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Case Report

Thyroid cancer in Gardner's syndrome: Case report and review of literature

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Abstract

Gardner's syndrome is a variant of familial adenomatous polyposis. A multitude of extra-colonic manifestations including various endocrine tumors have been associated with this syndrome, the commonest of which is thyroid cancer. Majority of the patients with thyroid cancer and Gardner's syndrome are females. Here we describe a male patient with Gardner's syndrome who subsequently developed thyroid cancer.

Key words: Gardner's syndrome, thyroid cancer, polyposis, osetoma

Introduction

Following the original description of Gardner's syndrome consisting of a classic triad of colonic polyps, osteomas and soft tissue tumors, various other extraintestinal manifestations and endocrine tumors have been reported to be associated with Gardner's syndrome, thyroid cancer being the most common. Here we report one such case and briefly review the literature.

Case Report

A 40-year-old gentleman with no previous medical or family history was referred to our hospital with a diagnosis of adenocarcinoma of the rectum. At our institute, a colonoscopic evaluation revealed multiple polyps scattered throughout the colon. He underwent panproctocolectomy with ileostomy. The histology showed tubulovillous and adenomatous polys in caecum, colon and rectum with a moderately differentiated adenocarcinoma of rectum. All lymph nodes were negative [Figure 1]. Fifteen months later, he had a swelling around the stoma site. CT scan showed a 9.5x5.6x7.5 cm peritoneal mass at the site of ileostomy with multiple smaller similar lesions throughout the abdomen. The tumor was excised (R1 resection) with reconstruction of the abdominal wall, histologically showing it to be a desmoid tumor The patient was given weekly systemic therapy with vinblastine, methotrexate and tamoxifen (methotrexate 30 mg/m^2 weekly intravenously, vinblastine 6 mg/m^2 weekly intravenously and tamoxifen 20 mg/m^2 twice a day orally daily) for 6 cycles. Six months later (21 months following the diagnosis of colon carcinoma), CT scan showed a partial response of the desmoid tumors. A new thyroid nodule was detected at a screening ultrasound of the neck. FNAC confirmed the diagnosis to be papillary carcinoma of thyroid [Figure 2]. Total thyroidectomy was done which revealed a well-differentiated papillary carcinoma of the thyroid. The patient is currently on maintenance doses of thyroxine and is continued on tamoxifen. . Almost 3 years since the initial detection of Gardner's syndrome, the patient continues to remain stable.

Discussion

Familial adenomatous polyposis (FAP) is a syndrome caused by mutations in the adenomatous polyposis coli (APC) gene. The gene is located on chromosome 5q21. The normal gene protein is a classic tumor suppressor protein. Mutations of the APC gene are inherited in an autosomal dominant fashion. The disease is characterized by hundreds to thousands of colonic adenomas developing at a young age which almost invariably turn malignant if

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Table 1: Details of cases of thyroid cancer occuring in association of Gardner's syndrome/fap

Sex	Age at diagnosis of thyroid cancer	Age at diagnosis of gs/fap	Colectomy status with findings	Post colectomy recurrence of colonic cancer	Histology of thyroid cancer	Outcome	Ref no
Male	30	39	Refused	NR	P+F	NR	[1]
Female	19	28	Yes;HP--	NR	P+Alveolar	NR	[2]
Female	20	29	Unresectable sigmoid cancer	-	P	Death	[2]
Female	28	25	Yes; adenomas only	26 years later	P	Alive at 30 years	[3]
Female	27	23	Yes;HP--	NR	P	Alive at 15 years	[4]
Female	29	16	Yes;HP--	NR	P	Alive at 15 years	[5]
Female	26	21	Yes; adenomas + carcinoma	6 years later	P	Death	[5]
Male	35	18	Yes; adenomas only	NR	P+F	Alive at 2 years	[6]
Female	24	22	Yes; adenomas only	NR	P+F	NR	[7]
Female	27	23	Yes; adenomas only	NR	F	Death	[8]
Female	24	24	Yes; adenomas only	NR	P	NR	[9]
Female	22	21	Yes; adenomas + carcinoma	3 years later	P	Death	[10]
Female	26	19	Yes; adenomas only	NR	P+F	Alive at 7 years	[10]
Female	31	31	Yes; adenomas + carcinoma	NR	P	Alive at 13 years	[10]
Female	23	27	Yes;HP--	NR	P	Alive at 19 years	[10]
Female	20	20	Deferred	NR	NR	NR	[10]
Female	16	28	Yes; adenomas + carcinoma	NR	NR	NR	[10]
Female	34	17	Yes;HP--	NR	NR	Alive at 11 years	[10]
Female	37	33	Refused; biopsy - adenomas only	-	P	Death	[11]
Female	19	26	Not offered; biopsy - adenomas only	-	P	Alive at 12 years	[12]
Female	18	17	Yes;HP--	NR	P	NR	[13]
Female	23	32	Yes; adenomas + car in situ	NR	P	Alive at 11 years	[14]
Female	21	14	Yes; adenomas only	NR	P+F	Alive at 16 years	[15]
Female	31	25	Yes;HP--	NR	Medullary	Alive at 7 years	[16]
Male	72	44	Yes; adenomas + carcinoma	NR	P	Alive at 35 years	[16]
Female	27	25	Yes;HP--	NR	P	Alive at 13 years	[16]
Female	20	11	Yes; adenomas only	NR	P	Alive at 2 years	[17]
Female	27	24	Yes;HP--	NR	F	Alive at 4 years	[18]
Male	24	24	DNA	DNA	P	Death	[19]
Female	36	35	DNA	DNA	NR	DNA	[20]
Female	DNA	DNA	DNA	DNA	DNA	DNA	[21]
Female	DNA	DNA	DNA	DNA	DNA	DNA	[21]
Female	34	31	DNA	DNA	P	DNA	[22]
Female	19	17	DNA	DNA	P	DNA	[23]
Female	40	26	DNA	DNA	P	DNA	[23]
Male	40	42	Yes; adenomas + carcinoma	Not till 3 years	P	Alive at 3 years	This case

