

# A case report of an infant with both left-sided gastroschisis and septo-optic dysplasia and literature review: possible shared etiology?

## Abstract

The co-occurrence of gastroschisis and septo-optic dysplasia, two rare congenital anomalies of unknown etiology, has been reported in four cases. We report a fifth case, and the second where the gastroschisis was on the left side. The case involved a term infant with left-sided gastroschisis who was found to have optic nerve hyperplasia, diabetes insipidus, and hypothyroidism during her initial hospitalization. Gastroschisis and septo-optic dysplasia share some common risk factors, such as young maternal age, smoking, and illicit drug use. Providers should be aware of the potential for hypopituitarism and potential neuro developmental complications associated with gastroschisis, especially in the rare case where the gastroschisis is on the left side.

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## Introduction

Gastroschisis is a congenital abdominal wall defect with extrusion of the abdominal contents through a defect typically just to the right of the umbilicus. Gastroschisis has been associated with multiple risk factors but its pathogenesis remains unknown. There are theories that it is due to a vascular insult, with known associations of young maternal age, cigarette smoking, and illicit drug use.<sup>1,2</sup> The incidence of gastroschisis is ~5 per 10,000 live births, and may be increasing.<sup>3</sup> Left-sided gastroschisis is even rarer with only 18 reports found in our review of the literature. Septo-optic dysplasia (SOD) is a heterogeneous clinical disorder characterized by a combination of optic nerve hypoplasia, pituitary hormone abnormalities and midline brain defects. The incidence of SOD is not certain, but reported to likely be ~1 per 10,000 livebirths.<sup>4</sup> These two seemingly unrelated congenital anomalies have several features in common. While the incidence of most congenital anomalies is directly correlated with maternal age, both of these anomalies are more common in younger mothers.<sup>1,5-7</sup> They are also both postulated to be related to an insult around the 6th week of gestation.<sup>1,5-7</sup> Co-occurrence of gastroschisis and septo-optic dysplasia has been reported 4 times, with the gastroschisis on the left side in one case. We present a second case of both left-sided gastroschisis and septo-optic dysplasia occurring in an infant girl.

## Case

An infant girl weighing 2300g was born at 37 4/7 weeks gestational age to a 37 year old G5 P3 now P4 mother via cesarean section for a non-reassuring fetal heart tracing. Pregnancy had been uncomplicated. The mother denied any illicit drug use or smoking history. The infant was found on delivery to have a 3 cm abdominal wall defect to the left of the umbilicus. The entire midgut intestine and the distended bladder were eviscerated. The bowel was thickened, edematous, and matted with a meconium stained peel. The infant was placed

in an occlusive plastic bag up to the torso, covering the defect and exteriorized bowel. The infant required no other specific interventions and had Apgar scores of 9 and 9. After post-delivery stabilization, the infant was sedated, paralyzed and incubated immediately prior to surgery. Primary closure of the gastroschisis was not possible due to extent of distention and thickening of the bowel. The intestinal contents were placed into a Silastic premade silo. The infant was extubated on post-operative day 1 to room air. The eviscerated bowel was slowly reduced over 13 days when final abdominal closure was performed. The infant passed her first meconium stool on DOL 22. On DOL 23, her serum sodium was 148mEq/L; serum osmolality 309mosm/L; and urine osmolality 233mosm/L. Urine output at that time was 4ml/kg/h and increased to a maximum of 9ml/kg/hr over the next several days. She was diagnosed to have diabetes insipidus. An MRI showed hypoplasia of the optic nerves and optic tracts and absence of the pituitary bright spot. The corpus callosum, cavum septum pellucidum and the optic chiasm were all present. Further investigation revealed hypothyroidism which was managed with levothyroxine. The MRI findings, pituitary hypoplasia and pituitary hormonal deficiencies satisfied criteria for a diagnosis of septo-optic dysplasia, a clinical diagnosis characterized by two or more of the following features: optic nerve hypoplasia, pituitary hypoplasia, and midbrain defects.<sup>7</sup> She was discharged from the NICU on DOL 40 exclusively breastfeeding. Estradiol at 2 months of age and was below the normal range. She has normal development and growth and no other identified health issues at 4 months of age.

