Case report

Peutz-Jeghers syndrome and metastasising colonic adenocarcinoma

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Summary

A case of metastasising colonic carcinoma associated with Peutz-Jeghers syndrome in a 39 year old man is described. The caecal adenocarcinoma had metastasised widely to regional lymph nodes and was associated with several other colonic Peutz-Jeghers polyps, showing no evidence of dysplasia or malignancy. It was not possible to determine whether the carcinoma had arisen from a Peutz-Jeghers polyp. The patient also had gastric and small intestinal polyps. The serum carcinoembryonic antigen (CEA) was normal at presentation in this patient and in one other reported case. The use of this determination as a screening test for so-called high risk groups is, therefore, not supported by this report. The risk of malignancy is not known. It will only be determined by careful follow up of a defined Peutz-Jeghers syndrome population and comparison of carcinoma incidence with a matched sample of the general population. A national registry of Peutz-Jeghers syndrome patients in the United Kingdom would help to resolve this question.

First described by Peutz in 1921, and subsequently expanded by Jeghers, McKusick, and Katz in 1949, this syndrome consists of the association of gastrointestinal polyps mucocutaneous pigmentation and a familial incidence. The polyps may occur throughout the gastrointestinal tract but are most frequently found in the small intestine. Initially there were conflicting views as to the frequency with which malignant changes occurred in the intestinal polyps and this was because of the misinterpretation of the histological structure of the polyp. The irregular arrangement of normal epithelium and smooth muscle derived from the muscularis mucosae in the polyp suggested malignant invasion to earlier investigators. The polyps are now considered to be hamartomas. There are well documented case reports of malignant change in the stomach, gastroduodenal junction, duodenum, small bowel, and colon in patients with Peutz-Jeghers syndrome, which has led to the suggestion that there is an increased liability to carcinoma of the gastrointestinal tract. The familial occurrence of carcinoma in several of the reports also enhances the view of a genetic malignant trait. The exact risk is unknown, as is the incidence of Peutz-Jeghers syndrome in the general population. Moreover, two large series reviewing the risk of carcinoma in Peutz-Jeghers syndrome have reported conflicting results. This case is reported as it documents the occurrence of a metastasising carcinoma of the caecum in a patient with Peutz-Jeghers polyps of the colon.

Case history

A 39 year old white man was admitted on 21 January 1983, with a six month history of epigastric pain, weight loss of 8 kg and lassitude. He had had no previous episodes of abdominal pain. There was no family history of pigmentation, abdominal pain or rectal bleeding, although he had a 13 year old daughter with similar facial pigmentation.

On examination the patient was pale with pigmentation of the lips and about the eyes (Fig. 1). A firm, tender mass was palpable in the right side of the abdomen. Rectal examination disclosed fresh
blood on the examining finger, but no masses. Investigations showed a Hb of 8.5 g/dl, MCV 64 fl, MCH 18.8 pg, MCHC 29.4 g/dl. The ESR was 40 mm/h. The serum iron was 2.5 μmol/l. All other laboratory data, including glucose, blood urea nitrogen, uric acid, sodium, potassium, chloride, bicarbonate, calcium, phosphate, bilirubin, serum glutamic oxaloacetic transaminase, lactate dehydrogenase, alkaline phosphatase, albumin, globulins, and total serum proteins were normal. The serum carcinoembryonic antigen (CEA) on admission was normal (10 μg/l). At oesophagastroduodenoscopy carried out on 22 January 1983, one small polyp was seen in the stomach and two larger ones in the duodenum. Sigmoidoscopy showed fresh blood within the lumen but no mucosal lesions in the rectum. Barium meal and follow through examination showed one polyp in the duodenum and suggested that there were further polyps in the small bowel. Barium enema and air contrast examination (Figs. 2 and 3) showed a large polyp in the descending colon and a smaller one in the ascending colon in addition to a large carcinoma of the caecum. He was transfused 4 units of blood and underwent laparotomy on 14 February 1983. At operation 10 polyps, seven of them large, were felt in the small bowel. There was a 5×7 cm carcinoma in the caecum with small seedlings on the peritoneal surface of the ileocaecal mesentery and involved lymph nodes along the course of the superior mesenteric vessels and extending towards the hilum of the liver. Colonic polyps were also felt. Biopsies were taken of the peritoneal secondaries and of the lymph nodes in the mesentery, one close to the tumour and one high up at the origin of the superior mesenteric artery. The peritoneal polyps were a hamartoma with no evidence of dysplasia or malignancy (see Fig. 5).
A palliative right hemicolectomy was performed on 29 March 1983. He made an uneventful postoperative recovery. Histology of the right hemicolectomy specimen confirmed a poorly differentiated adenocarcinoma of the caecum. It was not possible to determine whether this had arisen from a hamartomatous polyp. Postoperatively he was started on a course of radiotherapy to the involved nodes and this was completed on 24 May 1983. After this he began adjuvant chemotherapy in the form of Adriamycin, Mitomycin C, and 5-Fluorouracil. His condition, however, gradually deteriorated and he died on 25 September 1983. No necropsy was performed.

