



Cate's Story: Hereditary Diffuse Gastric Cancer

Megan Rogers, RN, MHS

Cate is a 25-year-old woman who has a germline mutation in *cadherin 1 (CDH1)*, coupled with a significant family history of diffuse gastric cancer. Cate's journey started with her seeing her mother and sister die at a young age from this disease. Rather than being daunted by this adversity, she showed great resilience, coping with not only her grief but also simultaneously dealing with the impact of finding that she was a carrier of the same genetic disorder.

Gastric Cancer

Gastric cancer is a major cause of cancer-related mortality worldwide (Black, Kaneshiro, Lai, & Shimizu, 2014) and is thought to be responsible for about 10% of cancer-related deaths across the globe (Worster et al., 2014). Although it is a significant problem in the Western world, it is far more common in Asia (Macdonald, 2011), where it is a significant public health burden (Tan & Wong, 2012).

A small proportion of all gastric cancers (1%–3%) arise because of a known hereditary syndrome, the most common of which is hereditary diffuse gastric cancer (HDGC) (Pattison & Boussioutas, 2015). This is an autosomal dominant genetic disease characterized by an increased risk of developing diffuse gastric cancer at a young age. The gene responsible for HDGC is *CDH1*, also known as *E-cadherin*, a germline mutation conferring an 80% risk of developing gastric cancer during the lifetime of the carrier (Black et al., 2014, Pattison & Boussioutas, 2015). Overt gastric cancer frequently appears before 40 years of age but also

has been reported in teenage *CDH1* carriers (Framp, 2010). Females with germline *CDH1* mutations face an additional risk of developing lobular breast cancer, with a reported cumulative risk of 60% by the age of 80 years (Pattison & Boussioutas, 2015).

CDH1 Mutation Carriers

HDGC is characterized by high disease penetrance, and the management of identified carriers is complicated by the lack of a reliable surveillance method for effective early detection and diagnosis of the multiple signet ring cell carcinomas that are seen with HDGC. Routine endoscopy for known *CDH1* mutation carriers has proven to be ineffective in the setting of a cancer that is typically subtle, infiltrating beneath normal mucosa and leaving the stomach to appear normal (Pattison & Boussioutas, 2015).

Genetic Testing

Cate's mother and sister died of gastric cancer at ages 30 and 22 years, respectively. Before she died, Cate's sister had genetic testing and was identified as a carrier for the *CDH1* gene mutation. Cate's sister is the index patient in this family because the identification of her genetic mutation raised the

question of genetic testing for other relatives, including Cate, who was her only sibling (Fitzgerald & Caldas, 2006). Cate's mother came from a large family, and this diagnosis and its implications naturally generated much anxiety. The emotional impact of the diagnosis of a genetic disorder such as this cannot be underestimated and can have a huge impact on family members, forcing them to make difficult decisions about their future (Lynch et al., 2008; Mahon 2014). Given the clinical and psychological implications of testing positive as a carrier for a genetic disorder, at-risk individuals must receive counselling with a genetics service before any testing takes place (Fitzgerald & Caldas, 2006).

Management

CDH1 mutation carriers, such as Cate, should be managed by a team of healthcare professionals (Pattison & Boussioutas, 2015; van der Post et al., 2015). Prior to coming to the multidisciplinary clinic at the Peter MacCallum Cancer Centre in Melbourne, Australia, Cate attended a familial cancer center for genetic counseling and subsequent mutation testing. She demonstrated good insight regarding the implications of having a *CDH1* mutation. She was made aware of the statistics around her lifetime risk of developing gastric

Megan Rogers, RN, MHS, is an advanced practice nurse in Upper Gastrointestinal Services at the Peter MacCallum Cancer Centre in Melbourne, Australia. The author takes full responsibility for the content of the article. The author did not receive honoraria for this work. No financial relationships relevant to the content of this article have been disclosed by the author or editorial staff. Rogers can be reached at megan.rogers@petermac.org, with copy to editor at CJONEditor@ons.org.

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