Gardner syndrome

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INTRODUCTION

Gardner, in the early 1950s, described a kindred with intestinal characteristics of familial adenomatous polyposis (FAP), but also with a number of extracolonic growths, including osteomas, epidermal cysts and fibromas [1,2]. Dental abnormalities, desmoid tumors, and other lesions were later recognized as additional manifestations of the underlying genetic defect [3,4]. The constellation of inherited colonic adenomatosis together with these extracolonic lesions has become known as Gardner syndrome (GS).

This topic review will discuss each of the extraintestinal manifestations of FAP that historically have defined GS. Gastric, duodenal, and colonic polyp and cancer issues are discussed in a separate section on FAP. Genetic testing is now also available for FAP and GS since both arise from mutations of the same gene [5]. It should be noted that GS is now considered a subcategory of FAP, characterized by the extraintestinal manifestations to be reviewed below that occur in addition to the intestinal polyposis of FAP. Issues related to genetic testing are also presented in the section on FAP. (See "Clinical manifestations and diagnosis of familial adenomatous polyposis" and "Familial adenomatous polyposis: Screening and management of patients and families".)

DEFINITIONS

Shortly after discovery of the adenomatous polyposis coli (*APC*) gene, the gene responsible for familial adenomatous polyposis (FAP), it became apparent that both FAP and Gardner syndrome (GS) arose from *APC* mutations [3,4]. FAP is characterized by hundreds to thousands of colonic adenomatous polyps that most often emerge in the second and third decades of life. Colon cancer is inevitable if the colon is not removed. Polyposis is also usually observed in the stomach, duodenum, and small bowel, although the cancer risk in these locations is far less than in the colon. Inheritance is autosomal dominant with near complete penetrance of the gastrointestinal phenotype but with variable penetrance of the extraintestinal manifestations of the disease [6]. The APC protein is a complex scaffolding protein (brings together two or more proteins) with multiple domains relating to cell migration, cell adhesion, cell proliferation, cell differentiation, and microtubule binding that is involved in chromosomal segregation and mitotic progression. These multiple functional relationships contribute to the many intestinal and extra-intestinal manifestations of FAP/GS [7].

GS cannot be separated from FAP when considering studies that describe its overall prevalence. Estimates for the prevalence of the combined syndromes vary from 1 in 6850 to 1 in 31,250 people (2.29 to 3.2 cases per 100,000 persons) [8-10]. Prevalence appears fairly constant throughout the world with males and females affected equally. Twenty to 30 percent of newly diagnosed cases, ie, those not belonging to previously identified families, appear to represent new mutations [8]. New cases may also arise from mosaic inheritance, which implies that a mutation occurred in parent's sperm or egg cells, but not in other cells of the body, so the parent did not have clinical disease [11,12].

It was once believed that GS patients exhibited fewer and more distinct colonic polyps. However, continued study has demonstrated that the gastrointestinal polyp and cancer phenotypes, although variable, are identical for both GS and FAP. Colonic polyp number depends to some degree on where the mutation occurs in the *APC* gene [13]. Mutations in the center of the gene (often called the mutation cluster region) give rise to dense polyposis, with 5000 or more colonic polyps [14] when the disease is fully developed. If mutations occur proximal or distal to this central gene location, colonic polyps average approximately 1000 with full expression. Mutations in the extreme proximal or distal locations of the *APC* gene, or in certain areas of exon nine, are associated with many fewer polyps (often less than 100). This clinical variation is referred to as attenuated FAP. Extraintestinal growths also occur in the attenuated form of FAP, do not correlate with polyp density but have some correlation with mutation location [3,14,15].

The common extraintestinal manifestations associated with GS have been described in approximately 20 percent of patients with FAP. However, many more patients with FAP have these features if they undergo detailed physical and radiologic examinations [3]. Thus, the

difference between FAP and GS is somewhat semantic and GS is usually considered a subset of FAP [3]. On the other hand, the term GS continues to be commonly applied in the literature, particularly in families that exhibit frequent and obvious extraintestinal lesions.

