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Congenital Ampullary Atresia of the Fallopian Tube and the Coexistence of Fimbrial Tissue

Niamh Tallon[1], Ghadeer Akbar[1] and Peter McComb[1]*

Abstract

Objectives: To contribute 3 additional cases of congenital ampullary atresia to the 5 in our previously published case series. To document the constant coexistence of ipsilateral fimbrial tissue, to review the literature and to reconcile this finding with novel concepts of ovarian carcinogenesis.

Design: Case series.

Setting: Tertiary academic referral centre.

Patients: Cases of congenital ampullary atresia referred with infertility due to unilateral or bilateral ampullary obstruction over the years 2003-2012.

Intervention: Observation.

Main outcome measure: The presence of fimbrial tissue that coexists ipsilateral to a fallopian tube with congenital ampullary atresia.

Result: In all 3 cases fimbrial tissue was present ipsilateral to the congenital ampullary atresia.

Conclusion: There is a reliable finding of fimbrial tissue ipsilateral to congenital ampullary atresia in our series and, as can be reasonably ascertained, in all cases of CAA in the literature. This observation is consistent with a commonality of congenital celomic origin between fimbria and ovary, and with recent observations that there is molecular continuity between fimbria and the ovarian surface epithelium; and that niche cancer-prone stem cells populate the junction between fimbria and ovary.

Keywords

Congenital ampullary atresia; Fallopian tube oviduct

Introduction

Congenital ampullary atresia (CAA) of the fallopian tube is an unusual finding with an unknown prevalence in the general population [1]. CAA is likely under-reported due to the diagnostic subtleties associated with the condition [1] (Figure 1).

In infertile women with CAA, the ampullary obstruction is often identified at hysterosalpingography (HSG). However, the definitive diagnosis of CAA can only be made at surgery with the pathognomonic finding of a fallopian tube that is obstructed at the mid-ampullary region to form a hydrosalpinx. In the absence of the distal ampulla, the occluded mid-ampulla is connected by a 2-3 centimetre band of mesosalpinx to the outlying fimbrial tissue.

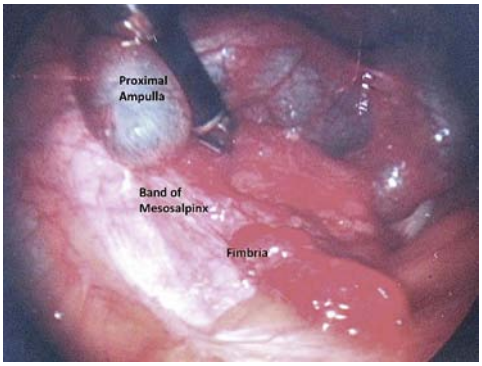

Figure 1: Laparoscopy: Case number 6. Left fallopian tube affected by CAA. Note the pristine serosal surfaces devoid of adhesions. The fimbrial tissue is separated from the proximal ampulla by a 2 centimeter band of mesosalpinx.

To improve fertility potential, surgical treatment consists of laparoscopic salpingostomy of the terminus of the occluded ampulla with approximation of the fimbria with microsuture. The fimbria is attached so that a cumulus oophorus retrieved by the fimbria will have access to the ampullary lumen [1]. Alternatively, when the CAA is unilateral, given the deleterious effect of the CAA hydrosalpinx upon embryo implantation, removal of the hydrosalpinx by salpingectomy may restore normal embryo implantation through the contralateral patent oviduct [2].

The anatomic defect in the fallopian tubal structure occasioned by CAA may predispose to an acute episode of pelvic pain due to torsion of the distal fimbrial tissue (with or without the ovary). This torsion may be perceived clinically to be the cause of the loss of the ampullary segment, rather than the torsion being a consequence of the pre-existing CAA.

Unless the CAA induces infertility or torsion this congenital condition is unlikely to be detected.

We have previously reported on 5 cases of CAA [1]. In 2005, Garrett and coworkers also identified 2 cases of CAA and noted the preservation of the fimbria in both [3]. They hypothesized that the fimbria has an embryologic origin that is distinct from the remainder of the fallopian tube. They also observed this hypothesis accords with the notion that 'ovarian' epithelial malignancies may arise from the fimbria as well as the ovary.

