

Case Study

Surgical decision for a young woman with familial adenomatous polyposis

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Summary

In the present case report, there are two particular learning points which are crucial. The first is that we must take serious symptoms seriously, even in young people. In this case study, we had a young woman with a change in bowel habit, with cancer being a differential diagnosis which would usually be further down the list. However, due process was followed which led to the diagnosis being made swiftly. Furthermore, we must remember that spontaneous mutation is present in over a quarter of cases of FAP so, again, take serious symptoms seriously. Secondly, a point which is important for this case is the optimization of a patient's condition prior to surgery. In the present case, the patient was admitted for TPN to help her recover some weight and strength to prior to surgery, to maximize her chances of a successful surgical outcome.

Abstract

Familial adenomatous polyposis (FAP) is a disease characterised by a multitude of polyps (hundreds to thousands), most often present in the colon, which have pre-malignant potential. The condition is due to a mutation in the adenomatous polyposis coli (APC) gene. Although the majority of these cases are inherited, a significant proportion arise due to a de novo mutation. The definitive treatment for the condition is surgery, but with multiple surgical options available, it is important to consider the trifecta of best evidence, clinical judgement and patient values in the selection process. In the present case report, a 36-year old woman diagnosed with FAP presented with a small bowel obstruction upstream of her stoma. Eight months previously, she underwent a panproctocolectomy and ileostomy with the creation of a ileal-pouch. The surgery was necessary as there was a suspected rectosigmoid cancer seen on CT. Reported is the information pertaining to her recent stay in hospital following the obstruction but the discussion explores the multi-faceted approach to determining which type of surgery was most suitable for this patient.

FAP - a summary

Familial Adenomatous Polyposis (FAP) is an autosomal dominant condition in which there is a germline mutation in the adenomatous polyposis coli (APC) gene on chromosome 5. The consequence of this mutation is characteristic polyp formation predominantly in the colon, but also at other sites such as the small bowel, which can develop into adenocarcinomas. Although named 'familial', it is believed that 10-30% of cases of FAP arise from de novo mutations¹. FAP is a rare disease, with estimates of frequency from 1 in 6,850 to 29,000 people². It is estimated that FAP is responsible for approximately 1% of colorectal cancer presentations³.

A brief history

The first reported case of polyposis was described in 1721 by Menzel⁴. This report was followed by many others in the subsequent decades, with an ill-defined suspected sequelae of events involving rectal haemorrhage leading to mucosal prolapse, inflammation, diarrhoea and rectal mucosal follicular hypertrophy⁵. At the beginning of the 20th century, the tendency for the polyp condition to have an inherited predisposition was illuminated⁵. Later that century, it was highlighted the pre-malignant potential of these adenoid polyps with surgery becoming an important treatment option. The first 3-stage proctocolectomy for the condition was performed in 1924⁶. A few years later, it was determined that the inheritance pattern for this condition was dominant⁷, and there began to appear the suggestion that offspring of affected individuals should undergo a prophylactic sigmoidectomy. The first proctocolectomy with a straight ileoanal anastomosis was successfully carried out in 1933. Later, Lloyd-Davies carried out the first colectomy and ileorectal anastomosis in St Mark's Hospital⁸. Much later, in 1978, another treatment option, called a restorative proctocolectomy was performed²². FAP does not just affect the colon, with extra-intestinal features described by Gardner in 1951 which include desmoid tumours, cyst-like tumours and bone tumours⁹.

Aetiology and pathogenesis

The characteristic gene affected in FAP is APC. The role of this gene is as a tumour suppressor gene, which is involved in controlling the Wnt signal transduction pathway¹⁰. The possibility of an association of a chromosomal deletion in 5q and FAP was proposed in 1986¹¹ and confirmed to be 5q21-22 by two independent groups in 1987^{12,13}.

The polyps which arise in FAP have malignant potential. There is a link between the site of mutation in

the APC gene and the degree of disease severity. Mutations at the far 3' and 5' ends of the APC gene are associated with a milder phenotype whilst mutations between codons 1251 and 1309 are associated with an increased polyp burden, as well as the presentation of colorectal cancer earlier in life^{14,15}. Furthermore, patients with a mutation 3' to codon 1400 have a significantly greater risk of intra-abdominal desmoid which is a serious cause of mortality in FAP patients¹⁶.

Presentation

The vast majority of patients with FAP are diagnosed prior to presentation as one of their parents will be affected the condition. Genetic testing is generally done around 12 years of age¹⁷. Surveillance plays a large role in preventing the onset of colorectal cancer. There have been numerous reports that centralised registration and prophylactic examination has improved the prognosis of FAP¹⁸⁻²⁰. However, as mentioned, up to 30% of FAP cases are spontaneous mutations¹. Therefore, it is possible for patients to present in their early middle age with non-specific abdominal symptoms such as bowel changes, decreased appetite, increased flatulence and intermittent per rectal bleeding²¹.

