Turcot syndrome
K K Jain MD  ( Dr. Jain is a consultant in neurology and has no relevant financial relationships to disclose. )
Rimas V Lukas MD, editor. ( Dr. Lukas of Northwestern University Feinberg School of Medicine received honorariums from AstraZeneca as an advisory board member and AbbVie as a guest speaker and advisory board member.)
Originally released September 28, 1999; last updated August 7, 2018; expires August 7, 2021

Introduction

This article includes discussion of Turcot syndrome, brain tumor polyposis syndrome, glioma-polyposis syndrome, familial adenomatous polyposis coli, and hereditary nonpolyposis colorectal cancer. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

Overview

Turcot syndrome is a genetic disorder clinically comprised of an association of primary neuroepithelial tumors of the central nervous system with familial adenomatous polyposis coli (APC) or hereditary nonpolyposis colorectal cancer. This article describes the pathogenesis and diagnosis of this syndrome. The management of patients with Turcot syndrome takes into consideration both the CNS lesions and colorectal lesions. Early detection of brain tumors in patients with familial adenomatous polyposis coli might improve outcome. Therefore, surveillance for brain tumors is considered worthwhile in these patients.

Key points

- Turcot syndrome is an association of primary neuroepithelial tumors of the central nervous system with familial adenomatous polyposis coli or hereditary nonpolyposis colorectal cancer.
- Turcot syndrome is a genetic disorder associated with mutations of 2 germline genes in each individual.
- An important differential diagnosis is metastatic brain tumor in cases with colorectal carcinoma.
- Early detection of brain tumors in patients with familial adenomatous polyposis coli might improve outcome.
- Prognosis in advanced cases is poor, and death is usually due to malignant brain tumor, but some patients die due to colorectal malignancy.
- An understanding (and classification) of the disease at the genetic level is likely to lead to the most impactful advances in its management.

Historical note and terminology

Turcot syndrome has been described as the association of primary malignant tumors of the CNS with adenomatous polyposis coli. The first case of polyposis coli associated with a medulloblastoma, as well as thyroid carcinoma, was described in a case report in 1949 (Crail 1949). In 1959, Turcot described 2 teenaged siblings with multiple adenomatous polypli of the colon that developed into adenocarcinoma and malignant CNS tumors, medulloblastoma involving the spinal cord in 1 sibling and glioblastoma multiforme in the other (Turcot et al 1959). The gene for adenomatous polyposis coli was mapped and cloned in 1991 (Groden et al 1991; Nishisho et al 1991). Familial adenomatous polyposis coli, Turcot syndrome, Gardner syndrome, and a few other syndromes were later considered to be associated with mutations in adenomatous polyposis coli gene. Another type of germline genetic defect, the mutation of a mismatch repair gene usually found in hereditary nonpolyposis colorectal cancer, also known as Lynch syndrome, was demonstrated in 1995 in the family originally described by Turcot (Hamilton et al 1995). Controversy persists regarding the mode of inheritance and whether Turcot syndrome constitutes a distinct genetic disorder. One common feature of these syndromes is association with inheritance of germline mutations in the DNA mismatch repair genes. It is now proposed that inheritance of 2 mismatch repair mutations in an individual along with the unique tumor spectrum should be defined separately from Lynch syndrome I and II, or the subtypes Turcot and Muir-Torre and termed Lynch III, to identify individuals with constitutively compromised mismatch repair associated with biallelic mutations (Felton et al 2007). Turcot syndrome overlaps with "constitutional mismatch repair deficiency (CMMRD) syndrome", a genetic disorder that results from biallelic germline mutations in 1 of the 4 MMR genes -- MLH1, MSH2,
**MSH6** or **PMS2** – and manifests in childhood with a broad spectrum of cancer including mainly hematological, brain, and intestinal tract tumors. It includes cases of Lynch syndrome, and it is likely that the original 2 cases described by Turcot in 1959 were the first cases of CMMRD and many cases described subsequently as Turcot syndrome should retrospectively be considered CMMRD patients (Wimmer et al 2014).

