Colorectal Adenocarcinoma in a Patient with Tuberous Sclerosis [Case Report]

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Abstract

Tuberous sclerosis (TS) is a neurocutaneous disorder that presents with the classic triad of seizures, mental retardation, and facial angiofibromas. In most cases there is a constellation of manifestations, including tumors in the brain, heart, kidneys, lungs, skin, and eyes. Two-thirds of the cases result from an autosomal dominant inheritance. The TSC1 and TSC2 genes encode for the hamartin and tuberin proteins, respectively. TSC1 and TSC2 are tumor suppressor genes.

We present the case of a 63 year-old white female with a history of nephrolithiasis, melanoma and a two-year history of worsening hematochezia. She has no family history of inflammatory bowel disease, colorectal cancer, polyps, or other gastrointestinal pathology. Medication included only omeprazole. She denied any alcohol, tobacco or illicit drug use.

Case Report

A 63 year-old white female presented with a history of nephrolithiasis, melanoma and a two-year history of worsening hematochezia. She has no family history of inflammatory bowel disease, colorectal cancer, polyps, or other gastrointestinal pathology. Medication included only omeprazole. She denied any alcohol, tobacco or illicit drug use.

Physical exam revealed a moderately obese white female. Blood pressure was 168/106, pulse 96, respiration 18, temperature 98.2°F. Abdominal exam revealed nonreactive bowel sounds, soft and nontender to palpation with no discernible fullness, mass, or organomegaly. Rectal exam was positive for occult blood. Laboratory studies revealed white blood cell counts of 7.88, hemoglobin 14.8, hematocrit 44.9, and platelets 288. Electrolytes, BUN, creatinine, albumin, bilirubin, ALP, AST, ALT, TSH, PT, PTT, alpha-fetoprotein, and LDH were normal.

CT of the abdomen and pelvis showed findings consistent with angiolipoma of the right kidney (Figure 3), and a 4 cm liver mass. MRI of the brain showed radial white matter bands along the migratory pathways of the neurons and glial cells (Figure 2). CT head showed left frontal bone uncertain for benign complicated cyst or venous lake. A colonoscopy, a 5 mm polyp in the ascending colon, a 25mm polyp in the rectosigmoid junction, and a rectal polyp were seen. Biopsy of the 25mm polyp revealed a low-grade adenocarcinoma. A biopsy of a rectal mass showed tubulovillous adenoma.

During this admission, the patient was clinically diagnosed (Figure 4) with TS based on one major criteria: renal angiomyolipoma, and several minor criteria: bone cysts, cerebral white-matter “migration” lines (Fig 1), and a hamartoma. At adenocarcinoma, a 5.5 mm polyp in the ascending colon, a 25mm polyp in the rectosigmoid junction, and a rectal polyp were found. Biopsy of the rectosigmoid polyp revealed a low-grade adenocarcinoma arising from a tubulovillous adenoma. Twenty-six lymph nodes were negative for metastatic disease. A biopsy of the rectal mass revealed a tubulovillous adenoma.

Although gastrointestinal malignancies are rare in patients with TS, there are some previous reports suggesting an association. TS is well associated with rectal hamartomas, but the association with colon adenocarcinoma has not been established. Our report of a patient with TS diagnosed with rectosigmoid adenocarcinoma and rectal adenoma adds to previous reports suggesting an association between TS and gastrointestinal tumor; however, knowing whether they are associated with the TSC gene abnormality or are merely coincidental will need further investigation.

Discussion

TSC1 and TSC2 genes play a role in the phosphoinositide 3-kinase pathway, which can lead to a wide range of malignancies if unregulated; therefore, mutation of the TSC genes may contribute to sporadic cancers such as astrocytoma and renal cell carcinoma. The patient in this case report raises a possible association between TS and gastrointestinal adenocarcinoma and adenoma.

Although gastrointestinal malignancies are rare in patients with TS, there are a few studies that suggest an association. In 1992, Mouis, et al reported the first case of invasive colorectal adenocarcinoma in a 24-year-old patient with well-documented TS. In 2000, Digno, et al described a 17-year-old TS patient with invasive rectal adenocarcinoma. In 2009, Ahemd, et al presented the first reported case of gastric adenocarcinoma in a TS patient. In 1999, Verheef, et al presented a 12-year-old TS patient with a malignant pancreatic tumor that metastasized to lymph nodes. In 1991, Byard, et al described a 16-year-old patient with two different tumors: basal adenoma in the salivary gland and a leiomyoma in the colon. In 1950, Budenz described a 38-year-old TS patient that underwent total colectomy for his polyps, which showed early malignant changes on histological exam. In 1988, Devroede et al found polyps in nine of twelve TS patients; five of those patients had hamartomas, three had adenoma, and one had villiganglioma carcinoma in situ.

Conclusion

TS is well known to be associated with rectal hamartomas, but the association with adenocarcinoma has not been established. In conclusion, we report the case of a TS patient who was diagnosed with rectosigmoidal adenocarcinoma and rectal adenoma. Our report adds to previous reports documenting an association between TS and gastrointestinal tumor; however, knowing whether they are associated with the TSC gene abnormality or are merely coincidental will need further investigation.

Major features

1. Facial angiofibromas or frenulated pterygium
2. Neurocutaneous stigmata or periorbital Rosai-Dorfman
3. Hypomelanotic patches (three or more)
4. Laryngeal rhabdoid tumor (speech and language delay)
5. Angiofibromatous hairy naevi
6. Cerebral tubers
7. Subependymal nodules
8. Subependymal giant cell astrocytoma
9. Cortical tubers, one or more
10. Renal angiomyolipoma

Minor features

1. Multiple, randomly distributed pink-to-red lesions
2. Hypomelanotic patches
3. Multiple, segmental cutaneous hypopigmentation
4. Cerebral white matter radial migration lines (≤3 of 5)
5. Neurofibromas
6. Renal angiomyolipomas
7. Subependymal nodules
8. Cortical tubers

Possible tuberous sclerosis complex

Either one major feature or one minor feature in addition

Probable tuberous sclerosis complex

Either two major features or two minor features

Figure 1. Brain MRI of a TS patient showing white matter migration tracts (StatDx.com)

Figure 2. MRI of the brain showed radial white matter bands along the migratory pathways of the neurons and glial cells associated with Tuberous Sclerosis.

Figure 3. Abdominal and Pelvic CT showed renal angioliopma (Right Kidney).

Figure 4. Diagnostic Criteria of Tuberous Sclerosis

- When both lymphangiomyomatosis and renal angiomyolipomas are present, other features of tuberous sclerosis should be present before a definite diagnosis is assigned.
- Histologic confirmation is suggested.
- Radiographic confirmation is sufficient.
- One panel member (M.R.G.) felt strongly that these or more radial migration lines should constitute a major sign.

References


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