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Review Article

Misdiagnosis of OEIS complex as omphalocele in autosite of epigastric heteropagus: a case report and literature review

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Abstract: Heteropagus twins are characterized by an incomplete component (parasite) that is normally smaller and dependent on the relatively complete host (autosite). Epigastric heteropagus refers to the attachment between the parasite and autosite to be in the epigastric region of the autosite. The associated abnormality in the autosite determined the clinical outcome. If the autosite is not associated with an omphalocele, but an OEIS complex (an acronym for omphalocele, exstrophy of the bladder, imperforate anus and spinal defects), the prenatal management is completely different because the prognosis of an OEIS complex is usually poorer than an omphalocele. Herein is reported an autosite associated with an OEIS complex, which was misdiagnosed as an omphalocele prenatally, and analyze similar published cases.

Keywords: Epigastric heteropagus, OEIS complex

Introduction

Heteropagus (asymmetrical form of conjoined twinning) is described entities that an incomplete component (parasite) is bound to a relatively normal entire member (autosite), which is an extremely unusual event with affecting 1 in 1-2 million live births [1]. Epigastric heteropagus refers to the attachment between the conjoined twins lies on the epigastrium of the autosite [1]. Twenty-six cases of epigastric heteropagus cases have been also reported in the English-language literature from 2002 to the present (**Table 1**). Reviewing these cases (**Table 1**), the parasite can be separated from the autosite in epigastric heteropagus and the clinical outcome depended on the associated abnormality in autosite. Therefore, accurate diagnosis prenatally is critical to prenatal management and consulting.

In the current era of mandatory antenatal check-ups and sonography, epigastric heteropagus is usually accurately diagnosed *in utero* during the anomaly scan. If the autosite is associated with the OEIS complex, rather than the omphalocele, which is a common complication, the prenatal diagnosis is challenging and the prenatal management is totally different due to the poor prognosis of the OEIS complex. Herein, an autosite associated with the OEIS complex is reported, which was misdiagnosed as an omphalocele prenatally, and the case represents a unique phenotype of epigastric heteropagus. In addition, this report includes a literature review of similar cases that have been reported in English for nearly 16 years.

Case report

A 27-year-old gravida 2 para 1 who had conceived spontaneously was referred to our hospital at 24 weeks gestation because of fetal multiple abnormalities. The woman's previous child had no congenital anomalies. Detailed ultrasonography at our maternal and fetal unit was performed. Ultrasound examination, however, revealed unexpected findings. One fetus

Table 1. Reported cases of epigastric heteropagus with associated anomaly in autosite (2002-2018)

Case No.	Study	Year	Sex	Congenital anomaly of autosite
1	De Ugarte et al. [2]	2002	M	Inferior sternal cleft, VSD, PFO, TGA, PDA, Co AOmphalocele, Meckel diverticulum
2	Martinez et al. [3]	2003	/	
3	Tongsin et al. [4]	2003	/	Omphalocele
4			/	Omphalocele
5			/	Omphalocele
6			/	CHD
7	MacKenzie et al. [5]	2004	F	Bilateral choroid plexus cysts, Dextrocardia, Omphalocele
8	George et al. [6]	2004	M	Talipes equinovarus
9	Bangroo et al. [7]	2004	M	
10	Bhansali et al. [8]	2005	F	Omphalocele
11			M	Omphalocele
12			F	
13	Kanamori et al. [9]	2006	F	Abducted/flexed LL
14	Hager et al. [10]	2007	F	VSD
15	Haga N et al. [11]	2009	F	Deformed right hip
16	Qasim M et al. [12]	2011	M	
17	Abubakar AM et al. [13]	2011	M	Omphalocele
18	Xie JT et al. [14]	2012	M	
19			M	Omphalocele
20	Kesan K et al. [15]	2013	M	Omphalocele, ASD, VSD, PDA, Overriding of aorta, Pulmonic stenosis
21	Calderoni DR et al. [16]	2014	M	Omphalocele, Deformed duplication of the right ear, PFO
22	Dar SH et al. [17]	2014	M	Omphalocele
23	Baskaran D et al. [18]	2015	M	Gastroschisis
24	Anca FA et al. [19]	2015	M	Omphalocele, Hydronephrosis, VSD, Septal aneurysm with low-pressure coronary sinus dilation
25	Raj P et al. [20]	2017	M	Omphalocele, PDA
26	Malik M et al. [21]	2018	M	Omphalocele
27	Present case		M	Holoprosencephaly, CHD, OEIS complex

PDA, patent ductus arteriosus; CHD, congenital heart disease; CoA, coarctation of aorta; VSD, ventricle septal defect; ASD, atrial septal defect; PFO, patent foramen ovale; TGA, transposed great arteries.