BENIGN EXTRAINTESTINAL LESIONS

Gardner syndrome (GS) is associated with several benign extraintestinal growths including:

- Osteomas and dental abnormalities
- Cutaneous lesions
- Desmoid tumors
- Congenital hypertrophy of the retinal pigment epithelium
- Adrenal adenomas
- Nasal angiofibromas

Osteomas and dental abnormalities — Osteomas, the first described extracolonic lesions of GS, are found in 60 to 80 percent of families with familial adenomatous polyposis (FAP) when careful physical and radiographic examination are done [2,7]. They are benign bone growths characterized by compact lamellar cortical or cancellous bone and are found most commonly in the skull and mandible but may occur on any bone of the body [1,7,8,16-18]. The size ranges from less than a millimeter to several centimeters in diameter, and they number from one to dozens. More than three osteomas is suggestive of GS [7]. Detection of these lesions on average precedes the diagnosis of FAP by 17 years and are thus a potential early diagnostic clue for FAP. Osteomas often occur in children and may continue to appear and grow throughout life. They have no malignant potential but may occasionally be of cosmetic concern. These bone lesions occur most commonly from codons 767 through 1578 in the *APC* gene [7].

Dental abnormalities are present in 30 to 75 percent of FAP patients (compared with 1 to 2 percent of the general population) and include unerupted and impacted teeth, congenitally missing teeth, hypercementosis, supernumerary teeth, dentigerous cysts, and odontomas [1,7,19-21]. Mutations of the *APC* gene appear to be of central importance to the development of supernumerary teeth [21]. Dental abnormalities may precede the development of colonic polyposis and, like osteomas, contribute to the early diagnosis of FAP and indicate the category of GS. Radiopaque jaw lesions not apparent on physical examination are evident by panoramic dental radiographs in up to 90 percent of FAP patients [22]. Surgical or orthodontic management is needed when lesions are associated with cosmetic or dental problems [23]. There is some correlation of bone, cutaneous, and desmoid tumor occurrence with location of mutation in the distal or 3' portion of the *APC* gene [3,24]. (See 'Desmoid tumors' below.)

Cutaneous lesions — Epidermoid cysts, fibromas, lipomas, and pilomatricomas can all occur in GS [3,4,25-29]. All of the cutaneous lesions can cause cosmetic problems.

- Epidermoid cysts occur in 50 to 65 percent of GS/FAP patients. They are most common on the legs, face, scalp, and arms, in that order, but they may be found anywhere on the surface of the body [2,25]. Their size ranges from millimeters to several centimeters. While they are also common in the general population, in GS they often appear before puberty and may precede the onset of polyposis. Epidermoid cysts in GS, similar to sporadic epidermoid cysts, are surgically removed when needed, usually for cosmetic reasons [30].

- Fibromas range in size from millimeters to centimeters and occur on the cutaneous surfaces of the scalp, shoulders, arms, and back. Fibromas appear to be the cutaneous equivalent of desmoid tumors. Gardner-associated fibroma is a histologically specific type of fibroma that appears specific for GS/FAP. It may be seen cutaneously in young patients and be an early clue of the diagnosis of FAP/GS [31].

- Lipomas are so common in the general population that they are not a helpful diagnostic feature of GS, and there is even some question as to whether there is actually an increased incidence of these lesions in GS compared to the general population.

- Pilomatricomas are common in children, but are a rare association with GS [32]. When present in GS, they may be millimeters to centimeters in size and are often multiple. A family history to rule out GS is indicated when pilomatricomas are present in children. Additionally, the presence of six or more pilomatricomas is highly suggestive of an inherited syndrome including GS [33]. These lesions are surgically removed.

None of the cutaneous lesions progress to malignancy.