**Discussion**

In a large review of patients with Peutz-Jeghers syndrome,\textsuperscript{11} colonic polyps occurred in 53% and rectal polyps in 32%. The question of an increased risk of colorectal carcinoma in patients with Peutz-Jeghers syndrome and colonic polyps is thus very important. Part of the debate surrounding the malignant potential of Peutz-Jeghers polyps is centred on whether the Peutz-Jeghers polyps have undergone malignant transformation, or whether the malignancy has arisen coincidentally in a pre-existing adenomatous polyp. It is generally accepted that there is an adenomatous polyp/cancer sequence in the rectum and colon, although the majority of adenomas do not become cancerous during a normal adult life span.\textsuperscript{30,31} The hamartomatous nature of the colonic polyps in Peutz-Jeghers syndrome is well established.\textsuperscript{4-6} Adenomatous colonic polyps, however, have also been described in patients with Peutz-Jeghers syndrome\textsuperscript{28,32} and these last authors also mention the existence of hamartomas in the same patients. In addition, Perzin and Bridge\textsuperscript{24} report a case of Peutz-Jeghers syndrome in which histology of a single duodenal polyp showed areas of hamartomatous and adenomatous cellular arrangement with \textit{in situ} carcinoma. It was not possible to determine whether the \textit{in situ} carcinoma had developed from the hamartomatous or adenomatous element of the polyp. Although invasive carcinoma has been shown to have arisen in Peutz-Jeghers polyps in the small bowel,\textsuperscript{8,21} there are no recorded cases where a colonic carcinoma has been unequivocally shown to have arisen from a Peutz-Jeghers colonic polyp. Areas of severe glandular dysplasia have been recently noted in a hamartomatous polyp removed from the colon of a 35 year old man with Peutz-Jeghers syndrome.\textsuperscript{33} Other hamartomatous polyps removed from the colon at the same time showed no such dysplasia. These authors suggest that Peutz-Jeghers polyps are
Peutz-Jeghers syndrome and metastasising colonic adenocarcinoma

proliferative and may be premalignant. Areas of severe dysplasia in a Peutz-Jeghers polyp removed from the rectum have also been described.

In our case it was not possible to determine whether the carcinoma had arisen from an adenomatous or hamartomatous colonic polyp. Other polyps removed from the colon and small bowel at the same time were hamartomatas with no evidence of dysplasia or malignancy. Although histological observations such as these are very important and provide good circumstantial evidence of the malignant potential of the polyps, the ultimate answer can only come from detailed prospective studies of a defined Peutz-Jeghers syndrome population and comparison of carcinoma incidence with a matched sample of the general population.

In a group of 21 patients with Peutz-Jeghers syndrome seen at the Mayo Clinic and followed up to 45 years (median follow up 33 years), there was no evidence of intestinal carcinoma arising from a hamartomatous polyp, with possibly one exception where it was impossible to tell whether the primary lesion was of colonic or ovarian origin.

In addition, there was no evidence of decreased survival when compared with a matched general population. In contrast with a large national survey of 222 patients with Peutz-Jeghers syndrome in Japan, 11 (5%) patients with carcinoma of the colon were identified in the surveyed group. The cause of death of eight patients was registered as caused by carcinoma of the colon. In six patients the diagnosis was histologically confirmed. Mortality was lower than in patients with familial polyposis coli, but higher than in the general population.

Clearly further prospective studies of this nature are needed to resolve the question of cancer risk. It is unlikely that the true incidence of the syndrome and the risk of malignancy will be established without a national registry.

This report and one other both record normal CEA values at the time of presentation when the colonic carcinoma had already metastasised. The use of this determination as a screening test for carcinoma in patients bearing colonic polyps is therefore not supported by this report. This report endorses the conclusion of the NIH consensus statement that the use of CEA to help with surveillance of so-called high risk groups in whom CEA producing tumours may develop remains to be established.

Fig. 4 Photomicrograph of mesenteric lymph node removed at laparotomy showing invasion of the node with adenocarcinoma. (H & E original magnification ×150).
Fig. 5 Photomicrograph of colonic polyp removed at colonoscopy. The polyp shows the typical features of a Peutz-Jeghers hamartomatous polyp. The glands are irregular and the stroma is composed of branching muscularis mucosae (arrowed). There is no evidence of dysplasia or malignancy (H & E original magnification ×30).

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