Diffuse gastrointestinal polyposis with ectodermal changes

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EDITORIAL COMMENT A patient with diffuse gastrointestinal polyposis and abnormalities of nails, skin, and hair is described. This is the fourth case to appear in the literature. The other three cases are reviewed and possible mechanisms responsible for the changes of ectodermal structures are discussed. These cases differ from the Peutz-Jeghers syndrome and from familial polyposis coli.

Hereditary polyposis of various parts of the alimentary tract has been well recognized for several decades and, in a recent review, McKusick (1962) described six distinct varieties. On the other hand only three cases of diffuse gastrointestinal polyposis, associated with ectodermal changes, have been described. These patients had no family history. They presented with diarrhoea, atrophy of the nails, pigmentation of the skin, and alopecia. They were found to have polyposis involving the stomach, small intestine, and colon and died from the disease a few months after the diagnosis was made (Cronkhite and Canada, 1955; Johnston, Vosburgh, Wiens, and Walsh, 1962). It seems likely that such cases belong to a distinct syndrome in view of the lack of family history, and the peculiar associated ectodermal changes. Recently we had the opportunity to study a patient with the characteristics of the syndrome described by Cronkhite and Canada, who had polypoid mucosa from the cardia to the rectum, and whose condition improved dramatically after partial gastrectomy and replacement therapy.

CASE REPORT

The patient, a dustman, aged 61 (case no. 351370), was married with two healthy children. There was no family history of alimentary disorders, and his own parents had died aged 75 and 80. His health had been good until December 1962 when he developed diarrhoea, which settled spontaneously. In September 1963, he was admitted as an emergency case to his local hospital with a recurrence of diarrhoea of two months' duration. He was passing four to six fluid, yellow stools daily with no evidence of blood or slime. He was extremely weak and lethargic, could barely walk, complained of leg cramps and had lost 28 lb. (13 kg.) in weight.

Serological investigations showed the following:—
Na 149 q./l. K 2.2 mEq./l., Cl 98 mEq./l., Ca 8.8 mg%.

The haemoglobin was 109% and the packed cell volume 49%.

Despite vigorous therapy, the diarrhoea continued and the electrolyte picture remained unaltered. Stool cultures were negative.

A barium meal showed a bizarre gastric outline interpreted as being due to masses of polyps, and follow-through films showed multiple, small round filling defects in the small bowel. A barium enema showed similar

FIGS. 1 and 2
Finger nails
and toenails
showing gross
changes.

FIG. 1.

FIG. 2.

FIG. 3.
*Palmar pigment-
ation and
nodule in
palmar
fascia.*

lesions in the ascending colon with a shaggy outline in the rest of the colon. A provisional diagnosis of diffuse gastrointestinal polyposis was made, and the patient was transferred to the Nuffield Department of Medicine at Oxford under the care of Professor L. J. Witts.

The patient was now extremely ill, showed evidence of marked weight loss, and was bed bound. Abdominal examination was not contributory. Various ectodermal changes, noted beforehand, were confirmed. The finger and toe nails (Figs. 1 and 2) had a striking appearance. They were thick, white, brittle, and splintered easily. According to the patient these changes had been present for several years. There was pigmentation of the palmar creases and contracture of the palmar fascia of the right hand (Fig. 3), and numerous pigmented spots on the forearms and back. The scalp hair was thin and there were a few areas of alopecia, although this finding was not striking and could well have passed unnoticed. Trousseau's and Chvostek's signs were positive.

HAEMATOLOGY Hb 15.7 g./100 ml., M.C.H.C. 35%, haematocrit 45; W.B.C. 16,900/c.mm. (neutrophils 88%, lymphocytes 11%); E.S.R. 29 mm. in one hr.; serum folic acid 1.6 μ g./ml.; serum iron 148 μ g./ml.; serum vitamin B₁₂ 850 μ g./ml.; prothrombin time (Owren's) 46%; plasma proteins, total 4.8 g./100 ml. and albumin 2.0 g./100 ml.

SEROLOGY This showed evidence of a gross hypokalaemic alkalosis, consistent with severe diarrhoea and loss of extracellular fluid. The serum calcium and magnesium were consistently low.

SIGMOIDOSCOPY Dr. S. C. Truelove saw generalized cobblestoning appearances. The changes were similar to those noted in the small bowel at operation.

