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xx February 2008

Familial Adenoma Polyposis (FAP)

Introduction

Familial Adenoma Polyposis or FAP is an autosomal dominant inherited colorectal cancer syndrome that is the most common adenomatous polyposis type and which accounts for about 1 percent of all colorectal cancer cases. The name itself spells out what sufferers should come to expect of the disease; “F” which stands for familial means that it is basically inherited and thus runs in families; the “A” for adenomatous refers to the kind of polyps which grow in the small intestine and the colon and for which has the potential to become cancerous; and finally, the “P” is polyposis which refers to the condition of having an abnormally large amount of colon polyps.

From a genetic perspective, the adenomatous polyposis coli (*APC*) gene has a germline mutation which results in the production of non-functional protein; along with a virtual stoppage of apoptosis and thus allowing the abnormal accumulation of b-catenin and paving the way for the growth of adenomas.

Sufferers of FAP often discover that the syndrome hits at a young age, often starting in adolescence; at this stage, there is already the presence of hundreds to thousands of colon polyps in the colon and the small intestine. Eventually by the age of 40 or so, the possibility of getting colorectal cancer is almost 100 percent (Goldberg, Delaini, 2006).

The expected treatment is usually surgery in which FAP sufferers must have their colons and even their rectums removed to prevent the development of colon cancer. Further complications can also occur because of the fact that the genetic abnormality that causes FAP is also present in other cells of the body and that other organs may develop cancer as well.

Over 80 percent of all FAP patients experience the development of polyps in their small intestines and colons; polyps in the upper part of the stomach are called fundic gland polyps which may only manifest in some FAP patients while others may don't have them at all. The good news however is that these particular polyps are not predisposed to becoming cancerous and are virtually harmless although an initial biopsy should be conducted to find out if they are indeed fundic gland polyps (Galiatsatos, 2006).

On the other hand, the polyps which are found at the lower or bottom portion of the stomach which are called antrum may be precancerous; again, a biopsy is necessary for confirmation and once confirmed, surgical removal is advised.

The polyps found in the first part of the small intestine or the duodenum are adenomas and therefore, could also be cancerous. It is significant to point out that cancer of the duodenum or duodenal cancer causes plenty of cancer deaths among FAP sufferers (second leading cause of death) with the overall risk percentage at about 4 percent and as high as 25 percent if the patient has an advanced case of duodenal polyposis. The challenge in diagnosis is that duodenal polyps are especially difficult to detect in some cases while in some, they could be so apparent as to actually occupy a large portion of the duodenum (Galiatsatos, 2006).

Another potential source for concern is the papilla which is found right at the opening of the bile duct and the duodenum. Often appearing in large numbers, doctors see no need to

remove them however it is advised that they be checked on a regular basis and that if necessary, biopsies should also be performed as well.

Other crucial organs of the body that need to be looked out for possible presence of growths and tumors include the human skin, the eye (because of the possibility of congenital hypertrophy of the retinal pigment epithelium occurring), bones, abdomen for desmoid tumors and the thyroid. Other related disorders include Gardner's syndrome Attenuated FAP. Attenuated FAP is actually a variant of FAP which is characterized by the presence of a smaller number of polyps in the colon though the risks for cancer are still very much present. In attenuated FAP however, the resulting cancers only develop at a later stage.

Exploring the age of Diagnosis

The first significant clue towards a successful diagnosis of FAP is looking at the family history- it is highly possible that a family history of numerous colorectal polyps and cancers presupposes the predisposition to the disorder. It is estimated that a substantial number of all FAP sufferers (60 to 70 percent) have acquired the defective gene from their parents.

In this regard, it is recommended that screening for FAP be done at the age of 12.

Of this number, about 30 percent of all patients with FAP acquired the abnormal gene at the time of conception and have been discovered to have no family history of the disease- this however does not bode well for their progeny who stand to inherit the abnormal gene.

It cannot be denied that advances in genetic testing have paved the way for better and more comprehensive diagnosis of FAP. In particular, genetic tests have uncovered the gene present in chromosome 5. This means that families with a history of the disease can have their blood tested to look for the specific FAP gene mutation APC. In most cases where this type of

test was undertaken, about 80 percent of the mutation was detected although there is about 20 percent in which genetic tests are unable to reveal the mutation.

It has to be pointed out that genetic testing does not reveal cancers or polyps, but only provides the proof that a person has the gene mutation and full blown FAP.