We support this hypothesis with the findings from our 3 cases added to our previous 5 case series and the findings of recent research.

Objectives

This paper has three objectives. Firstly to report the observation that fimbrial tissue adjacent to the ovary is always presenting ipsilateral to the CAA in 3 women. This report adds to the 5 CAA cases that we have reported previously.

***Corresponding author:** Peter McComb, Division of Reproductive Endocrinology and Infertility, UBC Department of Obstetrics and Gynecology, D409-4500 Oak Street, Vancouver, BC Canada, V6H 3N1, Tel: 1-604-2288112; E-mail: pmccomb@mail.ubc.ca

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Second, to review the literature for CAA to determine whether others have also identified preservation of the fimbria.

Third, to reconcile the finding of fimbrial preservation with novel concepts of fimbrial and ovarian carcinogenesis.

Materials and Methods

Standardized health data from women referred for infertility to an individual consultant was gathered prospectively at the time of initial assessment at our tertiary care center over the years of 2003 – 2012. At the time of consultation this information was entered into an ongoing administrative database system, dBase III (Ashton-Tate, Culver City, Ca) [4].

The subsequent clinical assessment included HSG and laparoscopy. The laparoscopic findings determined whether tubal obstruction identified at HSG was of infectious etiology or due to CAA. The presence of fimbrial tissue ipsilateral to the CAA was assessed at laparoscopy and documented by photography.

Those afflicted with CAA underwent corrective surgery at the same laparoscopy. The procedures were either a terminal neosalpingostomy and fimbrial approximation with microsuture, or a salpingectomy of the CAA oviduct.

The diagnosis of CAA was entered postoperatively into the same database to allow later identification and retrieval. The cases are collated here for review. This series augments 5 cases reported by one of us previously [1]. Those cases derived from the years 1987-2002.

A literature review was conducted through Pubmed and Web of Science using the following key words in combination and separately: fallopian tube, oviduct, isthmus, ampulla, anomaly, congenital, segmental, and atresia.

Results

Case series

Congenital ampullary atresia was identified in our database in an additional 3 cases, to bring the total combined with our previous series, to 8 such women (Table 1). We now refer to all 8 cases.

From the standardized historical information provided by each woman, there was no apparent pattern of etiology for the CAA. The variables documented were extensive and included a history of previous surgery, pelvic infections, use of an intrauterine device, detection of herpes, chlamydia and/or gonococcus, and exposure to diethylstilbestrol [4]. All positive information elicited is depicted in Table 1. At HSG, no congenital uterine anomalies were identified.

At laparoscopy, we documented healthy fimbrial tissue to be physically adjacent to the ipsilateral CAA in each of the 8 cases.

In the one instance of salpingectomy of the tube affected by CAA, the tissue specimen was described as a 4.3 x 0.8 centimeter tubular structure with attachment of a separate fimbria 1.3 x 0.8 x 0.4 centimeters in dimension. There were no histologic abnormalities.

After the reconstructive surgery, 5 women have delivered at least one healthy infant each; another has experienced a pregnancy of inconclusive site.

These 8 cases represent 3.9% of all salpingostomies performed by laparoscopy for distal tubal obstruction over the same 25 year period [4]. This includes those distal occlusions of infectious causation, but excludes iatrogenic occlusions such as fimbriectomy, segmental sterilization or excision of ectopic pregnancy.

At the time of referral, for all but one case, the diagnosis by the referring gynecologist was distal hydrosalpinx, or hydrosalpinges, of infectious etiology. This was so, irrespective of whether a laparoscopy had been performed. In the single case where the etiology of CAA was correctly identified before referral, that gynecologist had previously attended a case of CAA.

Literature review

In review of the literature regarding ampullary atresia, there are publications of cases that present clinically as infertility, and also as acute pelvic pain, usually related to torsion.