RECTAL BIOPSY Dr. W. C. D. Richards reported non-specific inflammatory changes.

RADIOLOGY Dr. K. Lumsden, reporting on the result of a barium meal (Fig. 4), said that the stomach was large in size with a most unusual appearance, although the presence of food residue might be partly responsible. There were a number of polyps in the fundus and it was noteworthy that no mass could be felt in the region of the stomach or pyloric part where the changes were most marked. Gross gastric polyposis appeared to be the diagnosis.

FIG. 4. *Gross gastric polyposis with gastric retention shown after a barium meal.*

BARIUM ENEMA This showed gross polyposis of the caecum and ascending colon. The mucosa of the rest of the colon was abnormal and the presence of small sessile polyps seemed the most probable cause of these appearances.

BIOCHEMISTRY OF FAECES Faecal fat 21.5 g./24 hr., faecal electrolytes (4 litres of stool), calcium 18.5 mg./100 ml. = 740 mg./24 hr., potassium 23.7 mEq./l. = 94.8 mEq./24 hr., magnesium 1.1 mg./100ml. = 44 mg./24 hr., sodium 65 mEq./l. = 260 mEq./24 hr., phosphate 10.0 mg./100 ml. = 400 mg./24 hr.

Adequate balance studies were impossible owing to the extremely poor general condition of the patient who was passing from 4 to 6 litres of stool in 24 hours with some degree of incontinence. In view of his poor intake, the faecal electrolyte loss, particularly potassium, was excessive. In addition, approximately 50 mEq. of potassium was being lost in the urine every 24 hours.

The patient continued to have profuse watery diarrhoea which did not respond to symptomatic treatment. Vigorous attempts to improve the electrolyte pattern with massive intravenous therapy had only a temporary effect. It was not clear how the catastrophic diarrhoea

FIG. 5. Antral end of stomach opened at operation; prolapsing gastric polyps.

FIG. 6. Jejunal biopsy (enlarged).

had started, but as the greatest mass of polyps was situated in the pyloric antrum, and tending to obstruct the stomach, it was argued that removal of this vast secretory mass might break the vicious circle and alleviate the patient's symptoms. It was also clear that desperate measures were required if the patient were not to succumb.

Accordingly, after one final effort to improve the biochemical disorders, operation (C.U.W.) was undertaken three weeks after admission to the Nuffield Department of Medicine.

The stomach was found to be enormous (Fig. 5), and lined with a mass of polyps prolapsing into the duodenum. The bulk were at the antrum, but the fundal mucosa was polypoid with several large discrete tumours which were diathermied. A three-quarter Polya gastrectomy was performed, it being noted that the jejunal mucosa at the site of anastomosis (Fig. 6) was covered by a carpet of tiny polyps. Lesions were also palpated in the ascending colon.

After operation, the condition of the patient improved dramatically. The diarrhoea ceased, and at the time of discharge from hospital on his fourteenth post-operative day, he was eating well and passed only two or three semi-formed stools per day. The electrolyte picture

became stable, although he was prescribed oral potassium and magnesium supplements.

PATHOLOGY The gross specimen was covered by glistening oedematous polyps so that the appearance resembled a hydatidiform mole. On section these were adenomatous with no frank evidence of malignancy. Inflammatory changes were few but interstitial oedema was marked. Elongated and cystic gastric pits were present in the stroma (Fig. 7).

The jejunal epithelium at the point of the gastrectomy anastomosis showed a diffuse picture of micropolyposis, cystic dilatation, and considerable mucosal oedema.

FOLLOW-UP The patient was readmitted for assessment at intervals. Eleven months after operation he was very well, having gained 42 lb. (19 kg.) in weight. His nails, although still grossly abnormal, were regrowing, and he thought that his hair had also regrown slightly. He had no diarrhoea and his bowels moved twice daily. There was still palmar pigmentation although this was not striking. The electrolyte picture was normal except for magnesium, which was 0.75 mEq./l. His plasma albumin level was 3.2 g./100 ml. but he still had gross steatorrhoea with 21.5 g. faecal fat in 24 hours.

FIG. 7. Photomicrograph of gastric polyps $\times 4$.