## Discussion

Gastroschisis is a congenital full thickness abdominal wall defect with associated evisceration of the abdominal organs. The classic description is of a smooth edged defect typically smaller than 4 cm and almost always to the right of the umbilicus.<sup>8,9</sup> It has an estimated incidence of 2-5/10,000 births and appears to be increasing over the past 20 years.<sup>8,10</sup> A recent CDC report from 14 states showed

an increased prevalence of 30% between 1996-2005 (3.6/10,000) compared to 2006-2012 (4.9/10,000).<sup>11</sup> Gastroschisis is more common in younger mothers.<sup>1,2</sup> Prevalence rates as high as 11.45 per 10,000 have been reported for mothers who are less than 20 years old compared with 0.51 per 10,000 for mothers 35 years and older.<sup>1,8</sup> A lower BMI, smoking and drug use are all associated with an increased risk for having an infant with gastroschisis.<sup>1,2,12</sup> Infection, particularly sexually transmitted infection during pregnancy was associated with higher risk of gastroschisis.<sup>1</sup> At least some of these risks appear to be additive, the odds ratio for gastroschisis was very high (26.5, 95% CI 7.9-89.4) for malnourished mothers who smoked more than a pack/day 3 months before or during the first trimester.<sup>12</sup> No definitive etiology of gastroschisis has been proven although several hypotheses have been proposed. These theories include a failure of mesoderm to form in the body wall during the 4th week of conception, rupture of the amnion around the umbilical ring, abnormal involution of the right umbilical vein, disruption of the omphalomesenteric artery, or abnormal folding of the body wall during embryogenesis.<sup>13-15</sup> However, none of these theories explain the full clinical presentation of gastroschisis. For example, they do not explain the unilateral nature of the lesion with a predominance of right-sided lesions and a few left-sided ones. The involution of the right umbilical vein, or occasionally the left umbilical vein, could explain the laterality of the lesion.

However in one report the ipsilateral umbilical vein was observed to be patent.<sup>16</sup> Several of these theories implicate events occurring at a similar time in fetal life – between the 4-8th week of gestation. Left-sided gastroschisis is quite rare,<sup>9,14,17-20</sup> but differs from the more common right-sided lesion in several ways. First, although the incidence of right-sided gastroschisis is similar between male and female infants, left-sided gastroschisis occurs more often in girls.<sup>9,14</sup> In our review of the literature, we found 18 reported cases of classic left-sided gastroschisis (Table 1). Of these, 12 were female; 4 were male; in 2 cases the sex was not reported. Extra-intestinal malformations were more common in cases of left-sided gastroschisis compared with right.<sup>14</sup> Among those 19 cases (including the current case), the incidence of other malformations was 47%, compared to an incidence of 32% reported for right-sided lesions.<sup>10</sup> Septo-optic dysplasia is a clinical diagnosis characterized by two or more of the following features: optic nerve hypoplasia, pituitary hypoplasia, and midbrain defects.<sup>7</sup> There is a wide spectrum of clinical disease severity.

The etiology of septo-optic dysplasia is currently unknown. Genetic abnormalities have only been identified in less than 1% of cases to date.<sup>7</sup> The association of pituitary and forebrain abnormalities have led to speculation that septo-optic dysplasia is a result of an injury between 4-6 weeks of gestation.<sup>7</sup> Young maternal age and antenatal drug use are identified risk factors for septo-optic dysplasia, but the mechanisms by which they increase risk is unclear.<sup>5,13</sup> Our patient is the fifth reported co-occurrence of gastroschisis and SOD, and the 2nd with where the gastroschisis was left sided. (Table 2) In 1981 Linarelli reported an infant with gastroschisis who developed diabetes insipidus on the 10th post-operative day. The infant was then found to have left cerebral atrophy and septo-optic dysplasia.<sup>21</sup> In 2008 Navti et al.,<sup>22</sup> reported a case of an infant who was born at 37 weeks with gastroschisis and schizencephaly. The infant was found to have sept-optic dysplasia on fundoscopy. The infant later developed diabetes insipidus, panhypopituitarism and generalized tonic clonic seizures.<sup>22</sup> In 2008 Suver et al.,<sup>14</sup> reported on three infants with left-sided gastroschisis.<sup>14</sup> One of these also had septo-optic dysplasia and Panhypopituitarism. No mention was made about whether or not

diabetes insipidus developed. In 2010, Kamien et al reported on a child with gastroschisis.<sup>23</sup> The child was later found to have bilateral optic atrophy and panhypopituitarism with decreased ACTH, TSH, and diabetes insipidus.<sup>23</sup> Gastroschisis is generally felt to be caused by an arrest or disruption of normal development, rather than genetically determined abnormal development.

Most co-existing anomalies, such as intestinal atresias, are considered to possibly be related to vascular or other disruption occurring at the same embryologic stage. Case reports that become a published part of the literature cannot accurately reflect incidence or associations of congenital anomalies. However, the reported co-occurrence of the two rare anomalies of gastroschisis and SOD raise the possibility of a common etiology. The over-representation of left-sided gastroschisis in reports of SOD and gastroschisis may be due to random chance and selective reporting of unusual combinations. However, it makes sense to proactively consider that babies with gastroschisis, particularly left-sided, may be at risk for developing endocrine complications associated with hypopituitarism, and neuro developmental complications associated with SOD.

