Case Report

A case of Turcot's Syndrome in a child with malignant transformation

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ABSTRACT

Turcot's syndrome or the glioma polyposis syndrome is a rare variant of the polyposis syndrome and it is characterized by colonic polyposis and central nervous system neoplasm typically a glioblastoma or a medulloblastoma. We present a case of Turcot's syndrome in a child with malignant transformation.

Keywords: Polyposis Coli, Turcot's Syndrome.

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Turcot's Syndrome or the Glioma Polyposis Syndrome was first described in 1959 by Jacques Turcot and his colleagues who identified colon and brain tumors in a teenage brother and sister.[1] It is considered a variant of the familial adenomatous polyposis and characterized by adenomatous colonic polyps as well as central nervous system (CNS) neoplasms. Familial colonic adenomatous polyposis is a well known hereditary precancerous disease transmitted as an autosomal dominant with 100% risk of developing adenocarcinoma.[2] Although Turcot's syndrome is considered a variant of familial adenomatous polyposis, their mode of inheritance and biological behavior seems to be different. Patients with Turcot's syndrome are almost invariably identified in their 2nd decade of life, and not uncommonly the brain tumor manifests before the bowel lesions. This is a report of 2 siblings with Turcot's syndrome and review of the relevant literature.

Case Report. The patient is a 13-year-old male who presented to our hospital with a 6-month history of bleeding per rectum. The bleeding was associated with a protrusion of a mass from the anus. There was no history of any other problems but 10 years ago he had craniotomy followed by radiotherapy for a large right sided cerebellar medulloblastoma, and from that aspect he is otherwise well. His examination revealed a thin built, pale patient. No masses could be felt apart from a large rectal polyp. His investigations showed hemoglobin of 7.9 g/dl and white blood cell count of 8.30×10^3mm, platelets of 356000/mm^3, total protein of 54g/l, albumin of 24g/l, urea of 3.3mmo1/l and creatininine of 47mmo1/l. His liver function tests were normal. His abdominal ultrasound was reported to be normal. He had a barium enema prior to his referral to our hospital that showed a large mass at the rectosigmoid region with almost total occlusion of the lumen. He underwent examination under anesthesia with the possibility of a laparotomy and total colectomy. Sigmoidoscopy revealed a large rectal polyp that was excised transrectally and sent for frozen section. This revealed a rectal polyp with severe atypia. Laparotomy was carried out through a lower midline incision. There were multiple colonic polyps with a large one in the sigmoid colon and another one in the

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transverse colon. The colon was mobilized and total colectomy and ileo-rectal anastomosis was carried out. Postoperatively, he did well and was discharged home in a good general condition. Histology of the polyps excised transanally showed one to be an adenomatous polyp with severe epithelial dysplasia and another one to be a moderately differentiated invasive adenocarcinoma. Sections of all polyps identified in the colon revealed adenomatous polyps with severe epithelial dysplasia. In 2, there was also possible invasion of the stalk although the base of stalk was clearly free of any malignant change. A 3rd polyp showed moderately differentiated mucinous adenocarcinoma of the colon that infiltrated through the bowel wall at the mesenteric edge. No vascular invasion was identified. So in the colectomy specimens 9 polyps were identified, 2 showed adenocarcinoma and 7 were adenomatous polyps with varying degrees of dysplasia and their size ranged from 2-5 cm in diameter. In total, 52 lymph nodes were identified. All were reactive but in the most distal group of lymph nodes there was however a small focus of intramesentric tumor which does not appear to be within a lymph node. Three months following his discharge he was seen in the clinic. He was well, but per rectal examination revealed a small nodule at the site of previous anastomosis. This was excised transrectally and histology showed it to be a tubulodenomatous polyp with moderate dysplasia. The whole situation was discussed with the father as well as the necessity to excise the remaining rectal mucosa. The patient as well as the father refused the idea of having a permanent ileostomy, so it was decided to excise the remaining rectal mucosa and carry out an ileo-anal anastomosis. He underwent laparotomy through the previous incision. The liver as well as the abdominal cavity was free of any masses. The site of the previous anastomosis was mobilized, the small bowel divided and the rectal stump inverted through the anal opening where excision of the mucosa was carried out and the terminal ileum was pulled through the anal opening and ileo-anal anastomosis was carried out. Postoperatively, the patient did well apart from an initial period of diarrhea, which settled with time. Now he is 8 months postoperatively and well. He passes stools 3-4 times per day and has full bowel and urinary control. His mother and father are parental cousins and he has a brother and a sister. His family pedigree is shown in Figure 1. His brother is 25 years old now and well, and both his father and mother are well. His sister died at the age of 17 years. She was diagnosed to have multiple polyposis coli at the age of 4 years because of bleeding per rectum. She had total proctocolectomy and permanent ileostomy, but one month later she developed severe headache and proved to have a brain tumor. This was biopsied and proved to be an astrocytoma grade 3. She subsequently died because of multiple abdominal metasteses at the age of 17 years.