In 2006, Nawroth and coworkers published a report of a single case of CAA [5]. In addition, 18 cases of either unilateral or bilateral segmental atresia were identified from 12 earlier publications. In 11 cases the atresia involved the ampullary segment. In 5 cases, the atresia included the isthmus. In 3 cases there was an absent distal tube and/or ovary; Nawroth considered these to be consistent with loss of tubal tissue due to torsion. Otherwise, in 11 cases there was preservation of fimbrial tissue and ovary ipsilateral to the CAA [5].

Since the publication of Nawroth's series, Dahan in 2006 reported a case of unilateral CAA with preservation of the fimbria; the histology showed no inflammation [6]. Ganesh et al. reported 3 similar cases of CAA all treated surgically by creating an ampullary neostomy and suturing the edges through a slit in the (preserved) fimbria. One conceived a term pregnancy [7]. Garrett et al. reported experience of 2 cases of CAA; an 11 year old female with episodes of acute pelvic pain, and a 20 year old female with hydrosalpinx [3]. In both, the pristine ipsilateral fimbrial tissue was noted. An embryologic relationship between fimbria (distinct from the rest of the oviduct) and ovary was hypothesized. In this context, the relevance of their observation for a fimbrial origin of 'ovarian' malignancies was conjectured.

Besides these cases, that are unequivocally examples of CAA, there are other reports that may involve CAA. Eustace in 1992 published 2 cases: the first case manifest bilateral stumps of isthmus, a cystic ovary on the left, and absent distal tube and ovary on the right [8]. The second case had a normal left adnexum and an isthmic stump with no distal tube or ovary on the right side. The etiology was considered to be a vascular insult, or congenital atresia predisposing to torsion. Uckuyu et al. published 4 cases of segmental tubal loss [9]. The etiology in each instance is unclear, but associated pelvic adhesions in 2 cases may imply torsion and/or infection.

Sankaran et al. reported a case of tubal 'autoamputation' in 2009 [10]. The findings on the right side were a necrotic distal ovarian complex mass (excised) with isthmic stump. The left tube was patent and the left ovary was pexed to the uterus to prevent torsion.

Kopec et al. published on a 14 year old female proven to have a congenital uterine anomaly and absent left kidney [11]. The acute left tubal torsion with hematopyosalpinx was conjectured to be subsequent to a congenital tubal anomaly.

Pabuccu et al. reported unilateral absence of fallopian tube and ovary and suggested that congenital atresia was a predisposition to the torsion [12].

Table 1: Fertility outcome of women with congenital atresia of distal ampulla after neosalpingostomy and fimbrial approximation or salpingectomy at our institution: years 1987-2012.

Author (y)	Presentation	History	Tubal Anomaly	Treatment	Fertility Outcome
Johnston and McComb [1]	Case 1	Positive chlamydial culture	Bilateral distal ampullary atresia	Laparoscopy-bilateral salpingostomy	Term birth
	Age: 27	Renal calculi		Endosalpinx attenuated	
	Primary infertility for 4 years	Identical twin sister			
	Case 2	Positive chlamydial culture	Left distal ampulla atresia	Laparoscopy-left salpingostomy	Not pregnant
	Age: 31	Oligomenorrhea		Endosalpinx normal	
	Primary infertility for 8 years	Varicocele therapy Myomectomy 7 cm fibroid			
	Case 3	Previous miscarriage at 9 weeks gestation	Left distal ampulla atresia	Laparoscopy-left salpingostomy	Live birth 35 weeks' gestation
	Age: 31			Endosalpinx normal	
	Secondary infertility for 18 months				
	Case 4	Hypothyroid	Right distal ampulla atresia	Laparoscopy-right salpingostomy	hCG 208 IU/L
	Age: 35			Endosalpinx normal	Pregnancy site unknown
	Primary infertility for 25 months				
	Case 5	Positive chlamydial culture	Right distal ampulla atresia	Laparoscopy-right salpingostomy	Term birth
	Age: 28			Endosalpinx attenuated	
	Primary infertility for 18 months				
Tallon, Akbar and McComb	Case 6	Polycystic ovarian syndrome	Left distal ampullary atresia	Laparoscopy- left salpingectomy	Term birth
Since 2003	Age: 33	Oligo-ovulatory			
	Secondary infertility for 18 months	Clomiphene therapy			
		History of herpes type II			
		Childhood asthma			
		No history of pelvic inflammation			
	Case 7	Previous missed abortion at 9 weeks' gestation followed by dilatation and curettage	Left distal ampullary atresia	Laparoscopy- left salpingostomy	Term birth
	Age: 33	Non-ruptured appendicitis		Endosalpinx normal	
	Primary infertility for 24 months	Takes various herbal supplements including vitamins and folate			
		No history of pelvic inflammation			
	Case 8	Non-ruptured appendicitis	Left distal ampullary atresia	Laparoscopy-left salpingostomy	No pregnancy
	Age: 23	No history of pelvic inflammation		Endosalpinx normal	
	Primary infertility for 18 months	Infantile febrile seizures			
		Mononucleosis at age 15 years			

