DOI: https://doi.org/10.47275/2379-6707-118
Volume 9 Issue 1
Research Article

Scholit Publishers

Journal of Pediatrics and Congenital Disorders

Gastroschisis and Related Disruptive Disorders Associated with Amyoplasia: Implications for Decreased Maternal Age Effects, Increasing Rates, and Pathogenetic Heterogeneity

Mark Lubinsky*
Wauwatosa, WI, USA

Abstract

Introduction: Gastroschisis and amyoplasia are disruptive disorders that are usually found separately, but that can occasionally associate. Their relationship is examined to help understand the pathogenetic processes involved.

Methods: Data was re-examined from extensively studied amyoplasia cohorts published previously.

Findings: Although gastroschisis has increased in frequency 30 - 40-fold or more over several decades, this has not occurred for amyloplasia associated cases, indicating a different pathogenesis for the abdominal disruption here. A lower decreased maternal age effect for gastroschisis with amyoplasia compared to isolated cases supports this difference. The sex ratio for amyoplasia with gastroschisis and/or intestinal atresia unexpectedly showed an apparently significant excess of females, despite a small excess of males with amyoplasia alone.

Keywords: Gastroschisis; Amyoplasia; Hypoperfusion; Maternal age

Introduction

Gastroschisis and amyoplasia are disruptive disorders that are usually found separately, but that can occasionally associate. Their relationship is examined to help understand the pathogenetic processes involved. Gastroschisis, a congenital abdominal wall defect, has increased 20 to 30-fold over the past several decades [1], and the strongest and most consistent risk factor is decreased maternal age [2]. However, there are indications of pathogenetic heterogeneity [3]. In particular, patients with amyoplasia show a roughly 5% association with gastroschisis, even though gastroschisis, which is much more common, shows a much smaller frequency of amyoplasia. Here, data from the literature [3,4] is reanalyzed to examine this relationship, and its implications for the pathogenesis of gastroschisis and related disruptive disorders.

Materials and Method

Data was reviewed from an extensively studied amyoplasia cohort detailed in Reid et al. [3] and Hall et al. [4], plus additional review of the literature.

Findings

In a group of 560 patients with amyoplasia where information was available, the mean maternal age was 27.4 years. When gastroschisis was also present, it was 23 years, and with both gastroschisis and bowel atresia, also probably of vascular origin [3] 23.2 years. However, with bowel atresia alone, it was 26.2 years [5].

Of these 560 patients, 225 had been reviewed earlier [3]. Comparing the two studies, associated gastroschisis rates went from 5.3% to 4.5%; when bowel atresia was also present, it went from 2.7% to 1.2%.

Correspondence to: Mark Lubinsky, Wauwatosa, WI, USA, E-mail: mlubinsky@wi.rr.com

Citation: Lubinsky M (2023) Gastroschisis and Related Disruptive Disorders Associated with Amyoplasia: Implications for Decreased Maternal Age Effects, Increasing Rates, and Pathogenetic Heterogeneity. J Pediatr Congenit Dis, 9(1): 118. DOI: https://doi.org/10.47275/2379-6707-118

Received: July 25, 2023; **Accepted:** August 21, 2023; **Published:** August 23, 2023

Twinning was seen in 6.6% of patients with amyoplasia, 37 monozygotic and 4 dizygotic. The monozygotic twins had a sex ratio of 1.64, with 23 males and 14 females. An additional 3.2% of patients had twins documented in early pregnancy, for a total of 9.8%. No twin had gastroschisis, but 5 (13.5%) had intestinal atresia.

For amyoplasia, there were 295 males and 264 females, for a sex ratio of 1.12. Cases with gastroschisis and/or intestinal atresia showed a significant excess of females, with 31 females and 20 males. For isolated amyoplasia the ratio was 1.17.

Discussion

The number of reported patients with amyoplasia associated gastroschisis is small, and ascertainment was biased, and may have changed over time [4], so decreasing rates for associated gastroschisis are likely artifactual. Significant increases are unlikely, and the differences between these rates and the huge increases for gastroschisis in general (again, 20 to 30-fold) [1] is convincing evidence that this is a very real finding.

A lowered standard decreased maternal age effect for combined cases compared with isolated gastroschisis consistent with pathogenetic heterogeneity. While several pathogeneses have been proposed for gastroschisis, recent work supports disruptions related to normal right umbilical vein involution, with key roles for both thrombophilic and vascular factors. The most common cause appears to be thrombophilia related to maternal estrogen, which is higher with decreased maternal age during the first trimester [5,6].

However, this mechanism may also be heterogeneous sinceestrogen affects thrombosis in several ways [7]. Epidemic rises in gastroschisis presumably reflect an endogenous factor or factors [8], but this agent may not affect all forms of estrogenic thrombophilia, explaining why certain thrombotic predispositions fail to associate with gastroschisis [8].

With this, estrogenic thrombophilia is more common with younger mothers. However, the epidemic factor(s) may not affect all these mechanisms. Therefore, when alternative mechanisms are primarily involved in pathogenetic events, sequelae will not show increasing frequencies. This is probably the case with body stalk anomalies, another likely vascular derivative, which can also have decreased maternal ages, but which have not been noted to be becoming more common [9].

