Malignant Tumors of the Central Nervous System Associated With Familial Polyposis of the Colon: Report of Two Cases.*

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FAMILIAL POLYPOSIS of the colon was first described by Cripps[1] in 1882. Since then, case reports and family histories have been eagerly studied, and it has become apparent that many patients afflicted with this disease have a tendency to develop adenocarcinoma in one or more polyps before they have attained the age of 50 years.[11]

It was not felt,[1, 4] however, that this proclivity of the familial type of polyps to transform into cancer was greater than in cases of isolated polyps; except that in multiple polyposis the chances of transformation are multiplied by the greater number of polyps. In other words, this tendency of polyps of the colon to undergo malignant transformation does not seem to be a characteristic of the hereditary type of the disease alone.

In recent years another interesting characteristic has been noted in patients with polypoid disease of the colon. It has been observed that different tissue tumors involved other anatomic sites in cases of diffuse polyposis and that this tendency seemed to be peculiar to familial polyposis only. Gardner[5, 6] in 1952 reported six cases of familial polyposis in which multiple osteomas were associated; O'Brien[12] reported in 1955, six cases of polyposis with soft tissue tumors, most of which were fibrous; Laberge, Sauer and Mayo in 1957[8] reported on their study of a connective tissue tumor of the mesentery in a patient with diffuse polyposis.

Many other studies and observations have been reported in recent medical literature.[7, 10, 13, 15] Enquist[3] studied 876 patients with isolated polyps of the colon and was unable to discover any correlation with other tissue tumors such as nevi, keratosis, lipomas, etc. Thus, the occurrence of various tumors of other parts of the body in association with familial polyposis appears to be of more significance than mere coincidence.

In this connection, it appeared to us that this report of two cases of diffuse polyposis of the colon in teenagers in whom there was subsequent development of malignant tumors of the central nervous system, would be interesting.

Case Reports

Case 1. This 15-year-old, white boy came to the hospital on November 9, 1950, complaining of diarrhea and bloody stools. For the last four years he had noticed blood in his stools occasionally and he had had frequent episodes of diarrhea.

The past history was not contributory and did not reveal that any pathologic disorder of importance had occurred in childhood or infancy. The family history for two generations failed to disclose any other occurrences of significant gastro-intestinal disorders, except the case of a sister, 13 years of age, whose history will be discussed in the second case report.

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FIG. 1. Segment of excised colon with multiple polyps. One is carcinomatous. Case 1.

Physical examination revealed a pale and rather thin boy, with no evidence of organic disease except that which involved his large bowel. Protoscopic and roentgenologic examinations of his colon showed many large polypoid masses in the rectum, sigmoid and upper segments of the colon. Biopsy of a rectal polyp failed to show any evidence of malignant transformation.

On November 28, 1950, a laparotomy was performed. Many polypoid masses were palpated through the wall of the distal portion of the colon and a malignant tumor of the sigmoid 3 or 4 cm. in diameter was found (Fig. 1). An anterior resection of the left portion of the colon was performed and an end-to-end anastomosis was made of the transverse colon with the rectum. Two weeks later, on December 15, 1950, a large rectal polyp was removed. From the specimens removed at these two operations, the pathologist reported two malignant tumors: one was an adenocarcinoma of the sigmoid and the other was a small adenocarcinoma developing on a rectal polyp (Fig. 2).

From January 1951 to July 1952, the patient was hospitalized five times and on each occasion examination of the colon disclosed the growth of new polyps situated chiefly in the rectum. These polyps were removed by excision or coagulation. On these occasions the histologic picture was always the same: the polyps were benign but in them were areas of hyperplasia possessing precancerous characteristics.

All through the course of the disease, the advisability of doing more radical surgery was discussed but the boy's father would not agree to the performance of an ileostomy. Finally, it was decided to do a right colectomy with anastomosis of the ileum to the rectum. Unfortunately the patient did not return to us for the operation but he had to be hospitalized on November 7, 1952, as an emergency in another hospital because of acute myelitis.

He died on January 19, 1953, and at autopsy it was discovered that he had a complete destruction of the spinal cord by a malignant tumor diagnosed as a medulloblastoma invading the medulla spinalis (Fig. 3). The brain was not examined.

Case 2. A 13-year-old girl (sister of the boy reported in case 1) was admitted on November 8, 1950, complaining of diarrhea and red blood in her stools. She had had acute otitis media as a child and her ears were still susceptible to this infection. Proctologic and roentgenologic examinations revealed the same condition as that discovered in her brother; namely, multiple polyposis of the rectum and many filling defects seen on x-ray films, which indicated that the polypoid disease involved other portions of the colon.