At least 180 cases resembling Turcot syndrome have been reported in the literature to date. In some cases, the histological confirmation of the lesions is not available. Some of the case reports also include reviews of previously reported cases (Schröder et al 1983; Jarvis et al 1988; Jamjoom et al 1989; Zink et al 1992; Cervoni et al 1995; Hamada et al 1998; Tomaras et al 1998). Several classification systems have been proposed. Lewis proposed 3 groups (Lewis et al 1983):

1. Cases in which siblings are affected and there is family history of brain tumors
2. Cases in which 2 or more generations in a family presented with polyposis of the colon
3. Isolated nonfamilial cases

A classification of glioma-polyposis syndrome based on a review of 127 cases is as follows (Itoh et al 1993):

1. Cases of Turcot syndrome that had characteristic colonic and brain manifestations
2. Cases of familial adenomatous polyposis coli associated with glioma
3. Suspicious cases of glioma polyposis
4. Cases other than glioma-polyposis syndrome.

A simple classification based on molecular evidence and genetic background divides Turcot into 2 entities (Sunahara and Nakagawara 2000):

1. True Turcot syndrome (autosomal recessive). Intestinal polyps are large, fewer in number than 100, and are apt to undergo a malignant change. Associated brain tumor is usually a glioblastoma or an astrocytoma. Mismatch repair genes might be involved.
2. Familial adenomatous polyposis-associated type (autosomal dominant). There is a predisposition to development of medulloblastoma.

**Definition.** The earlier cases of Turcot syndrome included only brain tumors of neuroepithelial origin, but some authors have reported other tumors as well. One of the original cases of Turcot had a 3 mm chromophobe adenoma of the pituitary in addition to the glioblastoma multiforme. Several other tumors of organs besides the colon and brain have been reported in some cases of Turcot syndrome. It is difficult to define the exact components of this syndrome. The synonym "glioma-polyposis complex," sometimes used to describe the syndrome, does not adequately describe it because it restricts the brain tumor to glioma and the colon lesions to polyposis. Because neuroepithelial tumors other than gliomas and nonpolyposis colorectal cancer are recognized as components of Turcot syndrome, the following definition of Turcot syndrome would be more appropriate: Turcot syndrome is an association of primary neuroepithelial tumors of the central nervous system with familial adenomatous polyposis coli or hereditary nonpolyposis colorectal cancer. It is generally agreed that CNS tumors of nonneuroepithelial origin such as meningiomas, pituitary tumors, craniopharyngioma, and CNS lymphoma should not be included as components of Turcot syndrome.

**Clinical manifestations**

**Presentation and course**

Most Turcot syndrome patients are younger than 30 years of age at the time of presentation. Rarely, the syndrome may present in old age. For example, a woman presented for the first time at 67 years of age with clinical manifestations of a glioblastoma; she was found to have multiple colonic polyps with adenocarcinomatous changes (Castillo and Wilson 2002). In another patient diagnosed with glioblastoma at 60 years of age, there was a history of hereditary nonpolyposis colon carcinoma (Grips et al 2002).

The usual presenting symptoms are those of a primary CNS tumor, often a brain tumor and rarely a spinal tumor. The primary brain tumor is usually a glioblastoma, an astrocytoma of higher grade, or a medulloblastoma. Ependymomas have also been described in patients with Turcot syndrome (Torres et al 1997; Mullins et al 1998). The majority of cases with tumors of astrocytic lineage (astrocytomas, glioblastoma) were described prior to the inclusion of IDH mutational status in the formal classification of these tumors. The neurologic signs and symptoms depend on the location of the tumor. There is usually a family history of familial adenomatous polyposis coli or colorectal carcinoma.

Some of these patients have a history of familial adenomatous polyposis coli. In some cases, the diagnosis of familial
adenomatous polyposis coli was established after that of the CNS neoplasm, or the adenocarcinoma of the colon developed years after the primary brain tumor. Medulloblastoma usually presents at a younger age than colonic polyps. It is very rare for a patient with Turcot syndrome to develop more than 1 type of CNS neoplasm (McLaughlin et al 1998).