There are also case reports of that may lead to surgical findings similar to those of CAA, but of unrelated etiology. For example, in 2007, Grover published on torsion of a midsegment of tube associated with a paratubal cyst [13]. The fimbria was intact. She pronounced that this etiology was evidence that CAA was over-reported.

Of these reports, those of Dahan et al. [6], Ganesh et al. [7], and Garrett et al. [3], and coworkers (6 cases), consist unequivocally of CAA with adjacent healthy fimbriae (Table 2). In the reports [8-12] with a total of 9 cases, each author and coworkers postulated that a congenital oviductal anomaly may have predisposed to torsion of fallopian tube and/or ovary in some or all of their cases. However, it cannot be ascertained as to whether fimbriae were present, pre-torsion, in the majority of their cases. Grover's case appears to be a singular exception, with clear evidence that factors other than oviductal atresia, such as a paratubal cyst may induce tubal torsion and lead to the loss of a segment of ampulla with preservation of the fimbria [13].

The 6 cases of definite CAA in the literature from 2006 to the

Table 2: Literature review: congenital ampullary atresia with coexisting ipsilateral fimbria.

Author (and co-workers) Year	Number of cases	Findings	
		Bilateral	Unilateral
Nawroth et al. [5] (review article 2006)	11	8	3
Dahan et al. [6] (2006)	1		1
Ganesh et al. [7] (2008)	3	3	
Garrett et al. [3] (2008)	2	1	1
Tallon (2013)	3		3
Total	20	12	8
*Includes our earlier 5 case series (1)			

present, added to the 11 cases of Nawroth (these included our earlier 5 case series) and the 3 cases that are the subject of this paper, bring the total to 20 cases of CAA that have preservation of the ipsilateral fimbria [5] (Table 2).

Discussion

Congenital ampullary atresia is a rare finding that is likely under-reported due to the diagnostic subtleties associated with the condition [1]. Those affected can be asymptomatic or misclassified, because the finding of an absence of a segment of the ampulla of the fallopian tube is often subtle and, specifically, can be misinterpreted as being an ampullary obstruction of infectious etiology [1].

Alternate mechanisms by which segmental tubal deletions may potentially occur include environmental factors, acquired infectious obstruction, or they may be secondary to vascular compromise due to torsion. Despite these diverse possibilities, CAA is a frequently reported cause of segmental absence of the ampulla [5]. Furthermore, CAA may well predispose to torsion due to loss of integrity of the tube with an increased tendency of the distal tube (and ovary) to twist.

In all of the 8 cases reviewed in our series, there was no history of acute undiagnosed pelvic pain to suggest acute torsion. The pathognomonic findings of CAA at laparoscopy and a total lack of intra-peritoneal infectious stigmata, as well as the high degree of fecundity achieved after salpingostomy with approximation of the fimbria, point to a true congenital etiology [1]. Occlusion sustained after pelvic infection is usually associated with damage to the ciliary mucosa and thus poor pregnancies rates after terminal salpingostomy [4].