HP: Histopathology not reported, NR: Not reported, P: Papillary, F: Follicular, P+F: Both papillary and follicular, DNA: Details not available

left untreated. Gardner's syndrome is a clinical variant of FAP. It is characterized by the association of FAP with the characteristic triad of desmoids tumors, osteomas and epidermoid cysts. Mutations in another gene, MUTYH can also lead to a phenotype similar to FAP but have lesser number of polyps (the attenuated FAP phenotype).

Table 2: Extra colonic manifestations associated with Gardner's syndrome

Sr.No.	Associated other abnormalities			
	Osteomas	Desmoids	Dental anomalies	Others
1	Yes; single	No	Yes; Edentulous	None
2	Yes; single	Yes	Yes; Unerupted and supernumerary teeth	Pigmented nevus, epidermal inclusion cyst, massive mesenteric fibrosis
3	No	No	No	Sebaceous cysts, lipoma
4	No	No	No	Epidermal inclusion cysts, in situ carcinoma of ampulla of Vater
5	No	No	No	None
6	No	No	No	None
7	No	No	No	None
8	No	No	No	Epidermal inclusion cysts, retinal pigmentation
9	No	No	No	Gastric fundic polyps
10	Yes; single	Yes	No	Subcutaneous fibroma, fibromatosis of head of pancreas, focal nodular hyperplasia of liver, epidermal inclusion cysts
11	No	No	No	Retinal pigmentation, epidermal cysts
12	No	No	No	None
13	No	No	No	None
14	No	No	No	None
15	No	No	No	None
16	No	No	No	None
17	No	No	No	None
18	Yes; single	No	No	Epidermal vulval cyst
19	No	Yes	No	Alopecia, hirsutism, ovarian cysts, adrenal hyperplasia
20	No	No	No	None
21	No	No	No	Duodenal, ileal and jejunal polyps, epidermal inclusion cysts, in situ lobular carcinoma of breast
22	No	No	No	Uterine fibroids
23	No	No	No	Odontoma, pigmented spots on buccal mucosa, epidermal inclusion cysts, gastric adenomyoma, duodenal adenoma
24	No	No	No	None
25	No	No	No	None
26	No	No	No	None
27	Yes; single	No	No	Retinal pigmentation, duodenal adenomas, adenoma of ampulla of Vater
28	No	No	Yes; supernumerary teeth	None
29	No	No	No	Medulloblastoma
30	No	Yes	No	None
31	DNA	DNA	DNA	DNA
32	DNA	DNA	DNA	DNA
34	DNA	DNA	DNA	DNA
35	No	No	No	None
36	No	No	No	None
Present case	No	Yes	No	None

HP: Histopathology not reported, NR: Not reported, P: Papillary, F: Follicular, P+F: Both papillary and follicular, DNA: Details not available

The association of thyroid cancer with Gardner's syndrome/FAP was first reported in 1949 by Crail. In 1968, independent reports by Smith and Camiel pointed out that there could be an association between thyroid cancer and Gardner's syndrome. We reviewed the cases of thyroid cancer occurring in association with Gardner's syndrome/FAP reported in English literature. The details of these cases are summarized in Table 1. Associated manifestations, in addition to colonic and thyroid cancer, are listed in Table 2. The vast majority of the cases occur in females, forming 86% of cases.Most patients present in the second or third decade of life. Colonic manifestations were seen earlier than thyroid cancer in nearly 65% patients. Most colonic cancers are well differentiated and the chances of local or systemic recurrence are rare if total procto-colectomy is carried out (<10%). Most thyroid cancers are

