

Pregnancy after prophylactic total gastrectomy

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Abstract Hereditary diffuse gastric cancer is an autosomal dominant inherited cancer predisposition syndrome characterized by susceptibility to diffuse gastric and lobular breast cancers. Since current screening options for diffuse gastric cancer are ineffective, prophylactic total gastrectomy (PTG) is a recommended option for unaffected germline *CDH1* mutation carriers. It is unknown whether pregnancy after surgery is possible or advisable due to potential maternal nutritional deficiencies. In this report we describe the pregnancy outcomes in three *CDH1* mutation positive women after PTG and in a *CDH1* mutation negative woman after total gastrectomy for early gastric cancer.

Keywords HDGC · Prophylactic total gastrectomy · Pregnancy

Introduction

Background

Hereditary diffuse gastric cancer (HDGC) is an autosomal dominant, inherited cancer predisposition syndrome associated with germline mutations in the epithelial-cadherin (*CDH1*) gene [1, 2]. The syndrome is characterized by an average life-time risk of 70% for diffuse gastric cancer in both male and female carriers of *CDH1* mutations and up to a 50% average life-time risk for lobular breast cancer in female mutation carriers [2].

Since the association of DGC with germline mutations in the *CDH1* gene was identified in 1998 [3], over a hundred other families world-wide have been described who carry mutations in this gene. Germline mutations in the *CDH1* are found in up to 50% of clinically defined North American families with HDGC from different ethnic backgrounds, predominantly from low incident populations [2]. Although it has been proposed that individuals who have a *CDH1* cancer-predisposing mutation undergo routine surveillance for gastric cancer, the optimal management of individuals at risk for a cancer is controversial because of the unproven value of current surveillance regimens [2, 4–7]. Given the high lifetime risk of stomach cancer in *CDH1* mutation carriers, and the lack of a proven effective screening test, prophylactic surgery is considered to be a realistic and reasonable option [8–10].

Gastrectomy is a major operation with many potential complications. Before undergoing this procedure, one must

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Table 1 Summary of patients history

Patient	CDHI status	Age at TG	Post-TG complications	Pregnancy history	Total wt gain during pregnancy	Dietary supplementation	Baby weight & GA	Pregnancy complications & medications	Tests and results	U/S
A	+	34	Significant nausea and vomiting on day 8 after solid foods. Resolved spontaneously. Discharged on day 14	Gravida 2, Para 1 1 Child pre-surgery is A&W	12.7 kg (73–85 Kg)	Yes Folate (8 mg day); ferrous gluconate (330 mg/day); vitamin B12 (intramuscular/month)	3,850 g 40 weeks	Seizure disorder—Valproic acid (250 mg day)	Fasting glucose-1 normal MSS negative	8 weeks; 16 weeks 2 days 18 weeks 3 days
B	+	39	None known	Gravida 7 Para 2 1 Child pre-surgery is A&W	13 kg (58.5–72 kg)	Yes Monthly B12 Calcium and multivitamins	4,082 g 40 Weeks	Pregnancy induced anaemia	MSAFP-normal; MTHFR heterozygote	Serial—every 4 weeks
C	+	21	Required endoscopic dilatation of oesophagojejunal stricture at 5 weeks and 3 months post op	Gravida 1 Para 1	No info	No information on dietary counselling B12 monthly; folate	3,425 g 40 Weeks	Blood transfusion at 7 weeks for Pernicious anaemia (HB 7.1);	MSAFP-normal	1 at 16 weeks—normal
D ^a	–	27	None known	Gravida 8 Para 3	16 kg (50–66 kg)	Yes	3,260 g 39 Weeks	Bilateral CPCs at 19 weeks-amino declined Ferrous sulphate Prenatal vitamins Preg induced anaemia-placed on ferrous sulphate	MSAFP-normal Fasting glucose—normal	Every 4 weeks from 8 to 35 weeks 1 day
					No info	Yes	3,175 g 38 Weeks		MSAFP-normal	Serial ultrasounds
					10 kg (60–70 kg)	Yes Folate 4 mg/day ASA .81 mg/day Prenatal vitamins	1,954 g 33 Weeks	Prenatal vitamins Cerclage for incompetent cervix in previous pregnancy; Preg induced anaemia-ferrous sulphate	MSAFP-increased risk for Tri 21-amino declined; MTHFR heterozygote	Serial ultrasounds

^a Patient D had a total gastrectomy after stage 1 DGC was diagnosed. There were very few records available on her second pregnancy. *MTHFR* methylene tetrahydrofolate reductase deficiency

consider the 1–2% risk of death associated with the procedure and nearly 100% risk of long term complications, including concern of possible malnutrition [9].