In genetic testing, there are two standard procedures for finding the mutations; the first one is a protein truncation test and the other is a direct DNA sequencing. One helpful advise for gene testing is that it should first be done on a family member who has been found to have FAP. If the mutated gene is discovered to be present then the rest of the family can be tested- multiple blood testing is both expensive and impractical because if the mutation is not found in a single individual the chances that the rest of his family has FAP is nil (Burt, 2005).

Another important consideration in genetic testing is that there are many other aspects to interpreting the results; it is advisable that the testing be done within a genetic counseling environment. This is because gene testing for FAP doesn't begin and end with the testing; there are other significant psychological and family related issues which need to be brought up and discussed with the family concerned.

Another consideration is the substantial number of people who develop the disorder outside of anything hereditary. FAP sufferers with so called new or spontaneous FAP gene mutations may be disadvantaged in the sense that they may never know they have the disease until it is almost too late. Too often with the disorder reaching its more visible symptoms in the later stage, these patients with no family history of the disease may struggle for years understanding why they have bloody stools, rectal bleeding, low blood counts, consistent abdominal pain and sudden weight loss. Eventually, accurate diagnosis that focuses in the examination of the colon will reveal the tell-tale presence of polyposis.

If such symptoms become frequent, one should immediately schedule a colon examination. A doctor may prescribe numerous ways of examining the colon; a popular method is the use of a scope which is a thin flexible piece of tubing that is inserted into the body, or through a barium enema which is a type of x-ray examination. The usual warning sign that FAP may be the culprit is the presence of an abnormally large number of colorectal polyps. If these are detected confirmation can be made using the scope test which is used to evaluate the lining of the colon; the versatility of this test is that a biopsy of the polyps can be made during the procedure itself. With a flexible instrument called the sigmoidoscope, examination of the lower portion of the colon can be conducted (Brosens, et.al, 2005).

It takes about less than 10 minutes for the sigmoidoscope to complete its testing; prior to testing, an enema is applied. Virtually painless and only slightly uncomfortable, sedation of the patient is not necessary. In some tests where the entire length of the colon must be examined, colonoscopy is used which has enough length to study the entire 6-foot length of the colon. Patients are asked to drink a colon cleansing solution the night before the test; and because the entire length of the colon is examined, a sedative is provided. The entire procedure is done in less than 30 minutes.

Method of treatment

The fact that FAP colonic polyps form in clusters by the hundreds and even thousands makes individual or even mass removal difficult and unnecessary. In this regard, removing the colon itself through surgery is the most viable option and the only alternative. There are no options for not availing surgery because 100 percent of the time, FAP sufferers without any kind of intervention for the disorder end up getting cancer.

In both cases where FAP is either the result of genetics or new mutations, the polyps inevitably begin forming at adolescence. At this stage where surgery is not yet an option, endoscopic surveillance is normally recommended. Flexible sigmoidoscopy is also recommended as a regular procedure to be performed every 1-2 years starting at the age of 10 up to the age of 12.

Colonoscopic surveillance is also recommended to take out large polyps in patients who have yet to undergo operation. This is crucial because colectomy can only be performed at an appropriate age; the only exception however is when the polyps exhibit very advanced histological characteristics that makes it imperative for early surgery.

Surgical procedures for FAP have seen tremendous advances in recent years; most operations are actually performed in a often less than invasive means normally through laparoscopy in which small holes are made in the abdomen, or through laparotomy which makes use of typical incisions on the abdomen.

For patients with relatively a small number of rectal polyps, the option is usually for total colectomy and ileorectal anastomosis (IRA). In this procedure, the entire colon is removed except for about 5 inches of the rectum which is then attached surgically with the ileum or the small intestine. This still enables the patient to experience normal bowel functions.

With Colectomy with ileoanal pouch (or restorative proctocolectomy), the doctors remove both the colon and the rectum but leave out the anal canal as well as the anal sphincter muscles. A new rectum is then constructed using parts of the small intestine which is then attached to the anal canal. In some cases, it may actually be necessary to create an ileostomy or a stoma in the abdomen which functions as a temporary opening for bowel functions. But this is later closed once the operation is completed and the wounds healed. This however works for a

small portion of FAP patients and is not generally recommended unless deemed necessary by doctors.