Treatment

The mainstay of treatment for FAP is surgical intervention. The rationale is to reduce the risk of colorectal cancer by removing the colon before any cancer can develop. From the late 1940's the only surgical options available were total proctocolectomy, where the colon, rectum and anus were removed or colectomy with ileorectal anastomosis (IRA), where the colon was removed and the ileum was joined to the rectum⁵. However, in 1978, another surgical option, restorative proctocolectomy, with an ileal pouch anal anastomosis (IPAA) was described and became widely used in FAP prophylaxis²².

Case Presentation

Patient details

Day 1 Jan 12 2018
Name: WD
Date of Birth: 13/10/1982

Presenting Complaint

A 36 year old woman, Whoopie Dale, was admitted to SEU with abdominal pain and vomiting. Whoopie had not passed stool into her stoma bag throughout the day. She had experienced two episodes of vomiting.

No dysuria. No cough. No chest pain.

History of Presenting Complaint

Whoopie has had a four week history of abdominal pain. She describes it as being crampy 'like being in labour' every 10 minutes. The pain was worse on movement. In this time she has had variable stoma output but has been passing flatus. She has also had small amounts of PR discharge.

The patient had presented to the surgical emergency unit two weeks previously with similar, but less severe complaints. Then, it was determined that her obstructive picture was likely to be due to slow bowel transit. She was given buscopan and sent home.

Past Medical History

Chemotherapy 2018 (August)

Panproctocolectomy and ileostomy with pouch 2018 (May)

Familial Adneomatous Polyposis 2018 (March)

Forceps live birth delivery 2017 (March)

Miscarraige < 12 weeks 2016 (May)

Miscarraige >12 weeks with ERCP 2016 (October)

Anti-phospholipid syndrome 2015

Factor V Leiden (heterozygous) 2015

Depression 2010

Drug History

Codeine

Loperamide

Tramadol 50 mg + Hyoscine 10 mg

Allergies: Tetanus vaccine

Social History

Whoopie lives at home with her husband and her 22 month old son.

Family History

There is no family history of note.

Systemic Enquiry

Cardiovascular, respiratory, gentio-urinary, neuro: No abnormalities detected

Examination

General Inspection: Alert and conversing.
Cardiovascular System: Heart sound 1+2 present with no additional sounds. Respiratory System: Breath sounds clear. Abdominal System: Abdomen soft, no guarding, no rebound. However, there was noted discomfort medial to the stoma on the right side. Stoma filled with light brown mushy faeces.

Initial Impression

Taking in to account the above history and clinical findings, it was suspected that Whoopie was experiencing bowel obstruction (possibly intermittent?) upstream of her stoma.

Investigations

Bloods:

Hb	121	g/L
WCC	12.1	x10 ⁹ /L
Neutrophils	9.3	x10 ⁹ /L
INR	1	(ratio)
Na	133	mmol/L
K	3.2	mmol/L
Urea	4.2	mmol/L
Creatinine	79	µmol/L
eGFR	71	ml/min/1.73 m ²
Bilirubin	12	µmol/L
ALT	11	Int Unit/L
ALP	104	Int Unit/L
Albumin	33	g/L
Ca	2.65	mmol/L
Phosphate	1.05	mmol/L
Amylase	110	Int Unit/L

Radiography:

18/01/2018CT abdo and pelvis with contrast:

The small bowel proximal to the site of the defunctioning ileostomy is dilated, measuring a maximum diameter of 6.7 cm. There is a very small volume of enteric contract seen within

ileostomy.

No pneumoperitoneum, free fluid or collection.

Normal liver, spleen, pancreas, kidneys and adrenals.

No enlarged lymph nodes.

Imaged lower lungs are clear.

No bone lesions.

Conclusion: Subacute small bowel obstruction just proximal to site of defunctioning ileostomy and is most likely adhesional in nature.

Management

Day 1: On the probability of there being an intermittent small bowel obstruction, it was determined that the patient should be admitted with a view to ease her pain and discomfort. This was achieved by intubation of the stoma which 'instantly' alleviated the pain.

Furthermore, Prof Cunningham decided that it was timely to close the ileostomy. The patient was deemed to be very poorly and had lost a lot of weight. As such, the decision was made that she needed to be admitted and given TPN to build her up for surgery to make the join in two weeks.

Day 12: surgery -

Incision: Laprascropy

Findings: The surgical team undertook an examination under anaesthetic and the pouch anal anastomosis was satisfactory. A sutured anastomosis was performed and the site of obstruction identified but this did not require resection when freed from the fascia.

Recovery - 12 hours post-op:

Self ventilating

Haemodynamically stable, normotensive

Warm and perfused

Afebrile

Alert and orientated (GCS 15)

Ongoing pain issues, commenced PCA morphine, bolus rate 1 mg

Also on regular IV paracetamol

Comfortable pain control

Wound clean and dry

24 hours post-op:

Feels well.

No flatus and no stools yet

Nausea and vomiting

PCA continued

48 hours post-op:

Watery stools being passed

PCA stopped and tramadol commenced

6 days post-op:

Continues to manage pain

Continues to pass stools

Discharge home

Discussion

The decision to perform a panproctocolectomy and ileostomy with the formation of an ileo-anal pouch was arrived at following the consideration of best evidence, clinical judgement and patient values.