When seen at an out-patient clinic in June 1966 he remained well, but was not working. He now continues on potassium, calcium, and vitamin supplements.

DISCUSSION

The unique nature of the syndrome of diffuse gastrointestinal polyposis makes this case report justifiable. The features of our case and the other three cases which appear in the literature are summarized in Table I.

These differ from the Peutz-Jeghers syndrome in which pigmentation of the face and mouth is associated with characteristically small intestinal polyposis often considered hamartomatous. In this

condition, as in familial polyposis coli, there is hereditary transmission due to a Mendelian dominant and an absence of the striking ectodermal changes found in diffuse gastrointestinal polyposis.

As in familial polyposis coli, the polyps of diffuse gastrointestinal polyposis appear to be true neoplasms, although in such a disorganized stomach minor inflammatory changes were not unexpected.

None of the recorded cases of diffuse gastrointestinal polyposis had a family history. Diarrhoea, atrophy of the nails, alopecia, skin pigmentation, and gastrointestinal polyposis were present in all of them. The first patient had no electrolytic disturbance; in the other three there was calcium and potassium deficiency. Plasma albumin was low in cases 2 and 4, and normal in case 3. Steatorrhoea was present in our patient. In all the patients the peripheral blood picture was normal. Cronkhite and Canada (1955), who described the first two patients, suggested that the ectodermal changes were part of a generalized deficiency state and that their clinical prominence might be related to the extensive distribution of the lesions in all segments of the digestive tract.

It appears certain that the changes of the ectodermal structures (nails, hair, and skin) seen in our patient were the consequence of the gastrointestinal polyposis. In view of the fact that the patient was aware of the nail changes for many years, the probability is that the polyps were present for a considerable time, but he had no severe constitutional disturbance until the diarrhoea occurred. The mechanism that triggered off the catastrophic diarrhoea was possibly some degree of pyloric obstruction due to polyposis, gastric stasis, and spilling of foul gastric contents into the small bowel.

The absence of electrolytic disturbance in case 1 and the normal albumin in case 3 suggest that the deficiency, responsible for the changes of the ectodermal structures, is not merely lack of albumin or the usual electrolytes. It is noteworthy that such ectodermal lesions are not described in patients

TABLE I

SUMMARY OF FEATURES OF FOUR CASES OF DIFFUSE GASTROINTESTINAL POLYPOSIS WITH CHANGES OF ECTODERMAL STRUCTURES DESCRIBED IN THE LITERATURE

No.	Sex	Age	Family History	Nail Changes	Hair Changes	Pigmentation	Diarrhoea	Abdominal Pain	Tetany	Electrolytic Imbalance	Steatorrhoea	Low Albumin Level	Blood Changes
1	F	42	—	+	+	++	+	+	—	—			—
2	F	75	—	+	++	+	+	+	+	+		+	—
3	F	51	—	+	++	+	+	+	—	+	—	—	—
Present Case 4	M	61	—	++	+	+	+	+	+	+	+	+	—

with longstanding malabsorption such as occurs in idiopathic steatorrhea.

The presence, for many years, of nail changes without constitutional disturbance in our patient probably means that he was losing either amino-acids or minerals necessary for the development of nails but not essential for other body functions.

Changes of nails, skin, and hair similar to the ones seen in the four cases with gastrointestinal polyposis have been described in patients with chronic hypoparathyroidism (Emerson, Walsh and Howard, 1941; Learner and Brown, 1943). In one of Emerson's patients the cystine content of the nail was abnormally low and an abnormality in sulphur metabolism was postulated. In this instance we were unable to confirm this hypothesis.

In our patient there was no evidence of gross hypoparathyroidism. The serum phosphorus level was low and that of urinary calcium was normal; however, it is possible that both in gastrointestinal polyposis and in chronic hypoparathyroidism there is a similar deficiency of substances necessary for the development of nails and hair and the low cystine content in the nails of Emerson's patient may be a significant finding.

We are grateful to Professor L. J. Witts and to Dr. S. C. Truelove for allowing us to publish this case. We wish to thank Dr. W. C. D. Richards for his help in the interpretation of the unique pathology.

ADDENDUM

Since this paper was accepted for publication, Jarnum and Jensen (1966) have added three additional cases from the literature and describe a further fatal case of the Cronkhite-Canada syndrome.

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