Proctocolectomy and ileostomy are procedures which are suggested for rectal cancer patients who for some reason, are not viable candidates for the previous surgical procedures mentioned. With these procedures, both the colon and the rectum are removed and the ileostomy that is created becomes permanent; wastes are eliminated by means of a bag which the patient has to wear at all times.

Surgery survival rates

The caveat for FAP surgery is that it is not a cure; surgery is only an intervention to save a patient's life from the grip of eventual cancer, but the mutation dictates that polyps continue to grow in the areas where it is genetically programmed to grow. There have been however advances in the formulation of medicines which have the ability to shrink polyps and even prevent the growth of new ones. By itself however, medication is not sufficient; it should be used in a comprehensive program to combat FAP combined with regular check-up and necessary surgery.

One of the first drugs that have been discovered to effect regression in colon polyps for FAP patients was sulindac which had anti-inflammatory properties. It was originally intended to help alleviate arthritis sufferers being a nonsteroidal anti-inflammatory drug (Thun, 2002).

Even without formal approval from the FDA, it has been used extensively in the United States and Europe to treat FAP. The downside however is that it has a high rate of users who experience extreme side effects such as painful stomach pains and ulcers.

Another arthritis medicine with the same anti-inflammatory properties called celecoxib has garnered FDA approval for use as colon polyp treatment. Being a COX-2 inhibitor, it offers

lesser side effects than sulidac. Studies have been extremely promising with results showing shrinkage of existing colorectal polyps with accompanying positive reaction from FAP patients.

With a regular daily dosage of 800 mg., it has proven to be quite effective in controlling adenomatous polyps on both the colon and rectum (Thun, 2002).

Recovery time after surgery and any follow-up medical care that may be required for the rest of their lives.

With less invasive surgical procedures, the usual stay in the hospital is less than a week although this also depends on the surgical procedures performed as well as the physician's discretion. Recovery is also nominally easy with recuperation lasting a month to six weeks at home. Normal but not too strenuous activities can be resumed in six to eight weeks after surgery although this could be on a case to case basis and should be discussed with the doctors on the first post-operative consultation.

One of the most common and significant questions asked by most FAP patient is, what lifestyle changes can be expected? The answer is usually very positive in the sense that there is a great deal of normalcy in diet and lifestyle expectations. One of the prominent changes would probably be more frequent bowel movements but not to the extent that it becomes debilitating or restricting. Social activities as well as sexual function will not be impaired and continue to be normal. There is also no effect on the ability to reproduce, both for men and women; women in particular will have no problems in having a normal pregnancy although infant delivery may have to be worked around the type of surgery performed on the mother previously.

Today an estimated 1 in every 6,859 people (some put it at 1 to 31,250) get FAP and the rate is constant across countries. In terms of mortality and morbidity, the leading cause of death among FAP sufferers is still colorectal cancer which inevitably develops in all patients unless

they get immediate treatment. With the average age of the onset of polyps at about 16 years, colorectal cancer appears at the median age of 39 with those who have adenomatous polyposis unaware of their condition because this type is normally asymptomatic.

Another significant cause of FAP mortality is through the complications brought about by diffuse mesenteric fibromatosis which is also referred to as a desmoid tumor.

This complication affects the intra-abdominal organs and vessels, creating gastrointestinal obstruction as well as the constriction of veins, arteries, and ureters. These tumors have been reported in about 4-32% of patients and that even after surgical treatment of FAP, about 20% of patients may still develop desmoid tumors after their colectomy; the mortality from these is about 10-50%. Adenocarcinoma of the duodenum and the papilla of Vater is the second most common malignancy in patients with FAP and affecting about 12% of patients. Other even rarer cancers which are associated with FAP include medulloblastomas (Turcot syndrome), hepatoblastoma, thyroid cancer, gastric cancer, pancreatic cancer, and adrenal cancer (Galiatsatos, 2006).

However, the prognosis is relatively good. For those extreme cases without treatment or even diagnosis, life expectancy is set at around 42 years although those who have had colectomy, life expectancies are greatly extended. Still, the most common causes of death even for those who have had colectomy are the recurrence of upper gastrointestinal cancers and desmoid tumors. It is in this regard that doctors emphasize regular surveillance programs to watch for recurrence (Goldberg, Delaini, 2006).

In both instances, the most important tool to address FAP continues to be patient education; patients are educated on the need for assiduous cancer surveillance after colectomy and that families with known histories of the disease should undergo screening.

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