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 polyps 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 9.5x6.6x7.5 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/m² weekly intravenously, vinblastine 6 mg/m² weekly intravenously and tamoxifen 20 mg/m² 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 well-differentiated 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
Table 1: Details of cases of thyroid cancer occurring 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                                     | DNA                       | P        | Death  | [19]  |
| Female | 36                             | 35                        | DNA                           | DNA                                     | RN                        | 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. | Osteomas | Desmoids | Dental anomalies | Associated other abnormalities |
|--------|----------|----------|------------------|------------------------------|
| 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 |
| 33     | DNA | DNA | DNA | DNA |
| 34     | No | No | No | None |
| 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 proctocolectomy is carried out (<10%). Most thyroid cancers are
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 done. 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 to 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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References

1. Smith WG. Familial multiple polyposis: Research tool for investigating the etiology of carcinoma of the colon? Dis Colon Rectum 1968;11:17-31.
2. Camiel MR, Mulé JE, Alexander LL, Benninghoff DL. Association of Thyroid Carcinoma with Gardner’s Syndrome in Siblings. N Engl J Med 1968;278:1056-8.
3. LaMont JT, Vickery AL Jr. Case 50–1982 – Liver Dysfunction after Total Colectomy for Intestinal Polyposis. N Engl J Med 1982;307:1866-73.
4. Heilman J, Goff JS. Letter to the editor – Case records of the Massachusetts General Hospital (Case no 50–1982). N Engl J Med 1983;308:906-7.
5. Delamarre J, Capron JP, Armand A, Dupas JL, Deschepper B, Davion T. Thyroid Carcinoma in Two Sisters with Familial Polyposis of the Colon: Case Reports and Review of the Literature. J Clin Gastroenterol 1988;10:659-62.
6. Kelly MD, Hugh TB, Field AS, Fitzsimons R. Carcinoma of the thyroid gland and Gardner’s syndrome. Aust N Z J Surg 1993;63:505-9.
7. Thompson JS, Harned RK, Anderson JC, Hodgson PE. Papillary carcinoma of the thyroid and familial polyposis coli. Dis Colon
Punatar, et al.: Thyroid cancer in Gardner’s syndrome

Rectum 1983;26:583-5.
8. Herrera L, Carrel A, Rao U, Castillo N, Petrelli N. Familial adenomatous polyposis in association with thyroiditis Report of two cases. Dis Colon Rectum 1989;32:893-6.
9. Bell B, Mazzaferr E. Familial adenomatous polyposis (Gardner’s syndrome) and thyroid carcinoma - A case report and review of the literature. Dig Dis Sci 1993;38:185-90.
10. Plail RO, Bussey HJ, Glazer G, Thomson JP. Adenomatous polyposis: An association with carcinoma of the thyroid. Br J Surg 1987;74: 377-80.
11. Schneider NR, Cubilla AL, Chaganti RS. Association of endocrine neoplasia with multiple polyposis of the colon. Cancer 1983;51:1171-5.
12. Smith WG, Kern BB. The nature of the mutation in familial multiple polyposis: Papillary carcinoma of the thyroid, brain tumors and familial multiple polyposis. Dis Colon Rectum 1973;16:264-71.
13. Hamilton SR, Bussey HJ, Mendelsohn G, Diamond MP, Pavlides G, Hutcheon D, et al. Ileal adenomas after colectomy in nine patients with Adenomatous polyposis coli/Gardner’s syndrome. Gastroenterology 1979;77:1252-7.
14. Lee FL, MacKinnon MD. Papillary thyroid carcinoma associated with polyposis coli – A case of Gardner’s syndrome. Am J Gastroenterol 1981;76:138-40.
15. Keshgegian AA, Enterline HT. Gardner’s syndrome with duodenal adenomas, gastric adenomyoma and thyroid papillary-follicular adenocarcinoma. Dis Colon Rectum 1978;21:255-60.
16. Reed MW, Quayle AR, Harris SC, Talbot CH. The association between thyroid neoplasia and intestinal polyps. Ann R Coll Surg Engl 1990;72:357-9.
17. Hizawa K, Iida M, Yao T, Aoyagi K, Oohata Y, Mibu R, et al. Association between thyroid cancer of cribriform variant and familial adenomatous polyposis. J Clin Pathol 1996;49:611-3.
18. Piffer S. Gardner’s syndrome and thyroid cancer – A case report and review of the literature. Acta Oncol 1988;27:413-5.
19. Crail HW. Multiple primary malignancies arising in the rectum, brain and thyroid. U S Nav Med Bull 1949;49:123-8.
20. Lockhart-Mummery HE. Intestinal polyposis: The present position. Proc R Soc Med 1967;60:381-8.
21. Alm T, Licznerski G. The intestinal polyposis. Clin Gastroenterol 1973;2:577-602.
22. Van Erpecum KJ, van Berge Henegouwen GP, Meinders AE, Bronkorst FB. Papillary thyroid carcinoma and characteristic pigmented ocular fundus lesions in a patient with Gardner’s syndrome. Neth J Med 1988;32:136.
23. Bulow S, Holm NV, Mellemgaard A. Papillary thyroid carcinoma in Danish patients with familial adenomatous polyposis. Int J Colorect Dis 1988;3:29-31.
24. Hamed RK, Buck JL, Olmsted WW, Moser RP, Ros PR. Extracolonic manifestation of familial adenomatous polyposis syndromes. Am J Radiol 1991;156:481-5.
25. Half E, Bercovich D, Rozen P. Familial adenomatous polyposis. Orphanet J Rare Dis 2009;4:22.

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