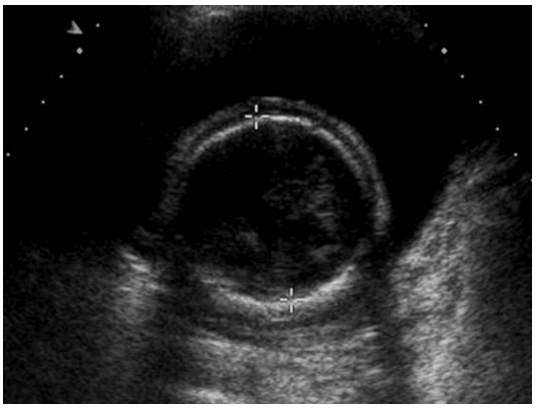

Figure 1. An axial sonographic image with biparietal diameter measurement showing a single ventricle cavity in the autosite.

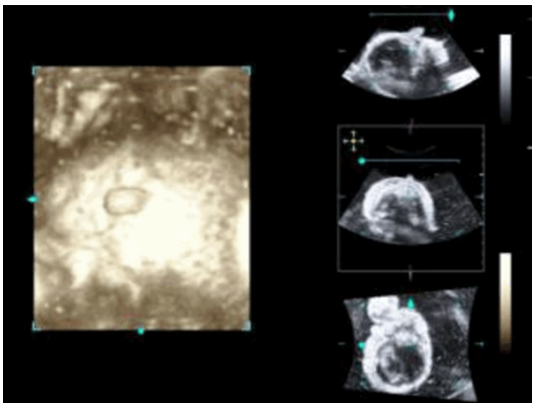

Figure 2. Three-dimensional ultrasound showing proboscis in the autosite.

(the autosite) had the following findings on 2D and 3D ultrasound: holoprosencephaly (**Figure 1**); proboscis (**Figure 2**); spinal bifida (**Figure 3**); cyclopia and an omphalocele (**Figure 4**); atrioventricular canal defect; and aortopulmonary window. In addition, a second body mass was detected that consisted of a fetal pelvis (the parasite) with a pair of lower extremities. A further detailed examination for twin B exhibited a pair of upper extremities. Therefore, the parasite was comprised of a pelvis and 4 completely formed extremities with no heart and head. No dividing membrane existed between the twins

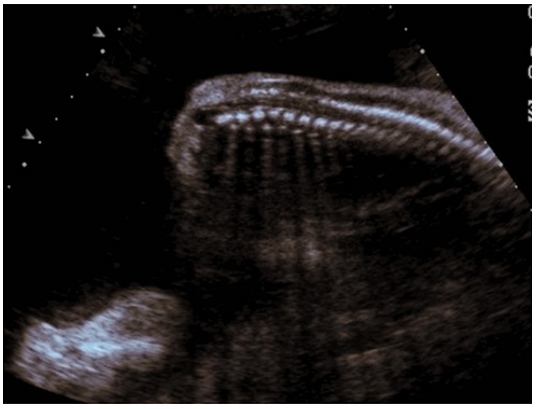

Figure 3. Sagittal sonographic image through a fetal spine showing spinal bifida in the autosite.

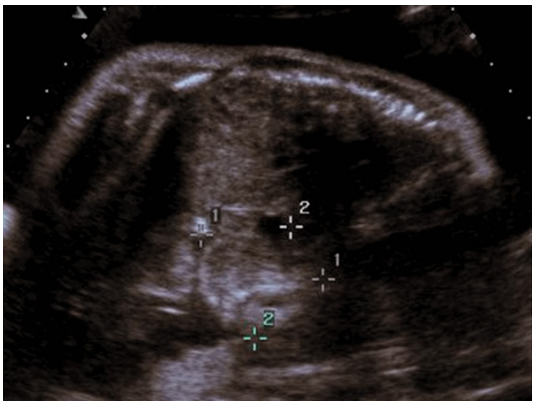

Figure 4. Sonographic image displaying an omphalocele in the autosite.

and a single placenta was located anteriorly to the uterus. A single umbilical cord was inserted from the autosite to the placenta. The estimated gestational age of the autosite was 24 weeks. Together, these prenatal findings suggested heteropagus and an autosite associated with holoprosencephaly, spinal bifida, cyclopia, a proboscis, an omphalocele, and congenital heart defects. Amniotic fluid samples were obtained from the conjoined twins via amniocentesis under ultrasonic guidance, and amniotic fluid cells were cultured for 1 week, followed by G-banding karyotype analysis using a Metascan Karyotyping System (Imstar S.A., Paris, France). The chromosomal phenotype of conjoined twins was 46XY. The family decided to terminate the pregnancy after consulting an obstetrician and pediatrician due to the poor prognosis of holoprosencephaly at the autosite.