With the advent of further awareness of HDGC and genetic testing for germline *CDHI* mutations, younger women, who have not started or completed their families, have either opted for or are contemplating this surgery. Understandably, there are concerns amongst both the women and their health-care providers with regard to the potential complications in both the mother and the foetus that may arise during pregnancy following PTG.

There are only a handful of case reports in the literature [11, 12] which explore the outcomes of pregnancy following gastrectomy. In this paper we report three women who each had successful term pregnancies after PTG. We also report on a woman who had three successful pregnancies after total gastrectomy following diagnosis of early DGC.

Case presentations

Methods

Information on the pregnancies and their outcomes was collected through medical records after patient consent was obtained.

Patient A is currently a 38 year old gravida 4 para 2 woman who had a laparotomy PTG with Roux-en-Y esophagojejunostomy. She has a healthy 7 year old daughter from a pre-PTG pregnancy. Approximately, a year after her PTG, she became pregnant. All pregnancy details are in Table 1.

Patient B is a 42 year old gravida 7 para 2 woman who had a laparotomy PTG with Roux-en-Y esophagojejunostomy. She had 5 first trimester losses, 2 of which were due to karyotypic abnormalities (Trisomy 22 and Trisomy 4). Parental chromosomes were done after the first loss and were normal. Her seventh pregnancy was conceived approximately 2 years after her PTG. Details of her pregnancy history are in Table 1.

Patient C is a 25 year old gravida 1 para 0 woman who underwent a PTG with a Roux-en-Y reconstruction. She became pregnant about 2½ years after her PTG. Pregnancy information is in Table 1.

Patient D is a 42 year old gravida 8 para 3 woman, underwent a TG (Roux-en-Y) after a diagnosis of DGC at 27 years. She did not receive any chemotherapy as the GC was detected at stage I. Her pre-cancer reproductive history was complicated by 4 first trimester spontaneous abortions caused by low levels of progesterone. She had 3 children within 8 years of her TG.

Conclusions

The risks of PTG are not trivial as one of the significant risks facing women contemplating pregnancy is malabsorption of nutrients such as vitamin B12, vitamin D, calcium, folate and iron [9]. Deficiencies in iron, vitamin B₁₂, folate, and calcium can result in maternal complications, such as severe anemia, and in fetal complications, such as neural tube defects, intrauterine growth restriction, and failure to thrive [13].

The long-term effects of total gastrectomy on nutritional status are not well known, neither is the role of nutritional support. Dietary counseling is usually individualized, but generally not well defined. Two studies in the English literature that discuss the issues of pregnancy after gastrectomy [11, 12] provide follow-up data on the pregnancy outcomes of 158 women who had gastrectomies for reasons other than cancer. Neither study revealed a change in the ability of a woman to conceive or deliver a baby after gastrectomy. Anaemia was noted in 20/33 pregnancies by Peck et al. suggesting the possibility of increased risk of anaemia after gastrectomy.

In view of the results of these 2 studies and studies investigating the ability of women to conceive and deliver normal infants post-bariatric surgery, it would appear that the anxiety over poor pregnancy outcomes may be allayed as long as the appropriate supplementation for likely nutritional deficiencies is implemented [14–17].

It is important that women of childbearing age who are undergoing PTG be counseled that pregnancies occurring post-gastrectomy will have specific nutritional requirements. These women will need to be monitored by both an obstetrician and a nutritionist throughout the pregnancy. Young women of childbearing age are especially encouraged to continue taking vitamins so that a deficiency at pregnancy onset can be avoided.

Here we report a total of 7 pregnancies in 4 women post-gastrectomy. All pregnancy outcomes were normal. However, until there is long-term follow-up data for both the women who are post-gastrectomy and the offspring of mothers who have conceived post-gastrectomy, continued caution regarding planned post-operative conception should still be undertaken.

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