Polyposis of the colon may be asymptomatic in the earlier stages. A large polyp can cause obstruction of the colonic lumen requiring emergency surgery (Shibata et al 1999). Carcinomatous changes usually lead to rectal bleeding.

Skin manifestations of patients with Turcot syndrome may include cafe-au-lait (as also seen with neurofibromatosis type 1) and other pigmented spots, sebaceous cysts, and basal cell carcinomas (Itoh et al 1993). Multiple cutaneous lesions are present in more than 30% of patients with Turcot syndrome.

Ophthalmological findings in Turcot syndrome include diplopia due to cranial nerve palsies resulting from a brainstem glioma and oval pigmented ocular fundus lesions (Ninclaus et al 2017).

Prognosis and complications

The prognosis of Turcot syndrome is generally poor. More than two-thirds of the patients die within 5 years of the manifestation of the disease’s first symptoms, but survival may be exceptionally long in some cases. Rarely, the diagnosis of Turcot syndrome is made at autopsy (Sarin and Bernath 2008).

The cause of death is usually the malignant brain tumor, but some patients die due to colorectal malignancy. Long survival is exceptional and most often occurs in cases with delayed development of the cerebral tumor. Survival to 22 years after development of astrocytoma was reported in 1 case (Cervoni et al 1995). The underlying germline genetic alteration may favorably influence the prognosis of glioblastoma (Hamilton et al 1995). One case of glioblastoma and Turcot syndrome survived for 14 years at the time of reporting and was under treatment for adenocarcinoma of colon (Rutz et al 1991). One explanation of long survival in patients with glioblastoma is misinterpretation of original histological slides, as some of these patients have turned out to have oligodendrogliomas (Taylor et al 1999). An additional explanation may rest on the IDH mutational status of the gliomas, which is an important prognostic factor that was first described in gliomas in 2009 but has not been included in the majority of reports on Turcot syndrome.

Clinical vignette

A 42-year-old man presented with headache and raised intracranial pressure with suspicion of a brain tumor. MRI revealed a glioblastoma of the right frontal lobe. The patient also had a family history of colon cancer but no gastrointestinal symptoms. After surgical treatment of glioblastoma followed by chemotherapy and radiotherapy, he underwent colonoscopy. Two adenomatous polyps were discovered and could be excised completely. Histological examination showed low grade dysplasia and no further treatment was considered necessary. Genetic testing of tumors revealed mutations of MMR genes MLH1 and PMS2, leading to the diagnosis of Turcot syndrome type 1. Repeat colonoscopy at 6 months showed no evidence of recurrence. However, the glioblastoma recurred after 1 year and the patient died a few months later despite treatment. No recurrence of cancer of colon was seen on autopsy.

Biological basis

Etiology and pathogenesis

Turcot syndrome is now considered to be a genetic disorder associated with 2 different types of germline genetic defects:

1. Mutation of the mismatch repair genes (MMR): MLH1, MSH2, MSH6, or PMS2, with chromosomal locus on 3p22.2, 2p21, 2p16.3, and 7p 22.1, respectively (Wimmer and Etzler 2008). hMLH1 and hPMS2 are usually found in hereditary nonpolyposis colorectal cancer associated with glioblastoma.

2. Mutations of the adenomatous polyposis coli (APC) gene are located on the chromosome 5q21. The discovery that adenomatous polyposis coli gene may have tumor suppressor activity indicates that predisposing germline mutation may be causally linked to neuroepithelial and colonic tumors (Lasser et al 1994). Medulloblastomas are more commonly linked to adenomatous polyposis coli mutations.

A classification of Turcot syndrome into 2 types on a genetic basis has been proposed (Paraf et al 1997).

Type I consists of patients with glioma and hereditary nonpolyposis colorectal cancer and their siblings with glioma and
colorectal adenomas. The tumors of these patients show germline alterations in DNA mismatch repair genes. Affected patients were younger than 20 years of age. The first case of type I Turcot syndrome was reported from Colombia in a 20-year-old male with a clinical presentation of both glioblastoma and multiple adenomatous colonic polyps who had a mutation in Kras Asp12 gene and altered expression of HMLH2 and HMLH6 genes in 2 of the colonic polyps (Dora et al 2012). This patient was still alive after 7 months of treatment at the time of reporting.