On December 6, 1950, she underwent a left colectomy with an end-to-end anastomosis of the transverse colon with the rectum (Fig. 4). Subsequently she returned every six months for examination of the remaining portion of her colon and rectum. On each occasion many polyps in her rectum were destroyed by coagulation and it was apparent that large polyps were growing in the right portion of her colon. On March 3, 1954, a right colectomy was done with

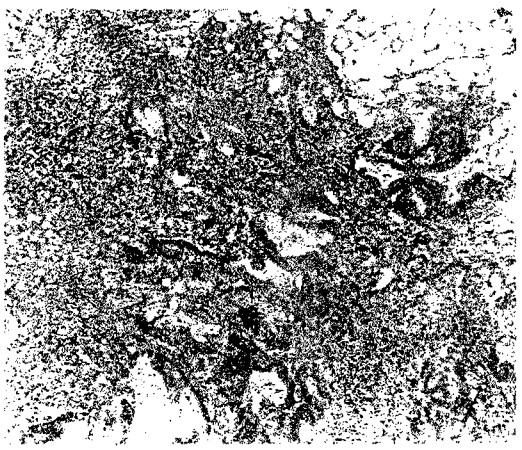

FIG. 2. Microphoto (from x180) of carcinomatous polyp. Case 1.

anastomosis of the ileum with the rectum and subsequently rectal examinations were repeated every six months.

In July of 1958, she experienced two or three episodes of headache during which she became unconscious. She was admitted to the hospital on August 10, 1958, and the clinical syndrome and examination of the ocular fundi indicated that she had a cerebral tumor. She was transferred to the neurosurgical service of L'Hopital de l'Enfant-Jésus, but she died suddenly, on August 15, 1958, before treatment could be administered. She was 21 years old. At autopsy a large tumor of the posterior zone of the left frontal lobe was discovered. The pathologist's diagnosis was glioblastoma of the left frontal lobe. The tumor was 5.5 cm. in diameter (Fig. 5). There was also a small chromophobe adenoma (3 mm. in diameter) of the hypophysis.

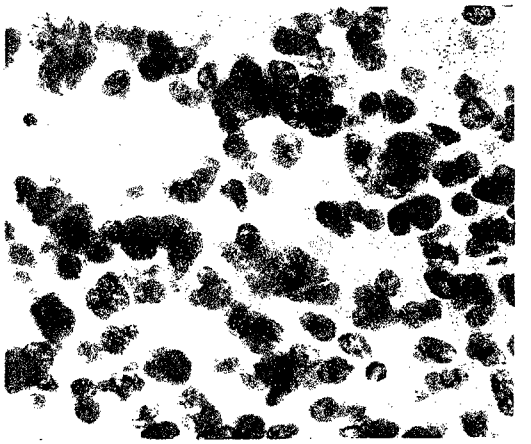

FIG. 3. Medulloblastoma: note the lymphocytoid cells with hyperchromatic nuclei. Case 1 (from x720).

Discussion

These two patients with very similar clinical patterns, beginning at puberty with polypoid disease of the colon tending to become transformed into cancer and terminating in both instances by development of malignant tumors of the central nervous system are indubitably very interesting and unusual cases.

Were they really cases of familial polyposis? The fact that the disease occurred in two children of the same family and that the polyps tended to recur after excision or coagulation convinced us that we were dealing with cases of hereditary polyposis, despite the fact that no authentic confirmation of the hereditary feature could be established.

The evolution of these cases was very different from that of the usual cases of isolated polyps of the colon.[3] They were also dissimilar to the syndrome of intestinal polyposis with pigmentation of the mucous membrane and skin of certain areas described by Peutz and Jeghers,[2] because in our cases the polyps were confined to the colon and there was no pigmentation of the mucous membranes or skin.

As discussed at the beginning of this paper, hereditary polyposis has been shown

FIG. 4. Segment of excised colon with many polyps. Case 2.

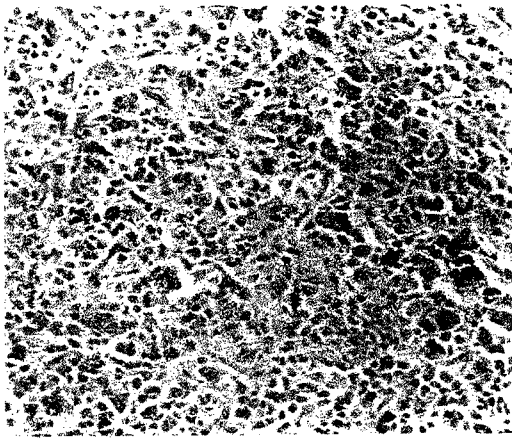

FIG. 5. Glioblastoma (from x180). Note the glial cells with atypical, multinucleated and hyperchromatic nuclei. Case 2.

in the last few years, to be associated with soft tissue tumors, chiefly of fibrous type, but to our knowledge, this is the first time that polyposis of the colon has been reported in cases in which it was associated with malignant tumors of the central nervous system. This unusual association of tumors of the nervous system with polyposis of the colon suggests an analogy with some hereditary diseases of the nervous system such as Bourneville's disease (tuberous sclerosis of the brain)[9, 14] in which there are sclerotic zones in the brain associated with lesions of the skin (adenoma sebaceum) and sometimes adenomas of the internal viscera such as the kidneys.

In conclusion, it may be said that these cases of familial polyposis associated with malignant tumors of the central nervous system are examples which support the theory that hereditary transmission of familial polyposis as a dominant characteristic can be associated with other potentialities residing in the same gene. Also, it should be emphasized that every case of familial polyposis must be followed and explored, not only by looking for new occurrences of polyps in the colon and rectum, when they are not removed, but also for the appearance of other tissue tumors elsewhere in the body.

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