Acta Dermatovener (Stockholm) 50: 381–384, 1970

ALOPECIA AREATA IN ASSOCIATION WITH INTESTINAL POLYPOSIS

The Relationship of Two Syndromes—Gardner's and Cronkhite–Canada

Allan K. Izumi,[1] Francis E. Rosato and Walter B. Shelley

From the Departments of Dermatology and Surgery, University of Pennsylvania School of Medicine, Pa, USA

Abstract. A case of Gardner's syndrome (familial intestinal polyposis, osteomas, soft tissue tumors) associated with alopecia areata is presented. The presence of alopecia in association with intestinal polyposis led initially to a consideration of the Cronkhite–Canada syndrome (diffuse gastrointestinal polyposis, alopecia, onycho-atrophy, hyperpigmentation), but the family history of intestinal polyposis and malignancy, presence of osteomas, and soft tissue tumor indicated that our patient had Gardner's syndrome. A critical review of the ectodermal changes in the reported patients with the Cronkhite–Canada syndrome revealed that the alopecia and nail changes could represent alopecia areata, and not inherent components of this syndrome.

Intestinal polyposis can be divided into a genetic and nongenetic group. McKusick (11) carefully reviewed the genetically induced group which includes familial polyposis, Peutz-Jeghers syndrome, Turcot's syndrome, and Gardner's syndrome (intestinal polyposis, osteomas, and soft tissue tumors). By contrast, the nongenetic group includes the majority of cases of isolated intestinal polyps, the rare cases of diffuse gastrointestinal polyposis (16), and the Cronkhite–Canada syndrome [diffuse gastrointestinal polyposis, alopecia, onycho-atrophy, hyperpigmentation (2)].

The unusual finding in the patient being reported was the accompaniment of alopecia areata with Gardner's syndrome. This fortuitous association prompted us to question whether the alopecia and onycho-atrophy in the Cronkhite–Canada syndrome were similarly a result of alopecia areata rather than an inherent part of that disease.

[1] Postdoctoral Trainee on PHS TI AM 05261.

CASE REPORT

J. D. is a 24-year-old Negro male referred to the Hospital of the University of Pennsylvania because of radiologic evidence of colonic polyposis. He was admitted on one other occasion 3 years ago for multiple chalazia, alopecia areata, and possible colonic polyposis. A barium enema was negative then, but a sigmoidoscopy examination revealed 4 to 6 polyps measuring 2 mm in diameter, approximately 5 to 10 cm from the anus. A history of alopecia areata, resistant to Grenz-ray treatment, intralesional steroids, and systemic steroids was present since age 13. A strong familial history of intestinal polyposis was obtained (Fig. 1). Approximately 1 month prior to admission, the patient's brother developed metastatic carcinoma of the colon.

A repeat barium enema on the patient revealed numerous polyps in the colon, and he was referred to the Hospital of the University of Pennsylvania. The patient had otherwise remained asymptomatic with no history of melena, diarrhea, abdominal cramps, weight loss or anorexia.

Physical examination revealed patches of diffuse alopecia of the scalp with almost total loss of eyebrows and eyelashes (Fig. 2). Axillary, pubic and body hair was normal. Linear pitting of the nail plate was present. Multiple immobile, hard, non-tender 2×2 cm nodules were present over the entire scalp, predominantly over the occipital and parietal areas. A non-tender 6×4 cm firm mobile mass was present under the right mandibular joint. The rest of the physical examination was normal.

Roentgenogram examination of the skull and colon respectively confirmed the presence of multiple osteomas and polyposis of the colon. Proctoscopic examination revealed multiple sessile polyps varying in size from 5 to 10 mm and present from the dentate margin up to 25 cm. A biopsy of a polyp at 14 cm confirmed the diagnosis of adenomatous polyp. Microscopic examination of plucked hairs from the scalp revealed clubbed and dystrophic hairs. A Wood's lamp examination of the scalp was negative. A scalp biopsy was consistent with alopecia.