Desmoid tumors — Desmoid tumors (also referred to as desmoid fibromatosis) represent a somewhat different disease in GS than in the general population (see "Treatment for tenosynovial giant cell tumor and other benign neoplasms affecting soft tissue and bone"). They are rare in the general population (5 to 6 per million per year) [34], but in FAP affect from 5 to 25 percent of patients [35-37]. Although more than 90 percent of desmoids occur in the general population, the incidence of desmoids in patients with FAP/GS is 800 to 1000 times that of the general population [38]. The risk of finding FAP in patients who develop a desmoid without a prior history of FAP is 4.8 percent [39]. The peak incidence of desmoid occurrence in GS is between 30 and 40 years, although they may occur at any age [38]. Independent predictors of their occurrence include *APC* gene mutations 3' (or distal) of codon 1444 [13,40], a family history of desmoids [37,40,41], female sex, and the presence of osteomas [42]. Surgery (including

colectomy) also appears to be an independent risk factor for desmoid disease in FAP, particularly with mutations in certain regions of the *APC* gene [37,43-45].

Desmoid tumors can arise in all musculoaponeurotic structures throughout the body but are most common in the abdomen where they begin as mesenteric plaque-like lesions that may progress to mesenteric fibromatosis and finally to desmoid tumors [46,47]. In both sporadic and FAP/GS desmoids, 80 percent of tumors occur intra-abdominally, 10 to 15 percent in the abdominal wall and approximately 5 percent extra-abdominally [36,38,48,49]. Most intra-abdominal desmoids are located in the mesentery. These tumors grow slowly, at approximately 2 to 9 cm per year [38]. Additionally, most desmoids pose a low risk of death, except those in FAP/GS, where this tumor is the third most common cause of death [2]. Approximately one-third of abdominal desmoids cause pain. In a series of 38 patients, the most common presenting feature was small bowel obstruction (58 percent) [50].

Desmoid tumors are considered to be benign because they do not metastasize. The tumors may enlarge gradually, stop growing, and even spontaneously regress [51,52]. Up to 20 percent spontaneous regression has been reported [52]. Surgery appears to stimulate their growth and a high rate of recurrence (>40 percent) is observed following surgery for both abdominal and extra-abdominal tumors [52-55]. Pregnancy may slow desmoid growth in some of these patients [56].

Although benign, desmoid behavior, especially in FAP/GS, can cause substantial morbidity, with an associated mortality of 10 to 50 percent [7,57,58]. They may infiltrate adjacent structures, extend along fascial planes, attach to and erode bones, and engulf and compress blood vessels, nerves, ureters, small bowel, and other hollow organs of the abdomen especially with the occurrence of mesenteric fibromatosis. Fistula formation with and between hollow organs and with skin also occur [59], and bowel perforation and abscess formation have been reported [38,60]. Severe and sometimes fatal problems can arise, especially if the mesenteric vessels or other hollow abdominal organs become obstructed [61]. Intra-abdominal desmoids may grow to massive sizes, sometimes occupying much of the abdominal cavity and encasing viscera (image 1). Desmoid tumors in FAP/GS are a common cause of mortality after colectomy [62]. However, progression is often gradual and survival 10 years after the diagnosis is approximately 63 percent [36,46,53].

GS-associated desmoids are histologically indistinguishable from sporadic desmoids, although there may be some differences between fibroblastic growths in GS and sporadic desmoids. A distinctive fibroblastic growth, called Gardner-associated fibroma, may be seen in young patients cutaneously and intra-abdominally, and appears to be the specific precursor lesion of desmoids in GS [63,64]. Desmoid tumors in GS are monoclonal growths, implying that they are

true neoplasms [65]. They arise from *APC* mutation inactivation and subsequent accumulation of beta-catenin in cells [66]. In contrast, *APC* mutations are uncommon in sporadic desmoids, which usually arise from beta-catenin gene mutations (*CTNNB1* gene) [67-71].