Type II consists of patients with a CNS tumor that occurs in a familial adenomatous polyposis kindred (familial adenomatous polyposis coli cases). These patients carry germline mutations in the adenomatous polyposis coli gene (APC).

A homozygous mutation in MSH6 in a family with Turcot syndrome is consistent with an autosomal recessive mode of inheritance (Hegde et al 2005). Two families with Turcot syndrome have been reported to have 2 germline mutations in each, 1 in the MLH1 gene and 1 in MSH2 (Lebrun et al 2007).

Multiple tumors may be seen in patients with Turcot syndrome, and a case has been reported with medulloblastoma, low-grade fibromyxoid sarcoma (following cranial radiation), pilomatrixomas, colonic adenomas, and abdominal desmoid tumor (following colectomy) (Fritch et al 2014). It is possible that immunosuppression associated with the treatment of 1 malignancy in some cases may have helped precipitate the development of other tumors. Although inherited APC mutations may be associated with ependymoma development in certain Turcot syndrome type II cases, mutation analysis of adenomatous polyposis coli and beta-catenin genes in sporadic ependymomas indicates that somatic mutations affecting these genes do not play a major role in the pathogenesis of sporadic ependymomas (Onilude et al 2006).

In patients with germline mutations of the adenomatous polyposis coli, inactivation of the second copy of the gene appears to be a factor in the development of the brain tumor (Hamilton et al 1995). Mutations of another tumor suppressor gene, p53, which is ubiquitous in various cancers, have also been reported in some patients with Turcot syndrome but did not involve the germline of these patients. This suggests that p53 may play a role in the progression, but not the initiation, of the disease (Kikuichi et al 1993). In 1 case, an adenomatous polyposis coli germline mutation and a somatic p53 mutation were identified in the colorectal carcinoma that developed a few years after the excision of an astrocytoma (Barel et al 1998). The p53 mutations observed in 2 different sites and stages of the disease indicate a multistep progression of the malignant events. Following the loss of mismatch repair function, p53 inactivation and chromosomal instability are not necessary for development of colorectal carcinoma but appear to be required for genesis of glioblastoma (Leung et al 2000). In another case of Type I Turcot syndrome, molecular genetic analysis detected microsatellite instability and p53 mutation only in the grade III astrocytoma tissue removed from the right frontal lobe, indicating a failure of the deoxyribonucleic acid mismatch repair system (Okamoto et al 2004).

A suggested explanation of the low penetrance and rarity of Turcot syndrome is that a carrier of a constitutive alteration in a caretaker gene will need at least 1 or 2 more hits (1 for an oncogene and 2 for a tumor suppressor gene) independently in each tissue to start the oncogenic process (Van Meir 1998). The penetrance of the adenomatous polyposis coli gene mutation in the colon epithelium is different from that in the brain because the colonic phenotype is present in about 100% of familial adenomatous polyposis coli patients by the age of 40, but few develop medulloblastoma.

In 1 reported case, normal colon mucosa, normal skin fibroblasts, and normal brain tissue showed high frequencies of severe replication error in contrast to usual hereditary nonpolyposis colorectal cancer patients in which rough endoplasmic reticulum was rare in normal tissues (Miyakai et al 1997). This suggests that extreme DNA instability in normal tissues causes the early development of multiple cancers in Turcot syndrome. Germline mutations of DNA mismatch repair genes associated with instability at the microsatellite region have been associated with the progression of Turcot colorectal tumors (Miyakai et al 2001). In 1 study of 3 patients with Turcot syndrome, each with colorectal adenocarcinoma and malignant glioma, all colorectal tumors showed a frameshift in the coding sequence of transforming growth factor beta type II receptor gene, but no such change was seen in any of the brain tumors (Chan et al 1999). Mutations in insulin-like growth factor type II receptor were found in only 1 glioma. These findings suggest that mutation may target different pathogenic pathways in the oncogenic process in the 2 organs.