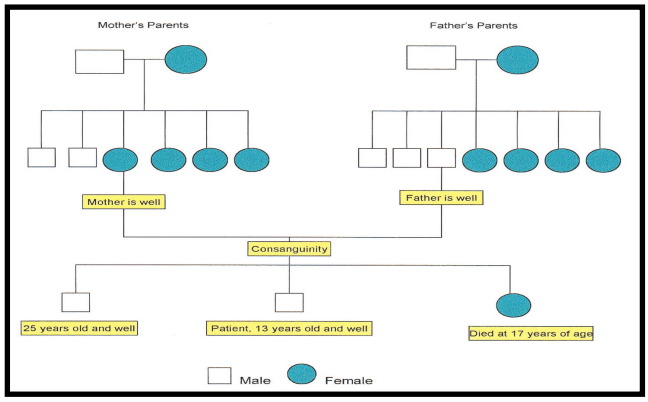

Figure 1 - Family Pedigree showing the affected patient and his sister as well as his parents who are first degree cousins.

Discussion. Familial adenomatous polyposis is classified into 3 main types: familial polyposis coli, Gardner's syndrome and Turcot's syndrome. Whereas colonic adenomatous polyposis is common to all 3 types, they differ in the extra colonic manifestations. Gardner's syndrome is characterized by multiple adenomatous colonic polyps with soft tissue and osseous tumors and it is inherited as an autosomal dominant.[3,4] Turcot's syndrome or the glioma-polyposis syndrome is a rare heritable disorder characterized by colonic polyposis and CNS neoplasm typically a glioblastoma or a medulloblastoma.[1] Lewis et al classified Turcot's syndrome into 2 main types.[5] In type 1, 2 or more siblings have multiple colonic polyps, and a malignant brain tumor, however neither the parents nor the other generations are known to have colonic polyps or CNS tumors. Our patient belongs to type 1. The parents of our patient were first degree cousins but neither of them have colonic polyps or CNS tumors. The presence of such consanguinity, as well as the absence of parental disease, have lead some authors to conclude that Turcot's syndrome is inherited as an autosomal recessive.[6] In type 2 Turcot's syndrome, consanguinity is lacking, but there are colonic polyposis in several generations. This type of Turcot's syndrome is said to be inherited as autosomal dominant. Lewis et al also described a 3rd type of Turcot's syndrome seen as isolated non-familial cases. Smith and Kern on the other hand proposed that all 3 disorders, familial polyposis coli, Gardner's syndrome and Turcot's syndrome are due to a single autosomal dominant pleiotropic gene that is responsible for multiple colonic polyposis which may occur alone or in association with other extra colonic phenotypes including the soft tissue and bony tumors of Gardner's syndrome or brain tumors of Turcot's

syndrome.[7] This possibility that all the 3 variants result from a pleiotropic gene is supported by the occurrence of gastric, duodenal and ileal adenomas as well as osteomatous change of the mandible in patients with familial polyposis coli[8] as well as the occurrence of Gardner's syndrome and Turcot's syndrome in different members of the same family.[9-14] The fact that the parents are sometimes not known to be affected is not unusual, as a negative family history is recorded in up to one 3rd of patients with familial polyposis coli which is inherited as autosomal dominant. This can be easily explained by spontaneous gene mutation and incomplete gene penetrance.[15,16] Not only this, but recent advancement of molecular biology have identified the genes responsible for familial adenomatous polyposis and its variants.[17] Adenomatous polyposis coli (APC) gene is a tumor suppressor gene associated with the familial polyposis and hMLH1 or hPMS2 are mismatch repair genes.[17] It was found that when Turcot's syndrome is caused by the APC gene, the patients develop medulloblastoma, but when it is caused by mismatch genes they develop glioblastoma.[8] This can explain the difference in the histology of brain tumors between our patient and his sister. He developed a medulloblastoma, while his sister had an astrocytoma. This was also the case in the brother and sister described by Turcot et al where the brother had a medulloblastoma, while the sister had a frontal lobe glioblastoma.[1] Although the colonic polyps of Turcot's syndrome are histologically identical to those occurring in familial polyposis coli, they seem to differ in their morphology and biologic behavior. Not only the number of colonic polyps is small; usually not exceeding 100, but the size is also different, as the polyps tend to be larger in size, which was the case in our patient. In familial polyposis coli, the colon is usually carpeted by 100's of small, sessile polyps. Add to this the fact that colonic malignant transformation occurs 10-30 years earlier than in familial polyposis coli which is attributed to the extreme deoxribonucleic acid (DNA) instability in patients with Turcot's syndrome.[18] Another interesting feature of patients with Turcot's syndrome is that whereas patients with malignant brain tumors rarely survive for long, surprisingly and for unknown reasons patients with Turcot's syndrome tend to survive long after excision of their brain tumors. Our patient so far survived more than 10 years and his sister survived 13 years following the discovery of their brain tumors. This was also the case in the patients reported by Lewis et al.[5] Contrary to our patient, the CNS malignancy develops more frequently after colonic resection for polyposis. Our patient and his sister, as well as those reported by others, had already undergone malignant transformation at the time of colectomy. In order to obviate this danger of malignant transformation in the colonic polyps, which is known to occur early in patients with Turcot's syndrome, the diagnosis should be suspected in any child with gastrointestinal symptoms and a family history of Turcot's syndrome or in children with gastrointestinal symptoms following excision of a brain tumor namely a glioblastoma or a medulloblastoma. With the discovery of the APC gene, it is now possible to diagnose asymptomatic gene carriers and because of the long term risk of malignant transformation offer them elective preventive surgery. Surgery for polyposis coli is indicated for acute therapy, for bleeding and obstruction as well as to obviate the risk of neoplastic transformation. A variety of surgical techniques have been adopted. These include total colectoproctectomy and permanent ileostomy or more commonly a sphincter preserving bowel reconstruction in the form of ileorectal anastomosis or ileo-anal anastomosis with or without an ileal pouch. Our patient was managed initially with ileo rectal anastomosis, but subsequently and because of dysplasia in the remaining rectal mucosa, it was decided to carry out rectal mucosectomy and straight ileo-anal anastomosis, which he tolerated well.