The specific location of mutations within the *APC* gene correlates with the occurrence of desmoid tumors, although desmoids can occur with mutations in any *APC* gene location [13]. Desmoid tumors occur more frequently when mutations are in the 3' end of the *APC* gene, specifically distal to codon 1444 [7,13,42,47]. One study showed desmoid tumors to be more common with *APC* mutations between codons 1444 to 1578 [72] and in another study between codons 543 to 713 and 1310 to 2011 [73]. Mutations between codons 1310 and 2011 are associated with a six-fold risk of desmoid tumors relative to the low-risk reference region (159 to 495) [15]. However, the specific phenotype varies with mutations within these regions [74,75]. A study of 269 patients found that tumors were present in 20 percent of patients with mutations 5' to codon 1444 compared with 49 percent of patients with mutations 3' to that codon [74]. In addition, desmoid tumors were present in 61 percent of patients with mutations between codons 1445 and 1580 compared with 18 percent of patients with mutations at sites 3' to that region. (See "Desmoid tumors: Epidemiology, molecular pathogenesis, clinical presentation, diagnosis, and local therapy", section on 'Adenomatous polyposis coli (APC) mutations'.)

The molecular events that lead to desmoid tumor formation in patients with *APC* mutations are incompletely understood. However, increasing evidence points to the primary involvement of the *APC* gene and beta-catenin in the initiation and molecular pathogenesis of desmoids both in GS as well as in sporadic desmoids [47,68,70]. (See "Desmoid tumors: Epidemiology, molecular pathogenesis, clinical presentation, diagnosis, and local therapy".)

Treatment — Screening for desmoid tumors is not routinely recommended. Imaging is indicated for physical examination findings, symptoms that may indicate a desmoid tumor, or prior to colectomy in patients at increased risk for desmoids. Treatment of desmoid tumors is indicated only when they cause symptoms, there is imminent risk to adjacent structures, or they create cosmetic concerns. Surgery is generally performed initially for extra-abdominal desmoids, although watch and wait is recommended in planning the appropriate time for surgery [68,76,77]. Surgery is no longer considered the first choice for treatment for abdominal wall or intra-abdominal desmoids [51,71]. A conservative approach is usually recommended for intra-abdominal tumors, such as treating with sulindac and/or increasing doses of tamoxifen [47,78]. Tyrosine kinase inhibitors have also been suggested as possible treatment agents in combination with nonsteroidal anti-inflammatory medicines [79].

In patients who do not respond or who lose response to these initial therapies, options include chemotherapy [47] (similar to that used for sarcomas), radiation therapy [80-82], and/or surgery

[51,83]. Intestinal perforation with chemotherapy for desmoids has been reported [84]. When combination chemotherapies are used, those including doxorubicin have been associated with the most favorable outcomes [85,86]. The biological agent imatinib has shown significant utility with progression-free survival of 66 percent at 12 months and objective tumor response in three of 51 patients [87]. The combination of methotrexate and vinblastine has also shown promise in treating desmoids [88] as has an oral gamma secretase inhibitor [89]. No agreed upon standard of care for desmoid tumors presently exists, partly because most studies reported represent case series or retrospective approaches. Perhaps the most promising study of treatment to date is a randomized, double blind, placebo-controlled phase 3 study of the tyrosine kinase inhibitor, sorafenib, administered for both abdominal and extra-abdominal desmoid tumors. Among 87 subjects, progression-free survival was significantly higher in the treatment group as compared with controls (81 versus 36 percent). Finally, total enterectomy with intestinal transplantation is an option for the most extreme cases [90-92].

The choice and order among these various treatments should be guided by a multidisciplinary team, all of whom should have experience with this difficult tumor [47,68,71,85,93-96]. Desmoid recurrence is frequent following surgery, particularly those in the abdomen [97]. It is recommended that patients with desmoid tumors be referred to specialty centers in view of the difficulty in treatment and the multispecialty approach needed for optimal outcome [71,98]. (See "Desmoid tumors: Epidemiology, molecular pathogenesis, clinical presentation, diagnosis, and local therapy" and "Familial adenomatous polyposis: Screening and management of patients and families", section on 'Desmoid tumors'.)