Best evidence

There are a number of surgical options available to a patient with FAP, and a number of considerations to attend to each one.

The first option is that of a total proctocolectomy which results in the total removal of all large bowel mucosa. The benefit of this is that it is completely protective against colorectal cancer and is thus oncologically the

best procedure. However, this is accompanied by profound emotional and psychological consequences and is therefore less commonly performed in FAP patients, unless there is low rectal insult or sphincter dysfunction²⁵.

Another option is a colectomy with ileo-rectal anastomosis (IRA). A major benefit of this procedure is the ability to perform it laparoscopically²⁴. Furthermore, a permanent ileostomy is not required, which is comparison to the total proctocolectomy²⁵. A major drawback of this procedure is the fact that as some of the mucosa remains, there is a risk of the development of carcinomas in time and routine surveillance is required. However, even with surveillance, cancer risk rises around the age of 50^{26,27}, which may require these patients to progress to a complete proctectomy.

The final surgical procedure of interest is a restorative proctocolectomy with ileo-pouch anal anastomosis (IPAA). The major benefit of this procedure is the advantage of removing virtually all of the large bowel reducing the risk of future cancers but does require a pelvic dissection to do so. As a result, there is an increased risk of both erectile and ejaculatory function in males as well as fertility in females^{25,28}. There is evidence to suggest that fertility in women can be halved following this procedure²⁹. Like the IRA, this procedure requires further surveillance of the anorectal transition zone where polyps may arise. It has also been reported that adenomas, and even carcinomas can arise from the ileoanal pouch which can subsequently lead to pouch removal^{30,31}.

A meta-analysis of the latter two surgeries included 12 studies including 1,002 patients with FAP²⁵. The findings were that multiple post-operative procedures such as bowel frequency, night defecation and the requirement for incontinence pads were significantly less in the IRA-treated patients than the IPAA group. However, faecal urgency was more pronounced with IRA than IPAA. Rectal cancer was only seen in the IRA group (5%) and most likely accounts for the greater requirement for abdominal reoperation on the rectum (28%) compared to IPAA (3%). In a case series comparing patient outcomes for IRA v IPAA, there were fewer side effects such as increased frequency, bowel discomfort and passive discomfort presenting in IPAA cases³². However, this case series only included 27 patients so should be met with caution. Another study which assessed 184 patients found no difference in either mental health summary score or physical health summary score between groups of patients who had either undergone IRA or IPAA procedures³³, suggesting the two procedures to be of equal merit as perceived by the patients. However, of the 184, only 32 were in the IRA group which could bias interpretation. Taken together, these analyses seem to suggest that there may be lesser side effects with the IRA procedure than the IPAA one, but this is accompanied by a greater risk of re-operation.

Clinical judgement

It was evident from the genetic testing and colonoscopy that FAP was the diagnosis for Whoopie. Therefore, an important next step was to consider which surgery might be best suited. Prof Cunningham is experienced in proctocolectomy, IRA and IPAA procedures, so all options were available to the patient. In this particular case, with such a young woman, Prof Cunningham was adamant that a proctocolectomy with an permanent ileostomy was not necessary and would significantly impair the patient's quality of life.

Both colectomy with IRA and restorative

proctocolectomy with IPAA were feasible options. However, with the polyp burden in the rectum of the patient as well as the tumour being present in the recto-sigmoid junction, IPAA was possibly more suitable. Therefore, Prof Cunningham believed that a restorative proctocolectomy with IPAA was the best option to remove disease as well as maintain a good quality of life for the patient.

Patient values

At the time of presentation, Whoopie was a 35-year old mother of a one year old son. She says that she was suspicious of the diagnosis of cancer in her bowel before it was delivered as she had had a long history of having blood in her stool and fluctuating bowel habits. When it came to attending the consultation with Prof Cunningham, the patient had done much research on the internet and was somewhat familiar with the options for surgery. She said that as a mother, her paramount responsibility was to do what she had to so she could be alive for her son. Therefore, she was willing to undertake whichever procedure was necessary, even if that meant the complete removal of the large bowel and a permanent stoma. However, Whoopie was convinced by Prof Cunningham's argument that the restorative proctocolectomy with IPAA would yield the best results for her in combination with a better quality of life. It would mean that she would have to maintain surveillance, but she was willing for this to be the case. There was of course the risk to her fertility, but Whoopie declared that she was not intending on having more children which removed the weight of this risk.

Conclusion

FAP is a condition in which 'cure' comes through surgery. There are a number of surgical options, and it is evident that there needs to be a consensus between best evidence, clinical judgement and patient values for the best option to be selected. In the current case, 36-year old Whoopie opted to have a panproctocolectomy with an ileal pouch anal anastomosis. According to the best available evidence, it was possible she would be at greater risk of having undesirable side effects, and also an increased risk that her fertility would be affected. However, Whoopie was willing to accept these risks on the basis that she had completed her family and that she was satisfied that IPAA, although with possible side effects, would allow her the best prognosis to ensure her future with her son.

Conflicts of interest

None.

Funding

None.

Consent

The patient has consented for the publication of this case study.

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