Clinicopathological and genetic features of 3 patients with Turcot syndrome type 1, all of whom had glioblastoma, have been reviewed (Lusis et al 2010). The study concluded that the giant cell variant of glioblastoma is overrepresented in Turcot syndrome, although gliosarcomas may also be encountered, and these patients usually
have long survival despite histological anaplasia (Lusis et al 2010).

**Epidemiology**

Turcot syndrome is a rare condition, but the occurrence of brain tumors in patients with familial adenomatous polyposis coli is more than an association by chance. Familial adenomatous polyposis coli constitutes about 1% of all cases of colorectal cancer. The Cleveland Clinic Familial Polyposis Registry found 13 patients with gliomas in 168 kindreds. This is a higher incidence than the expected rate of 8.2/100,000 in the general population (Kropilak et al 1989). True incidence of Turcot syndrome may be masked by early death of patients with medulloblastoma, which also prevents these young patients from passing on the genetic abnormality to a subsequent generation. Some published cases of brain tumor associated with colorectal carcinoma and PMS2 mutation are not indexed as Turcot syndrome.

The relative risk of brain tumor in patients with hereditary nonpolyposis colorectal cancer and their first-degree relatives was 6 times greater than in the general population (Vasen et al 1996). In a study based on the national Danish Hereditary Nonpolyposis Colorectal Cancer Register, brain tumors occurred in 14% of the families with significantly higher risks for individuals with MSH2 gene mutations and constitutional mismatch repair defects (Therkildsen et al 2015).

Most reported cases in the literature are from North America, Europe, and Japan (Edouard et al 2002). Further cases have been reported from Latin America and China.

**Prevention**

At present, no known method exists that will prevent the development of a brain tumor in patients with familial adenomatous polyposis coli. Prophylactic colectomy is usually carried out in patients with familial adenomatous polyposis coli to prevent the development of colon cancer. Presymptomatic diagnosis of hereditary nonpolyposis colorectal cancer is not yet possible as some additional responsible genes remain to be discovered. Prophylactic colectomy may not seem appropriate in a patient who has already been diagnosed with a malignant brain tumor.

Because the germline gene defects responsible for Turcot syndrome are known, germline gene therapy remains a theoretical possibility to prevent this syndrome in the offspring of families affected by this disease. It is also questionable that development of tumors in these patients can be prevented with a high degree of certainty by correction of genetic defects alone, as additional unknown factors may be involved in oncogenesis.

**Differential diagnosis**

The following are important among the conditions to be considered in the differential diagnosis of patients with multiple tumors, including those involving the gastrointestinal system and the brain. The important differentiating point would be the genetic basis.

An important differential diagnosis would be metastatic brain tumor in cases with colorectal carcinoma.

Another condition to be considered is the association of polyposis coli with multiple neoplasms, including gliomas, in the presence of an immune deficiency such as immunoglobulin A deficiency. A case of Turcot syndrome with gastrointestinal stromal tumor, the most common mesenchymal neoplasm gastrointestinal tract, has been reported (Bulus et al 2015). A patient with Turcot syndrome and a novel APC gene mutation presented with multiple tumors, including a low-grade fibromyxoid sarcoma, indicating the importance of a broad differential diagnosis (Fritch Lilla et al 2014).

Li-Fraumeni syndrome is a rare autosomal dominant disease that presents with multiple neoplasms including brain tumors and colon tumors (Scott et al 1993). This cancer predisposition syndrome is associated with germ line p53 gene mutations in most families.