Congenital hypertrophy of the retinal pigment epithelium — Multiple and bilateral patches of congenital hypertrophy of the retinal pigment epithelium (CHRPE), also called pigmented ocular fundus lesions, are a common manifestation of GS/FAP [99]. With careful slit-lamp examination, they occur in up to 90 percent of FAP patients compared with 1.2 to 4.4 percent of the general population [2,7]. The lesions are discrete, darkly pigmented, round, oval or kidney shaped, often with a halo, ranging in size from 0.1 to 1.0 times the diameter of the disc. The presence of bilateral or multiple (more than four) lesions is specific (94 to 100 percent) but only moderately sensitive (58 to 84 percent) for GS [100]. These lesions may exhibit an association with disorder of the cilia [101].

CHRPE lesions appear to be congenital and have been detected in patients as young as three months. Slit-lamp examination is usually required for detection. CHRPE is observed with mutations between codons 311 and 1444, although this varies somewhat depending on the study [3,7,13,15]. CHRPE is not known to cause clinical problems, although one case of malignant transformation was reported [102].

Adrenal adenomas — Adrenal adenomas have been reported in up to 15 percent of patients with GS/FAP (compared with approximately 5 percent in the general population) [103,104]. Most adrenal masses in GS are found incidentally (as they are in the general population), are non-functioning, and should be managed using similar principles [105-107] (see "Evaluation and management of the adrenal incidentaloma"). Adrenal adenomas in FAP harbor a somatic as well as germline *APC* mutation, indicating these tumors arise as part of FAP [108-110]. Malignancy of the adrenal is rare in FAP but has been reported [111].

Nasal angiofibromas — Nasal angiofibromas have been described in some patients with GS/FAP [112,113]. These are histologically benign but locally aggressive vascular tumors. They grow in the back of the nasal cavity and most often affect adolescent males [2]. Mutational studies indicate they involve the Wnt signaling pathway and are part of the syndrome [114,115].

EXTRACOLONIC MALIGNANCIES

Patients with Gardner syndrome (GS) are at increased risk for several extra-colonic malignancies. (See "Clinical manifestations and diagnosis of familial adenomatous polyposis", section on 'Extracolonic manifestations'.)

The following malignancies (and proportions of affected patients with GS/familial adenomatous polyposis [FAP]) have been described in various studies:

- Duodenal and periampullary (3 to 5 percent)
- Thyroid (2 to 12 percent)
- Pancreatic (2 percent)
- Gastric (0.6 percent)
- Central nervous system (<1 percent)
- Hepatoblastoma (1.6 percent)
- Small bowel distal to the duodenum (rare)
- Adrenal (rare)

Thyroid — Benign thyroid masses occur in almost 50 percent of FAP patients. Two to 12 percent of GS/FAP patients develop thyroid cancers, which are often multifocal and bilateral [7,116,117]. The cancer risk is increased approximately eightfold compared with the general population (relative risk [RR] 7.6, 95% CI 2.5-17.7) [118]. The mean age of diagnosis is 33 years [117]. There is elevated risk of FAP-associated thyroid cancer in females, in persons with thyroid nodules, and in those with a relative affected with this malignancy [116,119]. In a study from Japan, the risk of thyroid cancer was near 14 percent in FAP patients with an 8:1 female to male ratio [119].

The histology of thyroid cancer in FAP is predominantly papillary, commonly with a cribriform-morular pattern, which is somewhat specific for FAP/GS [120]. Thyroid cancer is associated with *APC* mutations in codons 1286 to 1513 in the 5' end of exon 15 [7,121]. The thyroid in FAP/GS patients is frequently nodular; as a result, ultrasound screening, in addition to palpation, should be used for thyroid surveillance in these patients [117]. (See "Overview of the clinical utility of ultrasonography in thyroid disease".)

Pancreatic — The risk of pancreatic adenocarcinoma in GS/FAP has been estimated to be increased more than fourfold compared with the general population (RR 4.46, 95% CI 1.2-11.4) [118]. The overall risk is about 2 percent [2]. In addition, duct obstruction has been described from benign and malignant tumors, sometimes giving rise to pancreatic cysts [122].

