intestinal tube)	Lordotic bending		-	Short	
13	Gastroschisis (bulge are liver, intestinal tube)	Angle the side		-	Short	
14	Gastroschisis and malformation (bulge are liver and intestine)	Lordotic bending	Miss left upper arm	-	Short	
15	Gastroschisis and malformation (bulge are liver, intestinal tube and gastric vesicle)	Side bending and twisting		-	Short	Single umbilical artery
16	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Lordotic bending	Lower limb fusion	-	Undetectable	
17	Gastroschisis (bulge are liver, gastric vesicles and intestinal tubes)	Torsion	Miss right lower limb		Short	
18	Acromphalus (bulge is liver)	Torsion	-		Short	Megacystis

absent umbilical cord combined with spinal abnormalities[19,20].

The sonographic characteristics of the 18 LBWC fetuses in our investigation can be summarized as follows: (1) The most common and severe malformation in LBWC is the thoracoschisis or gastroschisis [21,22]. Due to the absence of abdominal wall development, the defect area is large and may be accompanied by chest wall defects, resulting in the opening of the thoracoabdominal viscera to the amniotic cavity. Prenatal ultrasound shows a large defect at the insertion of the fetal umbilical cord on the abdominal wall, with abnormal echo masses at the defect site, and the fetal liver, stomach bubble, and intestine protruding into the extraembryonic coelom. The umbilical cord is difficult to display or appears too short. Daskalakis *et al*[23] and others believe that abdominal wall defects can be roughly divided into three types, gastroschisis, umbilical protrusion, and body stalk-like malformation. LBWC can be considered when accompanied by spinal curvature or torsion, anencephaly or encephalocele, facial abnormalities, and limb development abnormalities; (2) All 18 fetuses had spinal developmental abnormalities, manifested as spinal kyphosis, torsion or scoliosis, causing the fetus to be in a flexed or hyperextended state, making it difficult to obtain the mid-sagittal section required for measuring crown-rump length in prenatal ultrasound screening guidelines, and thus unable to accurately determine the gestational age of the fetus by ultrasound. In this study, all cases were calculated by menstrual age. In this group, the earliest large abdominal wall defect was seen at 11<sup>+2</sup> wk. In this group, all cases had varying degrees of thoracoschisis or gastroschisis and abnormal spinal curvature; (3) Increased fetal NT,

similar to the findings of Daniilidis *et al*[24]. In our study, 4 cases out of 18 LBWC cases were normal, 5 cases had increased NT, and 9 cases could not be measured due to spinal torsion or concomitant cranial abnormalities. Although LBWC fetuses often have abnormal NT thickening or fetal edema, 8 cases in this group underwent early pregnancy Down syndrome screening and all were classified as low risk. Previous studies[13,25] have shown that fetuses with LBWC have a normal chromosomal karyotype and the recurrence rate in subsequent pregnancies is very low; (4) Cranial abnormalities. In our 18 cases, 3 had encephalocele, and 1 had exencephaly; (5) Limb abnormalities. In our study, limb abnormalities were manifested as clubfoot, limb agenesis, or fusion; and (6) Short or absent umbilical cord. Other associated malformations include megacystis, fetal cystic hygroma, and abnormal development of the cloacal cavity.

### **Differential diagnosis of LBWC**

Owing to the numerous resemblances in ultrasound manifestations between LBWC and Cantrell's pentalogy[25], the latter primarily encompasses omphalocele, ectopia cordis, lower sternal defects, anterior diaphragmatic defects, and pericardial defects. Its hallmark features are omphalocele and ectopia cordis. Nevertheless, Cantrell's pentalogy does not involve spinal and limb developmental abnormalities, which serve as crucial distinguishing factors from LBWC[26].

## **CONCLUSION**

As LBWC is a lethal disease, enhancing early detection is of utmost importance. Prenatal ultrasound should be well-acquainted with the sonographic features of LBWC, such as thoracoschisis and gastroschisis, severe spinal scoliosis, neural tube defects, limb abnormalities, and absence or shortening of the umbilical cord. Furthermore, when spinal scoliosis and omphalocele are observed, the likelihood of LBWC should be strongly considered. In conclusion, early pregnancy ultrasound can effectively diagnose LBWC, and precise prenatal evaluation holds significant value for informing parental decision-making.

## **ARTICLE HIGHLIGHTS**

### **Research background**

There are relatively few reports on early pregnancy ultrasound screening for Limb body wall complex (LBWC). In this study, we retrospectively analyzed the sonographic data and post-abortion results of 18 cases diagnosed with LBWC in early pregnancy to explore the ultrasound features of prenatal diagnosis of LBWC in early pregnancy and enhance the understanding of LBWC.

### **Research motivation**

In this study, we retrospectively analyzed the sonographic data and post-abortion results of 18 cases diagnosed with LBWC in early pregnancy to explore the ultrasound features of prenatal diagnosis of LBWC in early pregnancy and enhance the understanding of LBWC.

### **Research objectives**

To explore the value of prenatal ultrasound in the diagnosis of fetal LBWC syndrome during early pregnancy.

### **Research methods**

The ultrasonographic data and follow-up results of 18 cases of fetal LBWC diagnosed by prenatal ultrasound during early pregnancy (11-13<sup>+</sup> wk) were retrospectively analyzed, and their ultrasonographic characteristics were analyzed.

### **Research results**

Among the 18 fetuses with limb wall abnormalities, there were spinal dysplasia (18/18, 100%), varying degrees of thoracoschisis and gastroschisis (18/18, 100%), limb dysplasia in 6 cases (6/18, 33%), cranio-cerebral malformations in 4 cases (4/18, 22%), thickening of the transparent layer of the neck in 5 cases (5/18, 28%), and umbilical cord abnormalities in 18 cases (18/18, 100%), single umbilical artery in 5 cases.

### **Research conclusions**

Prenatal ultrasound in early pregnancy can detect LBWC as early as possible, and correct prenatal evaluation provides important guidance value for pregnancy decision-making and early intervention.

### Research perspectives

As LBWC is a lethal disease, enhancing early detection is of utmost importance. Prenatal ultrasound should be well-acquainted with the sonographic features of LBWC, such as thoracoschisis and gastroschisis, severe spinal scoliosis, neural tube defects, limb abnormalities, and absence or shortening of the umbilical cord. Furthermore, when spinal scoliosis and omphalocele are observed, the likelihood of LBWC should be strongly considered. In conclusion, early pregnancy ultrasound can effectively diagnose LBWC, and precise prenatal evaluation holds significant value for informing parental decision-making.

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## FOOTNOTES

**Author contributions:** Ye CH contributed to the conception and design, administrative support, and manuscript writing; Ye CH and Ling L contributed to the provision of study materials or patients; all authors contributed to the data collection and assembly; Li S contributed to the data analysis and interpretation; All authors contributed to the final approval of manuscript.

**Institutional review board statement:** The study was approved by Institutional Review Board of Yijishan Hospital, Wannan Medical College.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Data sharing statement:** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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**Country/Territory of origin:** China

**ORCID number:** Cai-Hong Ye 0009-0009-5808-8897.

**S-Editor:** Yan JP

**L-Editor:** Filipodia

**P-Editor:** Yan JP

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