Consent for a full post-mortem examination was granted. Only one placenta was present with a single umbilical cord. The total weight of the abortus was 1110 g and 33 cm in length. External inspection showed that the autosite was connected with the parasite in the epigastrium, which had a pelvis, two well-developed limbs, and two rudimentary upper limbs. The autosite had cyclopia, a proboscis (**Figure 5A**) and an omphalocele and imperforate anus (**Figure 5B**). A detailed autopsy examination in the autosite disclosed exstrophy of the bladder, cryptorchism, a split penis, and multiple malformations, including holoprosencephaly (**Figure 5C**), spina bifida occulta, an atrioventricular canal defect (**Figure 5D**), and an aortopulmonary window in the heart (**Figure 5E**). Moreover, the vascular in the falciform ligament of the autosite was supplied to the parasite. A small intestine was observed in the pelvis of the parasite, but a large intestine and anus was absent. Finally, X-ray showed a widened pubic symphysis in the autosite and developed bones in the lower and rudimentary upper limbs of the parasite (**Figure 5F**). Post-mortem examination in the abortus suggested that an accurate diagnosis was epigastric heteropagus and an autosite associated with holoprosencephaly, congenital heart disease, and the OEIS complex.

Discussion

Conjoined twins are categorized as symmetric and asymmetric, and the asymmetric form is known as heteropagus [22]. In the heteropagus cases, the independent portion, namely the autosite, is commonly well-developed. A summary of epigastric heteropagus twins and the associated congenital anomaly in the autosite for nearly 16 years, including the present case, is shown in **Table 1**.

Based on analysis of the reported cases, several characteristics were found in the epigastric heteropagus. First, male accounted for most of these cases (15/6 [male/female]). Our case was also a male fetus which was in accordance with the published statistics. The reasons for such male predominance is unclear. Second, congenital cardiac malformations are noted in 9 autosites and 6 have multiple heart defects. An explanation for the development of cardiac abnormalities in the autosite is secondary to ischemic insults which result from the fact that