Hepatoblastoma — Hepatoblastoma occurs in 0.75 to 1.6 percent of children with FAP, but the risk of this tumor in children with FAP is 750- to 7500-fold greater than in the general population, which is about 1 per 100,000 children [2,123]. It occurs more commonly in males and has some association with *APC* mutations in the 5' end of the gene [3,104]. This cancer usually occurs between six months and three years of life, but some risk remains up to 16 years [104]. The *Wnt/*beta-catenin pathway appears to be of central importance in the development of hepatoblastomas, thus the importance of germline *APC* mutations in FAP/GS leading to this tumor [2]. In one study of children with hepatoblastoma, 14 percent were found to have germline pathogenic *APC* gene mutations [124]. The authors thus recommended that all children with hepatoblastoma malignancies undergo germline *APC* testing for FAP.

Central nervous system (CNS) — CNS malignancies, mostly medulloblastoma, are rare in FAP but show a distinct relationship [125,126]. *APC* mutations between codons 697 and 1224 exhibit a threefold increased risk of brain tumors and a 13-fold increased risk in medulloblastoma compared with FAP patients with other *APC* mutations [2]. When CNS tumors are present, the condition is actually called Turcot syndrome, now, like GS, also considered a subcategory of FAP. It is estimated that the risk for medulloblastoma in FAP is 92-fold greater than in the general population. The occurrence of this tumor in FAP is greatest before the age of 20 years [2].

Neoplasms of the gallbladder and bile ducts — Adenomatous change and cancer have been described in the gallbladder and bile ducts both of which may lead to biliary obstruction [2,127-130]. Neoplasms in these locations are unusual in FAP and their precise frequency is not known.

SCREENING FOR EXTRAINTESTINAL MALIGNANCIES AND DESMOIDS

Consensus has often not been achieved on optimal strategies for screening patients with Gardner syndrome (GS)/familial adenomatous polyposis (FAP) for extraintestinal malignancies and desmoids. However, general and helpful screening recommendations are suggested as given below:

- The thyroid should be subject to physical examination and ultrasound annually, starting at age 10 to 20 years [2,131].
- Screening for congenital hypertrophy of the retinal pigment epithelium (CHRPE) with slit-lamp and indirect ophthalmoscopy in patients with FAP. The presence of these lesions add significantly to the diagnosis when suspected, and additionally, NCCN guidelines recommend all persons with CHRPE should be screened for FAP [2].
- It is generally suggested that other possible extraintestinal cancer sites, such as the pancreas, should be evaluated only if symptoms occur or if these cancers have occurred in relatives. This recommendation is provisional and not accepted by all investigators in this area. An FAP study from the Netherlands found that screening for cancers in sites other than colon, duodenum, and thyroid did "not contribute significantly to the survival of patients with FAP" [62].
- Patients with FAP/GS should be questioned regularly regarding neurologic symptoms. In addition, periodic head magnetic resonance imaging is recommended if any family member has had central nervous system malignancy. The appropriate frequency is not known, but intervals of one to three years have been discussed, depending on the family history and presence of any possible related symptoms [2].
- Every six months, liver palpation, together with liver function tests, abdominal ultrasound examination, and alpha fetoprotein levels, should be considered to screen for hepatoblastoma, especially during the first five years of life in those with FAP/GS [132,133]. Screening, when regularly done, can be safely discontinued after age 15, and probably after age 10. The risk of occurrence of this tumor in neonates and children provides a rationale for performing genetic testing in the first year of life to determine which persons should be considered for screening. Although formal recommendations have not been given in this regard, genetic testing may be useful in patients if liver screening is to be anticipated. There is not yet consensus among experts on whether hepatoblastoma screening should be done for all FAP/GS patients, and thus depends on individual clinician and parental concern as well as family history [2].
- Annual liver function tests for biliary tumors, although the sensitivity of this approach is unknown [2]. Further evaluation should be performed only for symptoms or abnormal

liver function tests. Upper endoscopy every one to three years, with side viewing capability, is indicated for screening the stomach and duodenum in view of the risk of advanced duodenal polyposis and cancer [134]. It appears that there is even some risk of gastric cancer [135,136]. Obvious papillary abnormalities will be observed with this screening. Reasonably good endoscopic and surgical outcomes after finding advanced polyposis and/or duodenal cancer appear to justify these screening approaches [137,138].