In the literature, both unilateral and bilateral tubal atresias have been described, either involving the isthmic, ampullary or distal portions of the tube [1,3,5-7,14,15]. These are isolated findings in 30% of cases. The other 70% are associated with Müllerian anomalies [16]. When the abnormality is an isolated partial absence of the tube, it has not been associated with a renal tract abnormality [6]. It is notable, in our 8 case series, that HSG did not identify any uterine anomalies associated with CAA.

The fallopian tubes, uterus, cervix and upper vagina all derive from the paramesonephric (Müllerian) system; the pair of ducts that originates from the celomic epithelium of the urogential ridge between 8-16 weeks gestational age. The adjacent mesonephric (Wolfian) system acts as a developmental guide, directing normal paramesonephric fusion and canalization [17]. The fallopian tubes derive, embryologically, from the unfused cranial aspect of the paramesonephric ducts. Aberrant anti-Müllerian hormone has been considered contributory to Müllerian anomalies [18].

The master regulatory genes involved in development are known as the homeobox genes. These are highly conserved and are expressed in a co-linear fashion, leading to very controlled and ordered gene expression from the 3' to the 5' end of the gene. The *HOXA* genes are associated with the Müllerian system in the human female; *HOXA9* expression is highest in the fallopian tube, with *HOXA10* and *HOXA11* activity being found in the uterus [19].

A recent study has documented that fimbrial tissue develops at a later stage than previously thought - after 20 weeks' gestation [20]. Along these lines, Garrett and coworkers hypothesized that the embryologic origin of the fimbria is distinct from the remainder of the oviduct [3]. This is based upon their observation of fimbria ipsilateral to CAA. It also accords with the presence of fimbrial tissue juxtaposed with the ovary in females affected by type B Mayer Rokitanszki Küster Hauser (MRKH) syndrome, despite absence of the remainder of the fallopian tubes (and also the vagina and uterus) [19].

The fimbria has some commonality with the ovary; both the ovarian surface epithelium (OSE) and the fimbrial epithelium derive from celomic mesoderm.

Auersperg and coworkers have shown that there is an anatomical and molecular continuity in the epithelium of the fimbria and the OSE (they share differentiation mesenchymal and epithelial markers like N-cadherin, EpCAM, E-cadherin and OVGP1) [21]. This is considered to be a transitional area and the authors suggest a possible susceptibility to neoplastic transformation as is the case in the squamo-columnar junction of the uterine cervix or the esophageal-gastric junction.

Flesken-Nikitin and coworkers have carried out comparative gene expression profiling analyses on OSE by laser capture microdissection and have demonstrated that the OSE expresses many genes that are involved in somatic stem cell maintenance [22]. This is considered to be evidence of a stem cell niche at the junction of the OSE, mesothelium and tubal epithelium. They hypothesize that such junction-associated stem cell niches are predisposed to form cancer. They note that aberrations in the molecular and cellular mechanisms that govern epithelium regeneration may contribute to cancer.

After extensive collation of the current literature pertaining to a fimbrial origin of 'ovarian' cancer, Chene and coworkers have proposed a model of serous 'ovarian' carcinogenesis [23]. This model encompasses a tubal origin and an ovarian origin of epithelial malignancy. In the tubal origin, dysplastic tubal abnormalities, TP53 mutations, and associated genotoxic stress within the secretory cells of tubal epithelium, all lead to loss of cell cycle control and thus clonal expansion, which in turn evolve into serous tubal intraepithelial carcinoma. These lesions extend through endosalpingiosis to the ovary and peritoneum. For the ovarian origin, cortical inclusion cysts are subjected to a hyperactive stroma, which leads to dysplasia and malignant transformation with physical extension towards the tube and peritoneum.

We conclude that our finding of the consistent presence of the fimbria in all 8 cases of CAA, and in a total of 20 cases of CAA in the published literature, is circumstantial evidence to support the concept proposed by Garrett [3] that the fimbria may have a unique association

with the ovary that is distinct from the remainder of the fallopian tube. This also accords with the notion of many researchers [21-24] that ovarian carcinogenesis, specifically epithelial malignancies, may arise from fimbrial tissue as well as from the OSE.

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Author Affiliation

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[1]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, University of British Columbia, Vancouver, British Columbia, Canada

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