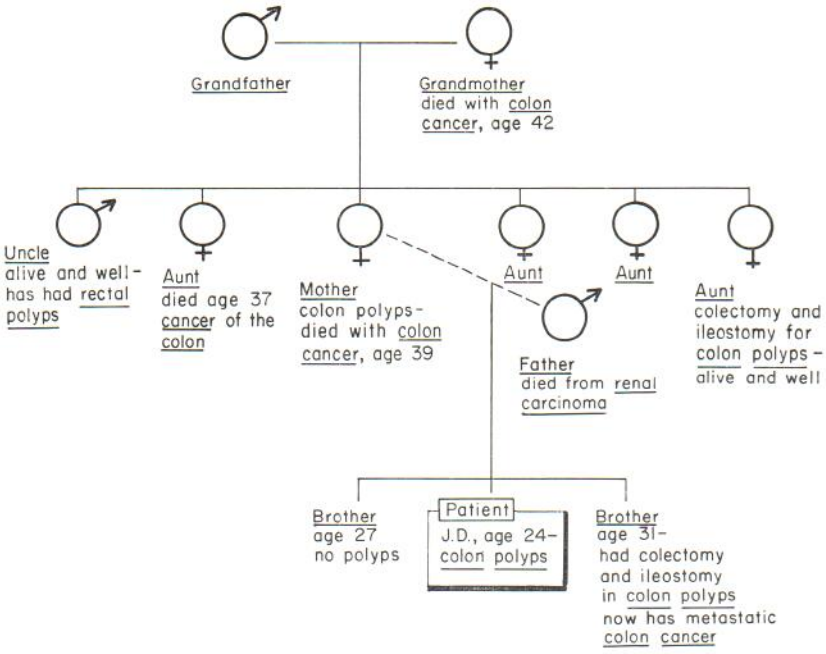

Fig. 1. Patient's genealogical history.

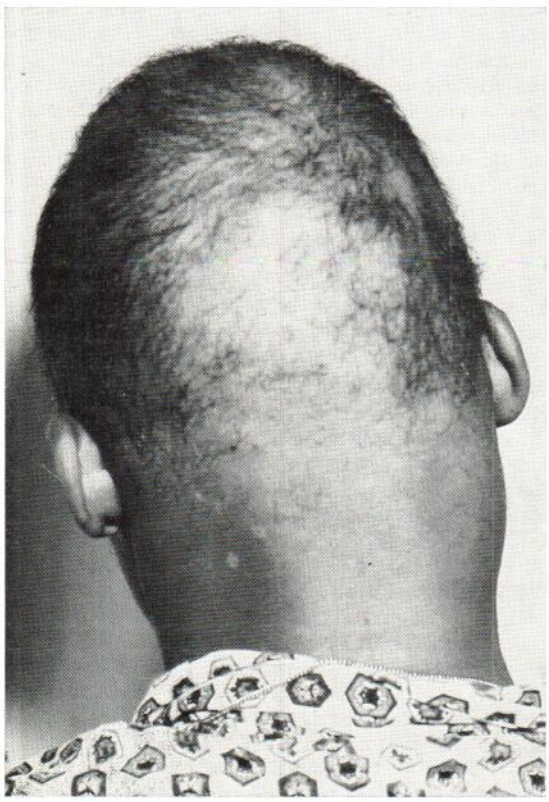

Fig. 2. Posterior view of patient showing alopecia areata of the scalp and soft tissue tumor of the right side of the neck. The osteomas of the scalp are not evident in this photograph.

The patient underwent a subtotal colectomy with anastomosis of the side of the terminal ileum to the end of the rectum leaving exactly 13 cm of the rectum and anus in place. Gross examination and pathologic specimens confirmed the diagnosis of multiple benign adenomatous polyposis.

By 5 weeks after surgery, he was having 2 to 3 formed stools a day, and on proctoscopic examination the polyp population was diminished by approximately 50%.

DISCUSSION

The ectodermal abnormalities in Gardner's syndrome are reviewed in the literature (5, 9, 17) (Table I). Although this is the first report of which we are aware of alopecia areata in this syndrome, we feel that this finding is fortuitous.

Cronkhite and Canada (2) described the syndrome of diffuse gastrointestinal polyposis, alopecia, onycho-atrophy, and hyperpigmentation. A total of 11 cases have been reported since their original paper (Table II).