- Screening is not routinely undertaken for desmoids, but evaluation should be pursued for palpable abdominal masses or symptoms of possible bowel obstruction prior to colectomy in patients with a history of fibromatosis or an *APC* mutation beyond codon 1444 [2]. On the other hand, some feel it is reasonable to obtain an abdominal CT with oral contrast every three years beginning at age 20 to 25 [129]. Particular attention should also be given to the biliary tree, gallbladder, pancreas, small bowel, and adrenal glands whenever abdominal imaging is performed.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hereditary colorectal cancer syndromes".).

SUMMARY AND RECOMMENDATIONS

- Gardner syndrome (GS) refers to the constellation of inherited colonic adenomatosis polyposis (familial adenomatous polyposis [FAP]) together with a number of extracolonic lesions. (See 'Introduction' above.)

- GS arises from a mutation in the adenomatous polyposis coli (*APC*) gene. As in FAP, the number of colonic polyps is related to the locus of the mutation in the *APC* gene. (See 'Definitions' above.)

- Several benign extraintestinal growths are associated with GS, including osteomas and dental abnormalities, cutaneous lesions, desmoid tumors, congenital hypertrophy of the retinal pigment epithelium, adrenal adenomas, and nasal angiofibromas. (See 'Benign extraintestinal lesions' above.)

- Patients with GS are at increased risk for certain extracolonic malignancies, including neoplasms of the thyroid, pancreas, liver, central nervous system, gallbladder, biliary tract,

duodenum, and stomach. (See 'Extracolonic malignancies' above.)

- Patients with GS should be screened for extracolonic malignancies. Desmoid tumors, including intra-abdominal, abdominal wall, and extra-abdominal, are a common feature of GS/FAP, and may result in significant morbidity and even mortality. Screening for desmoids is usually indicated if signs or symptoms occur and a multidisciplinary approach is indicated in their treatment. (See 'Screening for extraintestinal malignancies and desmoids' above and "Familial adenomatous polyposis: Screening and management of patients and families".)

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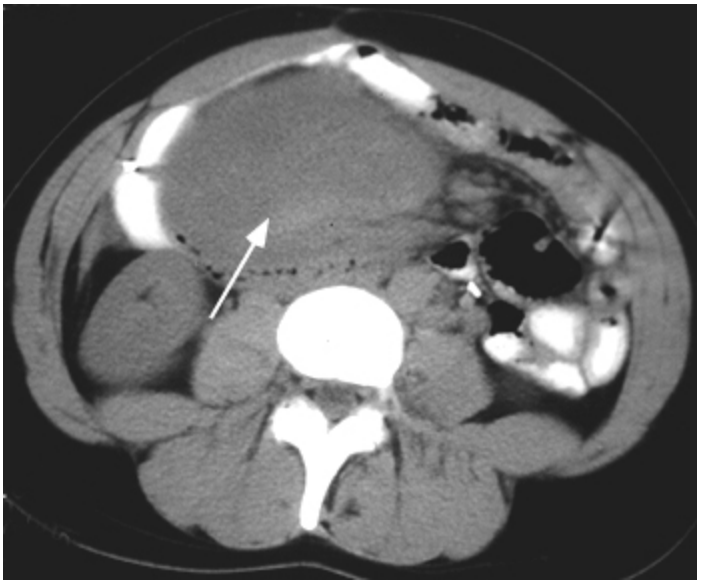
Topic 2598 Version 22.0

GRAPHICS

Intraabdominal desmoid tumor in familial polyposis



Computed tomography (CT) scan through the mid-abdomen demonstrates a large well-circumscribed soft tissue mass arising in the mesentery (arrow); the mass represented a desmoid tumor (aggressive fibromatosis).

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 54879 Version 5.0

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Randall W Burt, MD No relevant financial relationship(s) with ineligible companies to disclose. **J Thomas Lamont, MD** Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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