**Table 1** List of Cases of Infants with Left-sided Gastroschisis

| Case | Year | Authors                       | GA     | Sex | Associated anomalies   | Maternal age |
|------|------|-------------------------------|--------|-----|--|--------------|
| 1    | 1988 | Blair et al. <sup>1</sup>     |        |     |  |              |
| 2    | 1989 | Hirthler et al                | 27     | F   |  |              |
| 3    | 1989 | Hirthler et al                | "term" | M   |  |              |
| 4    | 1993 | Toth et al. <sup>18</sup>     | 35     | F   |  |              |
| 5    | 2000 | The pcharoennirund            | 37     | F   |  | 20           |
| 6    | 2000 | The pcharoennirund            | 40     | F   |  | 23           |
| 7    | 2001 | Pringle et al                 | 34     | M   |  |              |
| 8    | 2002 | Ashburn et al                 | 37     | F   |  |              |
| 9    | 2004 | Yoshioka et al. <sup>17</sup> | 38     | F   |  | 20           |
| 10   | 2004 | Orpen et al. <sup>19</sup>    | "term" | F   | Pseudoexstrophy<br>Pubic diastasis<br>Bifid clitoris<br>Double vagina<br>Anteriorly placed anus<br>ASD   |              |
| 11   | 2004 | Wang et al. <sup>16</sup>     |        |     | Situs inversus   |              |
| 12   | 2006 | Gow et al. <sup>9</sup>       | 39     | F   |  | 26           |
| 13   | 2007 | Prasun et al                  | 24     | M   | Bilateral multicystic dysplastic kidneys   |              |
| 14   | 2008 | Suver et al. <sup>14</sup>    | 34     | F   | Jejunal atresia<br>Microcolon<br>Septo-optic dysplasia<br>Panhypopituitarism<br>Blindness<br>Absent corpus callosum  |              |
| 15   | 2008 | Suver et al. <sup>14</sup>    | 35     | F   | AV malformations involving the posterior branches of the external carotid arteries, tentorial veins and dural sinuses and stenosis of the superior vena cava |              |
| 16   | 2008 | Suver et al. <sup>14</sup>    | 34     | F   | ASD Pulmonic stenosis  |              |
| 17   | 2010 | Patel et al. <sup>4</sup>     | 34     | F   | Small left colon   | 19           |
| 18   | 2013 | Mandelia et al                | "term" | M   |  | 20           |
| 19   | 2015 | Sullivan et al (current)      | 37     | F   | Bilateral optic Hypoplasia<br>Diabetes insipidus<br>Panhypopituitarism   | 37           |

**Table 2** List of Cases of Infants with Both Gastroschisis and Septo-Optic Dysplasia

| Case | Reference                | Gestational age (wk) | Birth weight (g) | Sex | Maternal Age (yr) | Findings described  |
|------|--------------------------|----------------------|------------------|-----|-------------------|---|
| 1    | Linarelli <sup>21</sup>  | 36                   | 2700             | -   |                   | In utero vascular accident<br>Right-sided gastroschisis<br>Diabetes insipidus<br>Optic atrophy<br>Left cerebral hemisphere atrophy                            |
| 2    | Navti <sup>22</sup>      | 37                   | 2180             | F   | 19                | Right-sided gastroschisis<br>Schizencephaly<br>Septo-optic dysplasia<br>Diabetes insipidus<br>Panhypopituitarism<br>Seizures                                  |
| 2    | Navti <sup>22</sup>      | 37                   | 2180             | F   | 19                | Right-sided gastroschisis<br>Schizencephaly<br>Septo-optic dysplasia<br>Diabetes insipidus<br>Panhypopituitarism<br>Seizures                                  |
| 3    | Suver <sup>14</sup>      | 34                   | -                | F   |                   | Left-sided gastroschisis<br>Septo-optic dysplasia<br>Blindness<br>Panhypopituitarism<br>Absent corpus callosum  |
| 4    | Kamien <sup>23</sup>     | -                    | -                | -   | 20                | Right-sided gastroschisis<br>Bilateral optic atrophy<br>Hypoplasia of the optic chiasm<br>Panhypopituitarism<br>Diabetes insipidus<br>Grey matter heterotopia |
| 5    | Sullivan et al (current) | 37                   | 2300             | F   | 37                | Left-sided gastroschisis<br>Bilateral optic Hypoplasia<br>Diabetes insipidus<br>Panhypopituitarism  |

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## Conflict of Interest

The author declares there is no conflict of interest.

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