The relationship of the alopecia and onycho-atrophy to the gastrointestinal polyposis in the Cronkhite–Canada syndrome is obscure. Three hypotheses are advanced to explain this relationship. Cronkhite (2) proposed that gastrointestinal malabsorption of essential vitamins, minerals and other vital substances was responsible for these abnormalities. Johnson (8), however, was not able

Table I. *Comparison of Gardner's and Cronkhite–Canada Syndrome*

	Gardner	Cronkhite–Canada
Genetic transmission	Autosomal dominant	Not genetically determined
Age	2–3 decade	5–6 decade
Gastrointestinal involvement	Colon	Diffuse (stomach, small bowel, colon)
Pathology	Pre-malignant adenomatous polyps	Benign adenomatous polyps[a]
Associated ectodermal abnormalities	Osteoma, soft tissue tumors (keratinous and sebaceous cysts, fibroma, desmoid)	Alopecia, Onycho-atrophy, Hyperpigmentation

[a] Adenocarcinoma reported in DaCruz's patient.

to demonstrate significant malabsorption, using I^{131} labelled triolein and oleic acid and fecal fat studies. Jarnum (7) and Orimo et al. (15) showed that these patients had a protein-losing enteropathy. Yet the alopecia and onycho-atrophy developed before significant malnutrition and hypoproteinemia occurred. One patient even regrew both hair and nails despite her progressive deterioration and subsequent demise (8). Manousos (12) suggested that the hair and nail changes were related to metabolic derangements, particularly hypoparathyroidism, but there was no evidence for this. Jarnum (7) felt that the ectodermal changes were an inherent part of this syndrome. Genetic analysis of these patients' families, however, was against this hypothesis.

The clinical features of the alopecia and onycho-atrophy in the patients with Cronkhite–Canada syndrome are consistent with alopecia areata (Table II). The sudden loss of hair in periods varying from 3 days to 2–4 weeks and the concomitant loss of eyebrow, eyelash, axillary and

Table II. *Cronkhite–Canada Syndrome*

Author	Family history	Sex	Age	Polyposis[a]	Alopecia	Onycho-atrophy	Hyperpigmentation
Cronkhite, L. W. and Canada, W. J. (2)	—	♀	42	S.D.I.C.	Scalp, facial, axillary, pubic	Atrophic fingernails – toenails	Dorsae hands, fingers, body folds
Kennedy, J. A. (10)	—	♀	75	S.D.C.	Scalp (alopecia totalis – 3 days)	Atrophic fingernails – toenails	Arms, legs
Martini, G. A. (13)	—	♀	69	E.S.I.C.	Scalp, axillary, pubic	Atrophic fingernails – toenails	Face, hands
Johnson, M. M. (8)	—	♀	71	S.C.	No comment	"Mycosis" of fingernails and toenails	No comment
Zdansky, E. (18)	—	♂	54	S.C.	Scalp	Atrophic fingernails – toenails	Hands
Jarnum, S. (7)	—	♀	58	S.D.C.	Scalp, axillary, pubic	Atrophic fingernails – some toenails	Diffuse
Manousos, U. (12)	—	♂	61	S.C.	Scalp	Atrophic fingernails – toenails	Palmar creases, forearms, back
Nishiyama, S. (14)	—	♂	61	S.C.	Scalp, eyelash, eyebrow, axilla, pubic	Atrophic fingernails – toenails	Hands
DaCruz, G. (3)	—	♂	64	S.I.C.R.	Scalp, axilla, pubic	Atrophic fingernails – toenails	No pigmentation
Orimo (15)	—	♂	64	S.D.J.I.C.	Scalp, eyebrow, eyelash, axilla, pubic	Atrophic fingernails – toenails	Palmar creases, soles, back

[a] E = esophagus. S = stomach. D = duodenum. I = ileum. C = colon. R = rectum.

pubic hair (7/11 cases) are characteristic of alopecia areata (i.e. alopecia universalis). Similarly, the thin, friable, atrophic nails seen in these patients can occur in alopecia areata, especially in alopecia universalis (4).

