A REVIEW OF PHYSICAL ABNORMALITIES IN FAMILIAL ADENOMATOUS POLYPOSIS

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ABSTRACT

Familial adenomatous polyposis (FAP) is an autosomal dominant condition wherein multiple polyps may be found in the gastrointestinal tract. Initially referred to as familial polyposis coli, it has become evident that virtually all patients with FAP develop adenomas in the upper gastrointestinal tract and thus the syndrome is now termed familial adenomatous polyposis. The number of associated conditions both malignant and benign has been increasingly recognized. Some of these lesions cause morbidity and mortality in affected individuals whilst others act as important clinical markers for identifying patients not yet expressing the phenotype. These abnormalities can arise from tissues of all three primary embryonic layers and are described in this paper.

Keywords: Familial adenomatous polyposis, upper gastrointestinal polyps, desmoids, congenital hypertrophy of the retinal pigment epithelium, Gardner's syndrome

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INTRODUCTION

Familial adenomatous polyposis (FAP) an autosomal dominant condition is perhaps the most interesting of a very heterogeneous group of gastrointestinal syndromes wherein multiple polyps may be found in the gastrointestinal tract. Initially thought to be limited to the colon and rectum the condition was originally referred to as familial polyposis coli. Subsequently it has become evident that virtually all patients with FAP develop adenomas in the upper gastrointestinal tract and thus the syndrome is now correctly termed familial adenomatous polyposis. In the early 1950s Gardner and his colleagues described a triad of multiple epidermoid cysts, multiple osteomas and familial polyposis[1-3]. The number of associated conditions both malignant and benign has now increased significantly with some of these lesions causing morbidity and mortality in affected individuals and some acting as important clinical markers for aiding identification of patients not yet expressing the phenotype[4].

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The abnormalities can arise from tissues of all three primary embryonic layers[5].

ABNORMALITIES OF THE TISSUES OF ENDODERMAL GERM LAYER ORIGIN

1. Colorectal polyps

The primary cause for concern in patients with FAP is the presence of multiple adenomatous polyps in the colon and rectum. Most people known to be at risk of developing FAP are not examined until they are teenagers. However, of those who have been seen younger, colorectal adenomas have been detected in an eighteen month old child. At the other end of the scale it has been known for a person to be negative during regular screening throughout teenage and up to the age of 34 when FAP was diagnosed.

Affected individuals have an average of 1,000 adenomas in the colon. However they may have as many as 10,000 but rarely less than 200. There are now reports of rectal sparing[6-11] and rectal or sigmoidoscopic examination alone might miss individuals so affected. With time, usually by middle age, there is a 100% risk of malignant transformation in at least one adenoma and timely surgery is necessary to prevent the development of colorectal carcinoma.

2. Gastric Polyps

Two histological types of gastric polyps are associated with FAP. Patients are commonly found to have fundic polyps which are usually harmatomatous and have little malignant potential[12-13]. However about 10% of patients have gastric adenomas[14] but very few cases of gastric carcinoma have been reported[15-17].

3. Duodenal/periampullary polyps

Duodenal polyps may be found in up to 100% of patients with FAP[18-35]. These polyps are most numerous in the second and third parts of the duodenum, especially around the periampullary region. Duodenal and periampullary carcinomas are more common than previously thought[14,36], and are now the second most common cause of cancer mortality in patients with FAP after colorectal carcinoma[37,38]. It is now thought that bile in FAP may have a co-carcinogenic effect[15,39].

4. Small bowel polyps

Adenomas are not infrequently found in the terminal ileum

and may also occur in the jejunum[40,41]. The risk of malignancy in these small intestinal polyps has been said to be small, however, cases of ileal and jejunal carcinoma are known[42].

5. Gall bladder, bile duct, pancreas and pancreatic duct tumours

Hepato-biliary and pancreatic ductal adenomas and their malignant counterparts together with pancreatic carcinoma have been reported with increasing frequency in patients with FAP[43-45].

6. Thyroid carcinoma

It has been shown that young females under 35 years of age have a 160x greater than expected risk of developing thyroid carcinoma if they have FAP[46]. The tumour is usually a papillary carcinoma and the prognosis is good[46 49].