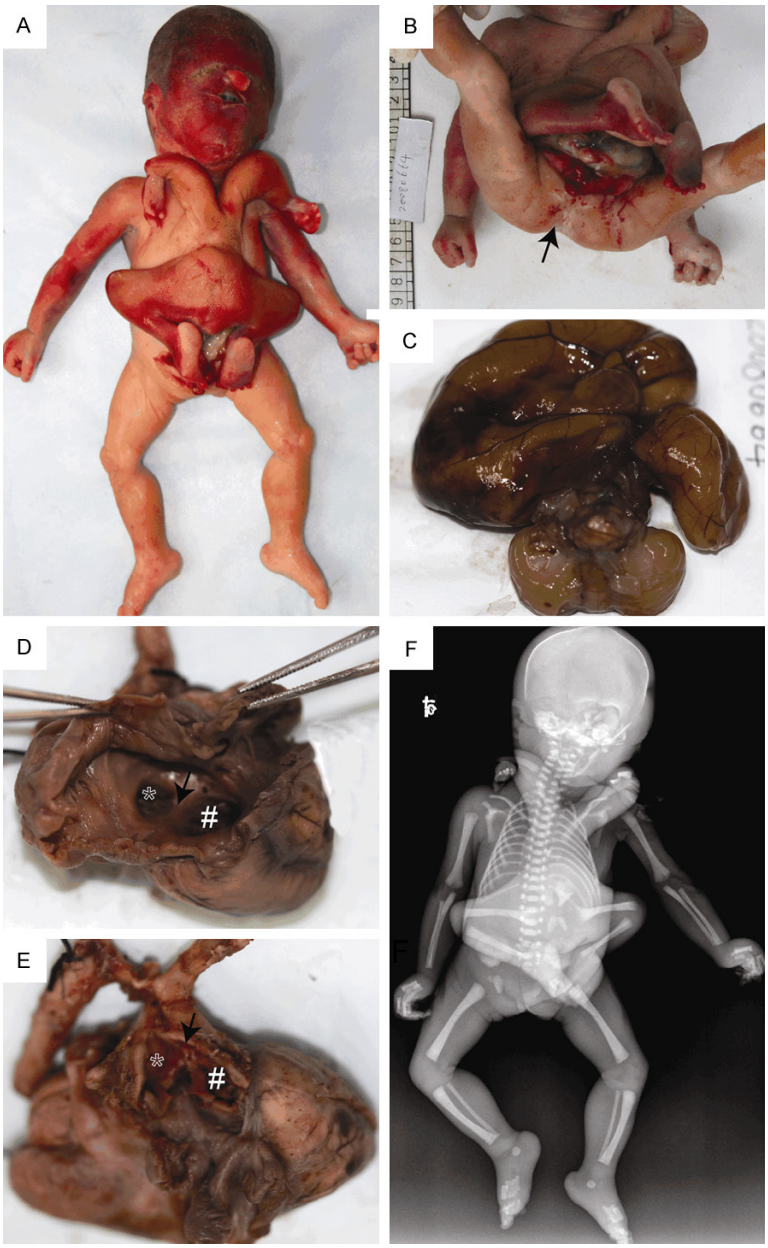

Figure 5. Photograph of a set of conjoined twins. A. The autosite with a proboscis and cyclopia. B. The autosite with the OEIS complex (arrow designating the diaper area with an imperforate anus). C. holoprosencephaly of the autosite. D. Atrioventricular defect of the autosite (asterisk designating the left ventricle, octothorpe designating the right ventricle, and arrow designating an interventricular septum). E. Window between aorta and pulmonary artery of the autosite. F. Co-twin radiograph showing the autosite with a spinal defect and splayed pubic tubercles.

the parasite poses a burden on the hemodynamic circulation [23]. Another potential reason of cardiac anomalies lies on the accident of a single injury at 3 weeks gestational age that result in both asymmetric twinning and disorder of early heart growth [24, 25]. Finally, an omphalocele was present below the epigastric connecting bridge in approximately 55.6% (15/27) of cases. Tempting explanation for the development of omphalocele lies on the face that the occurrence of the connecting bridge between the autosite and the parasite usually prevents mechanically the abdominal wall of the autosite from closing with the advance of gestation.

An obvious difference between the current case and previous cases is the association with the OEIS complex in the autosite. Due to the rarity of the OEIS complex, the etiology is unclear. Errors in monozygotic splitting has been suggested to contribute to the occurrence of the OEIS complex. Support for the suggestion is that twins, especially the same-genetic twin, has been observed to have a high incidence in patients with the OEIS complex [27, 28]. Similarly, the majority of epigastric heteropagus twins has commonly been considered as resulting from a fault during the process of fission in a single zygote, which leads to the growth of two centers of axial development rather than one [20]. Therefore, it can be speculated that an error in monozygotic splitting was responsible for the autosite with the OEIS complex and bearing the parasite in the present case.

Compared the postnatal autopy with the prenatal diagnosis, the OEIS complex was misdiagnosed as an omphalocoele. The reason for the misdiagnosis lies on the fact that absence of a visualized bladder was missed following an omphalocoele and an open neural tube defect in the autosite. Misdiagnosis would cause differential management to the fetus because the prognosis for the OEIS com-

plex and the omphalocele is different. For treatment of the OEIS complex, construction of bowel, bladder, and sexual function is challenging in most hospitals in our country. Conversely, treatment for an omphalocoele is usually successful. Therefore, an accurate prenatal diagnosis of the OEIS complex is required to give parents the option to terminate pregnancy.

Another unique phenotype in the autosite was the holoprosencephaly leading to the termination of the co-twins due to the poor prognosis. The exact etiology for the holoprosencephaly is unclear. With respect to etiopathogenesis, the attachment between conjoined twins may induce the occurrence of holoprosencephaly because a primary defect of ventral induction and patterning that accounts for total or partial failure of separation of the prosencephalon into two separate hemispheres results in classic holoprosencephaly [29].

In summary, prenatal diagnosis of a rare case of epigastric heteropagus is described here, in which the OEIS complex was misdiagnosed as an omphalocele. The autosite associated with the OEIS complex and holoprosencephaly was first reported in epigastric heteropagus in the English literature, expanding the clinical manifestation of epigastric heteropagus and adding benefit for accurate diagnosis and management of such rare conjoined twins.

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Disclosure of conflict of interest

None.

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