References

1. Turcot J, Despres JP, St Pierre FM. Malignant tumors of the central nervous system associated with familial polyposis of the colon: report of two cases. Dis Colon Rectum 1959; 2: 465-468.
2. Bussey HJR, Veale AMO, Morson BC. Genetics of gastrointestinal polyposis. Gastroenterology 1978; 74: 1325-1330.
3. Gardner EJ. Follow-up study of a family group exhibiting dominant inheritance for a syndrome including intestinal polyps, osteomas, fibromas and epidermal cysts. Am J Hum Genet 1962; 14: 336-390.
4. Watne AL, Core SK, Carrier JM. Gardener's syndrome. Surg Gynecol Obstet 1975; 141: 53-56.
5. Lewis JH, Ginsberg AL, Toomey KE. Turcot's syndrome. Evidence for autosomal dominant inheritance. Cancer 1983; 51: 524-528.
6. Baughman FA, List CF, Williams JR, Muldoon JP, Segarra JM, Volkel JS. The glioma-polyposis syndrome. N Engl J Med 1969; 281: 1345-1346.
7. 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: 264-271.
8. Babs S. Molecular biological background of FAP and HNPCC and treatment strategies of both diseases depend upon genetic information. Journal of Japan Surgical Society 1998; 99: 336-344.
9. Hamilton SR, Bussey HJR, Mendelsohn G, Diamond MP, Pavlides G, Hutcheon D et al. lleal adenomas after colectomy in nine patients with adenomatous polyposis coli/ Gardner's syndrome. Gastroenterology 1979; 77: 1252-1257.
10. Wennstrom J, Pierce ER, Mcknsick VA. Hereditary benign and malignant lesions of the large bowels. Cancer 1974; 34 (Suppl): 850-857.

11. Utsunomiya J, Kakamura T. The occult osteomatous changes in the mandible in patients with familial polyposis coli. Br J Surg 1975; 62: 45-51.
12. Utsanomiya J, Maki T, Iwama T, Matsunagu Y, Ichikawa T. Gastric lesions of familial polyposis coli. Cancer 1974; 34: 754.
13. Yaffee HS. Gastric polyposis and soft tissue tumours: A variant of Gardner's Syndrome. Arch Dermatol 1961; 89: 806-808.
14. Yao T , Ida M, Ohasta K, Watanabe H, Omae T. Duodenal lesions in familial ployposis of the colon. Gasterenterology 1977; 73: 1086-1092.
15. DeCosse JJ, Adams MB, Condon RE. Familial polyposis. Cancer 1977; 39: 267-273.
16. Pierce ER. Some genetic aspects of polyposis of the colon in a kindred of 1,422 members. Dis Colon Rectum 1986; 11: 321-329.
17. Hamilton S, Parsons RE, Papadopoulos N, Powell SM, Kursh AJ, Berk T et al. The molecular basis of Turcot's syndrome. N Engl J Med 1995; 332: 839-847.
18. Miyaki M, Nishio J, Konishi M, Kikuchi-Yanoshita R, Tanaka K, Muraoka M. Drastic genetic instability of tumors and normal tissues in Turcot's syndrome. Oncogene 1997; 15: 2877-2881.