7. Other endocrine tumours

A mixed bag of endocrine tumours including adrenal carcinomas[50 52], multiple endocrine neoplasia type 2b, pituitary adenomas and pancreatic islet cell tumours have also been reported[53,54].

ABNORMALITIES OF THE TISSUES OF MESODERMAL GERM LAYER ORIGIN

1. Skeletal abnormalities

Osteomas of the skull, jaw and less commonly other parts of the skeletal system are commonly found[1-3] and indeed occult osteomas may occur in more than 90% of patients with FAP[55]. These lesions are not important clinically except perhaps as an aid in identifying affected individuals before the development of colorectal polyposis.

2. Dental abnormalities

Dental pathology was described as part of the original Gardner's syndrome[2-3]. These abnormalities include early caries with teeth loss, supernumerary teeth, odontomas, dentigerous cysts and impacted permanent teeth[56-58].

3. Hepatoblastoma

It is now generally accepted that there is a higher than expected incidence of hepatoblastoma in the offspring of patients with FAP[59 60], some of which will present as stillbirths.

4. Desmoids

Desmoid tumours or fibromatosis may be found in about 10% of patients in FAP[61-64]. Two types of desmoid tumours are recognized; the intra-abdominal type and the musculo-aponeurotic type. Intra-abdominal desmoids are very vascular tumours. They may be well encapsulated or diffuse, and may occur within the mesentery or in the retroperitoneal region. Musculo-aponeurotic desmoids are usually more fibrous and may occur in the abdominal wall, within scar tissues or even within aponeurotic sites away from the abdomen. These tumours have varying growth rates in individual patients. In some, growth is rapid, others show a very slow growth rate and in a few, actual regression may be seen. Growth is said to be stimulated by pregnancy and surgery although this is debatable[65]. Intra-abdominal desmoids are very difficult to remove totally, have a high recurrence rate, and may bleed uncontrollably during surgery[66-67]. Patients with FAP have been noted also to have a high incidence of post-operative intestinal obstruction which may be related to a disorder of fibrous tissue formation[68].

ABNORMALITIES OF THE TISSUES OF ECTODERMAL GERM LAYER ORIGIN

1. Cutaneous lesions

Epidermoid and sebaceous cysts formed part of the original description by Gardner and co-workers[1-3]. These cysts are important clinically in so far as they often antedate the development of colorectal pathology and are, in fact rare in the normal prepubertal patient[69]. The presence of these cysts is therefore an indicator that a particular individual has inherited the gene. Absence of cysts does not mean that the gene has not been inherited. Unusual skin pigmentation and discoloration have also been recently described in relation with FAP[70].

2. Central nervous system tumours

Turcot and his colleagues described two siblings in a family with colonic polyposis in whom astrocytoma and medulloblastoma had occurred[71]. The relationship of Turcot's to FAP has given rise to considerable debate recently and the matter is still in doubt, partly because these tumours present at an early age and often prior to the development of colonic polyps[72-77].

3. Congenital hypertrophy of the retinal pigment epithelium (CHRPE)

CHRPE does not have any malignant potential but it has some significance clinically as a diagnostic marker of the presence or absence of the gene for FAP[75-85]. These lesions in patients carrying the gene for FAP may be multiple and appear at birth or shortly thereafter[85]. Multiple or bilateral lesions have a very high specificity and sensitivity as a clinical marker but patients with FAP have been known to have none. These ocular lesions are discrete, usually darkly pigmented and may be round, oval or bean shaped with a surrounding depigmented halo. Lesion size may range from 0.1 to 1.0 or more times the diameter of the optic disc. Small solitary or unilateral lesions are sometimes found in the normal population. Angoid streaks in the retina suggestive of connective tissue disorders has also been reported[86-87].

CONCLUSION

FAP is a multiple-system disorder. Awareness of the plethora of clinical manifestations of FAP will aid the health worker to better follow and manage patients who are known to have FAP, whilst the presence of clinical markers may help to identify individuals before colonic polyps are manifested but who have inherited the genetic defect. Such knowledge will be helpful in planning an appropriate treatment strategy for the affected patient[88].

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