The data also suggests that, while hypoperfusion may cause amyoplasia[4], subsequent factors linked to lower maternal ages, presumably an estrogen related thrombophilia, are necessary for the associated gastroschisis. With amyoplasia, gastroschisis is also associated with decreased maternal age both with and without accompanying bowel atresia, and this is probably true of gastroschisis without amyoplasia, although this has not, to our knowledge, been specifically studied. The lack of a major decreased maternal age effect when atresia alone occurs with amyoplasia is consistent with findings with atresia in general. However, the presence of a maternal age effect when atresia, gastroschisis and amyoplasia all occur together, suggests a different mechanism in that situation.

These findings call attention to the heterogeneity of thrombophilic and vascular mechanisms, and potential interactions in the pathogenesis of disruptive disorders. Gastroschisis with amyoplasia involves at least two different processes, both of which differ epidemically from those responsible for "standard" cases.

The primary cause is probably related to hypoperfusion. For amyoplasia, this is probably related to the association with increased twinning which, although numbers were small, did not seem to be the case when gastroschisis was also present. Similarly, gastroschisis in general does not seem to be related to plural births [11].

A decreased maternal age with gastroschisis with amyoplasia points towards a role for estrogen associated thrombophilia. But, again, the absence of rate increases differentiates this from the standard form.

The sex ratio for amyoplasia with gastroschisis and/or intestinal atresia unexpectedly showed an apparently significant excess of females, despite a small excess of males with amyoplasia, no particular sex-bias for gastroschisis on general, and typically male biased intestinal atresias[11]. This suggests that the specific combination of mechanisms here can result in novel epidemiologic features.

Conclusion

Gastroschisis and amyoplasia are usually found separately but can occasionally associate. This relationship clarifies the pathogenetic processes involved with the two disorders. For gastroschisis, associations with amyoplasia support hetrogeneous pathogenetic processes involving both thrombophilic and vascular mechanisms. Thrombophilic heterogeneity explains a decreased maternal age effect similar to that seen with isolated cases. However, when associated with amyoplasia, there were no increases in frequency over time as observed with isolated gastroschisis. For intestinal atresia, cases found with gastroschisis seem to involve a different mechanism from isolated cases, although twinning is increased in both situations. Thrombophilic and vascular mechanism can interact, and an unusual female excess in both amyoplasia associated intestinal atresia and gastroschisis may reflect a specific combination of atypical pathogenetic mechanisms.

Acknowledgments

As the sole author, I contributed everything to the paper.

Conflict of Interest

Author declare no conflict of interest.

Citation: Lubinsky M (2023) Gastroschisis and Related Disruptive Disorders Associated with Amyoplasia: Implications for Decreased Maternal Age Effects, Increasing Rates, and Pathogenetic Heterogeneity. J Pediatr Congenit Dis, 9(1): 118. DOI: https://doi.org/10.47275/2379-6707-118

References

1. Castilla EE, Mastroiacovo P, Orioli IM (2008) Gastroschisis: international epidemiology and public health perspectives. Am J Med Genet C Semin Med Genet 148: 162-179. https://doi.org/10.1002/ajmg.c.30181
2. Salemi JL, Pierre M, Tanner JP, Kornosky JL, Hauser KW, et al. (2009) Maternal nativity as a risk factor for gastroschisis: a population-based study. Birth Defects Res A Clin Mol Teratol 85: 890-896. https://doi.org/10.1002/bdra.20612
3. Reid CO, Hall JG, Anderson C, Bocian M, Carey J, et al. (1986) Association of amyoplasia with gastroschisis, bowel atresia, and defects of the muscular layer of the trunk. Am J Med Genet 24: 701-710. https://doi.org/10.1002/ajmg.1320240415
4. Hall JG, Aldinger KA, Tanaka KI (2014) Amyoplasia revisited. Am J Med Genet A 164: 700-730. https://doi.org/10.1002/ajmg.a.36395
5. Lubinsky M (2012) Hypothesis: estrogen related thrombosis explains the pathogenesis and epidemiology of gastroschisis. Am J Med Genet A 158: 808-811. https://doi.org/10.1002/ajmg.a.35203
6. Lubinsky M (2014) A vascular and thrombotic model of gastroschisis. Am J Med Genet A 164: 915-917. https://doi.org/10.1002/ajmg.a.36370
7. Tchaikovski SN, Rosing J (2010) Mechanisms of estrogen-induced venous thromboembolism. Thromb Res 126: 5-11. https://doi.org/10.1016/j.thromres.2010.01.045
8. Lubinsky M (2022) Evidence for an estrogen disruptor driven meta-epidemic including hygiene hypothesis related potentiation and beneficial effects related to the obesity paradox. Austin Environ Sci 7: 1072.
9. Cardonick E, Broth R, Kaufmann M, Seaton J, Henning D, et al. (2005) Genetic predispositions for thromboembolism as a possible etiology for gastroschisis. Am J Obstet Gynecol 193: 426-428. https://doi.org/10.1016/j.ajog.2004.12.010
10. Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E (2000) Body stalk defects, body wall defects, amniotic bands with and without body wall defects, and gastroschisis: comparative epidemiology. Am J Med Genet 92: 13-18. https://doi.org/10.1002/(SICI)1096-8628(20000501)92:1<13::AID-AJMG3>3.0.CO;2-8
11. Husain T, Langlois PH, Sever LE, Gambello MJ (2008) Descriptive epidemiologic features shared by birth defects thought to be related to vascular disruption in Texas, 1996–2002. Birth Defects Res A Clin Mol Teratol 82: 435-440. https://doi.org/10.1002/bdra.20449