Turcot syndrome overlaps with, but should be differentiated from, the tumor spectrum of a childhood cancer syndrome due to biallelic PMS2 mutations, which encompasses atypical brain cancers, hematologic malignancies, and colonic polyposis (Tan et al 2008). Early recognition of this familial cancer syndrome should prompt investigation for familial hereditary nonpolyposis colorectal cancer mutations.
Gardner syndrome usually presents with benign osteomas of the skull and facial bones, subcutaneous lesions such as epidermoid cysts, desmoid tumors, and dental abnormalities in a patient with familial adenomatous polyposis coli. Gardner syndrome should be differentiated from Turcot syndrome, familial adenomatous polyposis, and other attenuated forms of familial polyposis. Apart from characteristic polyps in the colon and osteomas, Gardner syndrome also exhibits abnormalities in the retinal epithelium that differentiate it from others (Juhn and Khachemoune 2010). There is 1 case report of Gardner syndrome, with a history of familial adenomatous polyposis, presenting as an isolated, giant cerebellopontine angle craniopharyngioma (Link et al 2002). There is no known genetic link between familial adenomatous polyposis and craniopharyngioma. The authors considered the possibility that this case was Turcot syndrome but, according to the criteria outlined in this article, it would not qualify for this diagnosis. Extracolonic carcinomas can also be a part of Gardner syndrome. This syndrome is genetically similar to Turcot syndrome because it is also due to a mutation of the adenomatous polyposis coli gene. Both Turcot and Gardner syndromes can occur simultaneously in a patient (Koot et al 1996).

Patients with Lynch syndrome also have an increased risk for colorectal cancer associated with cancer of other organs such as brain cancer. Carriers of MLH1 and MSH2 gene mutations have a 1% to 4% risk of brain tumors compared to the less than 1% in the general population (Kohlmann and Gruber 2018). Apart from mismatch repair mutations, genetic testing may reveal MYH-associated polyposis syndrome as an autosomal recessive, polyposis syndrome caused by biallelic mutations in the MYH gene (Goodenberger and Lindor 2011).

A patient who presented with sebaceous carcinoma, colon cancer, and a malignant astrocytoma was found to have Turcot syndrome with overlapping Muir-Torre syndrome, which is characterized by sebaceous neoplasms, keratoacanthomas, and internal malignancies due to a defect in DNA mismatch repair (Kleinerman et al 2012). Basis for this overlap is that patients have mutations in both the MLH1 and MSH2 genes in Muir-Torre syndrome, whereas patients with Turcot syndrome type I carry mutations in the MLH1, MSH2 and the PMS2 genes. Another patient with a history of being treated for colon adenocarcinoma and skin lesions leading to a diagnosis of Muir-Torre syndrome later developed a glioblastoma requiring surgical resection and pathology showed mutations in MSH2 and MSH6 mismatch repair genes (Grandhi et al 2013). One patient with Muir-Torre syndrome and colorectal cancer who showed loss of expression of proteins MSH2 and MSH6 had a son who died of glioblastoma; because of the paternal phenotype of Muir-Torre syndrome, it is likely that the son suffered from Turcot syndrome (Velter et al 2017). This case raises the issue if patients with Muir-Torre syndrome and their family members should be routinely screened for brain tumors.

**Diagnostic workup**

The diagnostic workup of a patient with a suspected CNS tumor is like that of primary brain and spinal cord tumors. Those with a family history of adenomatous polyposis coli should undergo screening and surveillance colonoscopy. Patients with Turcot syndrome should undergo genetic testing, and tissue removed at surgery should be genotyped. In some cases, reverse transcription polymerase chain reaction is revealing novel germline mutations that have not been reported previously. Polymerase chain reaction sequencing is a reliable method for screening the adenomatous polyposis coli gene for germline mutations. This method was used to test members of 6 Greek families with familial adenomatous polyposis, and 1 patient was found to have a medulloblastoma (Mihalatos et al 2003). This would be considered a case of Turcot syndrome, but this report was not coded as such.

Gene mutations are absent in 20% to 30% of patients with familial polyposis, as shown in the case of a 30-year-old woman with a positive family history of Turcot syndrome (Sahnane et al 2016). She was negative for APC and MUTYH, but fluorescent in situ hybridization analysis demonstrated that 5q22 breakpoint disrupted the APC gene. This case shows that where standard molecular tests are negative, cytogenetic testing is helpful in determining that the subject is a carrier of Turcot syndrome.

Although a clinical diagnosis of familial adenomatous polyposis can be made by colonoscopy, genetic testing is necessary because of the overlapping phenotypes of Mut Y homolog-associated polyposis with Lynch syndrome, Gardner syndrome, and Turcot syndrome (Hegde et al 2014). The American College of Medical Genetics and Genomics provides guidelines for clinical laboratories in validating testing for inherited colorectal cancers.