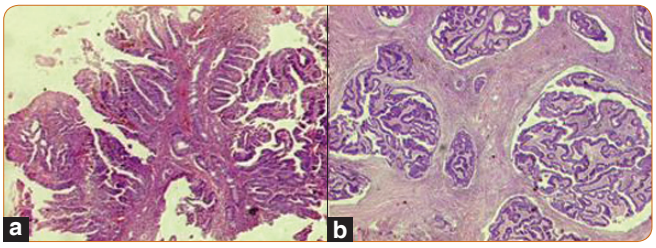

Figure 1: (a) Section from one of the multiple polyps in the surgical specimen shows features of a villous adenoma with moderate dysplasia. H and E stain, ×20 magnification, (b) Section from the tumor in the rectum shows invasive adenocarcinoma. Tumor is seen invading into the muscularis propria in this field. H and E stain, ×10 magnification

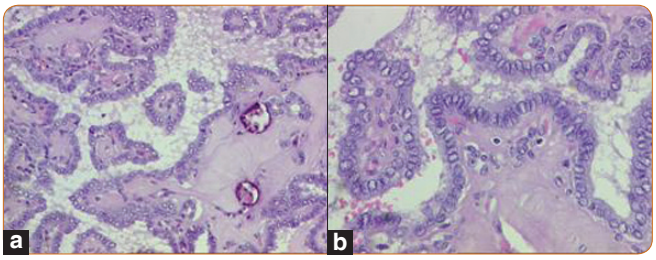

Figure 2: Papillary thyroid cancer - tumor with papillary configuration, showing prominent Orphan Annie eye nuclei, nuclear overlapping and grooves ((a) - at x200 magnification and (b) – at x400 magnification). The lower magnification picture shows bluish deposits (Psammomatous calcification)

also well differentiated and papillary cancer is the most commonly associated. An element of papillary cancer is found in 87% of the cases. Isolated follicular carcinoma is rare and found in only about 9% cases. Only one case of medullary carcinoma has so far been reported (case no 24; confirmed on. Immunohistochemistry with anti-calcitonin being strongly positive). Additionally, multicentric thyroid cancer is much more common in these patients as compared to the sporadically occurring thyroid cancer. No recurrence of thyroid cancer was seen if total thyroidectomy was performed. Metastasis from thyroid cancer was found in only one case, this patient had vertebral metastasis which showed a thyroid origin on biopsy (Case no 6). Although multiple osteomas are associated with Gardner's syndrome, none of these patients had multiple osteomas. Solitary osteoma was seen in <15% of patients. Among the dental abnormalities, supernumerary teeth were the commonest. Desmoid tumors, although common in Gardner's syndrome in general, were found be present in <15% of patients with thyroid cancer and Gardner's syndrome. Epidermoid inclusion cysts, retinal pigmentation, gastric fundic polyps, small intestinal polyps and carcinoma of ampulla of Vater are some of the other important reported associations. Gastric adenomyoma and uterine leiomyomas were found in one patient each.

Our patient had colonic polyps and adenocarcinomas as his presenting manifestation, as is seen in nearly 65% cases. His colonic malignancy was a moderately differentiated adenocarcinoma, as is seen in most patients with FAP/Gardner's syndrome [Figures 1 and 2]. His thyroid cancer was well-differentiated papillary carcinoma; more than 85% cases of thyroid cancer occurring in association with Gardner's syndrome have an element of papillary histology. To the best of our knowledge, our patient is the only male patient reported in the English literature with thyroid cancer and Gardner's syndrome who had multiple desmoid tumors associated with his syndrome.

Conclusions

Thyroid cancer may occur in patients with FAP/Gardner's syndrome and has a prevalence of around 0.6% in patients with FAP/Gardner's syndrome.[24] This amounts to a more than 150-fold increased risk as compared to the general population.[25] All patients diagnosed with Gardner's syndrome/FAP should be screened periodically by ultrasound for the early detection of thyroid cancer. Additionally, all young patients with thyroid cancer should be examined clinically for other manifestations of Gardner's syndrome and a meticulous family history should be taken. Total proctocolectomy should be offered to all patients because of the nearly 100% risk of developing a colonic carcinoma in untreated cases. When thyroid nodules are detected, total thyroidectomy should be done as partial thyroidectomy carries a risk of recurrent thyroid cancer in this patient group.

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