The etiology of alopecia areata is not known. The relationship, however, of preceding emotional and physical stress to alopecia areata is significant (6). In this regard, it is interesting that gastrointestinal symptoms preceded the alopecia in these patients in each case in which this association was recorded. Finally, Andrell (1) has reported alopecia areata in association with gastric polyps in 6 out of 13 patients. Although no conclusion can be made regarding the relationship of alopecia areata and gastrointestinal polyposis, it is noteworthy that all the patients with the Cronkhite–Canada syndrome had gastric polyposis.

REFERENCES

1. Andrell, O.: Gastric polypi and alopecia areata. Svensk Läkartidn *56:* 2 779, 1959.
2. Cronkhite, L. W. & Canada, W. J.: Generalized gastrointestinal polyposis; an unusual syndrome of polyposis, pigmentation, alopecia, and onychotrophia. New Eng J Med, *252:* 1 011, 1955.
3. DaCruz, G. M. G.: Generalized gastrointestinal polyposis: a unusual syndrome of adenomatous polyposis, alopecia, onycho-atrophia. Amer J Gastroent. *47:* 504, 1967.
4. Demis, J. D. & Weiner, M. A.: Alopecia universalis, onychodystrophy, and total vitiligo. Arch Derm (Chicago) *88:* 195, 1963.
5. Gardner, E. J. & Richards, R. C.: Multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. Amer J Hum Genet *5:* 139, 1953.
6. Greenberg, S. K.: Alopecia areata—a psychiatric study. Arch Derm (Chicago) *72:* 454, 1955.
7. Jarnum, S. & Jensen, H.: Diffuse gastrointestinal polyposis with ectodermal changes: a case with severe malabsorption and enteric loss of plasma proteins and electrolytes. Gastroenterology *50:* 107, 1966.
8. Johnson, M. M., Vosburgh, J. W., Wiens, A. T., & Walsh, G. C.: Gastrointestinal polyposis associated with alopecia, pigmentation, and atrophy of the fingernails and toenails. Ann Intern Med *56:* 935, 1962.
9. Jones, E. L. & Cornell, W. P.: Gardner's syndrome—review of the literature and report on a family. Arch Surg *92:* 287, 1966.
10. Kennedy, J. A. & Hirson, C.: A transient syndrome with Peutz-Jeghers features and ectodermal change. Proc Roy Soc Med *54:* 234, 1961.
11. McKusick, V. A.: Genetic factors in intestinal polyposis. JAMA *182:* 271, 1962.
12. Manousos, O. & Webster, C. U.: Diffuse gastrointestinal polyposis with ectodermal changes. Gut *7:* 375, 1966.
13. Martini, G. A. & Dölle, W.: Menetrier-Syndrome. Polyadenomatosis des Magens mit Eiweissverlust in den Magen-Darm-Kanal. Deutsch Med Wschr *86:* 2 524, 1961.
14. Nishiyama, S., Mori, S. & Harada, S.: Gastrointestinale Polyposis mit universeller Alopecie, Onychodystrophie und Pigmentation der Haut. Arch Klin Exp Derm *221:* 144, 1965.
15. Orimo, H., Fujita, T., Yoshikawa, M., Takemoto, T., Matsuo, Y., & Nakao, K.: Gastrointestinal polyposis with protein-losing enteropathy, abnormal skin pigmentation and loss of hair and nails (Cronkhite–Canada syndrome). Amer J Med *47:* 445, 1969.
16. Ravitch, M. M.: Polypoid adenomatosis of the entire gastrointestinal tract. Ann Surg *128:* 283, 1948.
17. Weary, P. E., Linthicum, A., Cawley, E. P., Coleman, C. C., & Graham, G. F.: Gardner's syndrome—a family group study and review. Arch Derm (Chicago) *90:* 20, 1964.
18. Zdansky, E. & Riederer, J.: Gastrointestinal polypose Adenomatose mit Hypoproteinamie und ektodermalen Storungen. Radiol Clin (Basel) *32:* 254, 1963.

Received April 13, 1970

Walter B. Shelley, M.D.
Hospital of the University of Pennsylvania
3400 Spruce Street
Philadelphia, Pa 19104
USA