Microsatellite instability due to mismatch repair gene mutations in tumor DNA can be type A or type B; the former is characterized by smaller, more subtle allelic shifts compared to the latter. Knowledge of the association between Turcot syndrome-related glial tumors and subtle type A microsatellite instability is important for full assessment of these patients and appropriate counseling (Giunti et al 2009).
Management

The management of patients with Turcot syndrome takes into consideration both the CNS lesions and colorectal lesions. Patients who present with a brain or spinal cord tumor are treated for these in the usual manner.

Management of brain tumors. Early detection of brain tumors in patients with familial adenomatous polyposis coli might improve outcome. Therefore, surveillance for brain tumors is considered worthwhile in these patients. Decision for surgery, if required, is made on neurosurgical consultation. Referral to a clinical cancer genetics program should also be considered. For more information, see the articles on medulloblastoma and malignant glioma.

Management of colorectal lesions. Additional considerations are the detection and management of colorectal lesions. This involves treatment of affected individuals, counseling of patients and their families, screening of at-risk individuals, and surveillance of affected patients for extracolonic cancers. Treatment of adenomatous polyposis is primarily colectomy during the second or third decade. It is known that a familial adenomatous polyposis coli patient whose adenomatous polyposis coli gene mutation locates at codon 1309 develops cancer 10 years earlier in comparison to the rest of the cases. Consequently, risky rectal mucosa should be removed in this group of patients.

Prevention. Finding better preventive agents, improving screening for extracolonic cancers, and applying new radiological and endoscopic technology to the diagnosis and management of extracolonic features will be the major challenges for the management of Turcot syndrome in the future. A boy with Turcot-like syndrome and a constitutional homozygous mutation of the mismatch repair gene PMS2 went into remission from his glioblastoma for 7 years after multimodal treatment followed by retinoic acid chemoprevention (Gottschling et al 2008).

References cited


Onilude OE, Lusher ME, Lindsey JC, Pearson AD, Ellison DW, Clifford SC. APC and CTNNB1 mutations are rare in sporadic ependymomas. Cancer Genet Cytogenet 2006;168(2):158-61. PMID 16843107


Shibata C, Sasaki I, Naito H, et al. Turcot syndrome with colonic obstruction and small intestinal invagination: report of


Wimmer K, Etzler J. Constitutional mismatch repair-deficiency syndrome: have we so far seen only the tip of an iceberg. Human Genetics 2008;124(2):105-22. PMID 18709565


**References especially recommended by the author or editor for general reading.**

**ICD and OMIM codes**

**ICD codes**

ICD-9:
- Adenomatous polyposis coli: 211.3
- Medulloblastoma: 191.6

ICD-10:
- Adenomatosis of colon: D12.6
- Malignant neoplasm of cerebellum: C71.6

ICD-O:
- Anaplastic astrocytoma: M9401/3

**OMIM numbers**
Adenomatous polyposis coli: \#175100
Mismatch repair gene MLH1: *120436
Mismatch repair gene PMS2: *600259
Turcot syndrome: \#276300

Profile

Age range of presentation

0-01 month
01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years
65+ years

Sex preponderance

male=female

Family history

family history typical
family history may be obtained

Heredity

heredity may be a factor

Population groups selectively affected

none selectively affected

Occupation groups selectively affected

none selectively affected

Differential diagnosis list

metastatic brain tumor
polyposis coli with multiple neoplasms
IgA deficiency
Li-Fraumeni syndrome
Gardner syndrome
Muir-Torre syndrome

Associated disorders

Cronkhite-Canada syndrome
Gardner syndrome
Lynch syndrome
Mismatch repair cancer syndrome
Peutz-Jeghers syndrome and mucous membranes

Other topics to consider

Gene therapy of glioblastoma multiforme
Low-grade astrocytoma in adults
Low-grade gliomas
Malignant astrocytomas
Medulloblastoma
Molecular diagnosis of brain tumors
Neurogastroenterology