Introduction:
Bannayan-Riley-Ruvalcaba syndrome (BRRS) is a rare autosomal dominant congenital disorder, characterized by macrocephaly, hemangiomata, lipomas, hamartomas, and pigmented macule in genitalia. Several dozen cases have been reported in the medical literature, but no case has been reported in Bangladesh. We report a case of BRRS in a 11-year-old male child with recurrent rectal bleeding with hamartomatous colonic polyposis & multiple subcutaneous lipomas on the anterior abdominal wall. In addition, patient had macrocephaly, intellectual impairment. Bleeding polyps were removed by colonoscopic polypectomy.

Case report:
Dihan 11-year-old boy 1st issue of nonconsanguineous parents admitted with the complaints of rectal bleeding for 3 months. Bleeding was intermittent, small in amount, painless, bright red drops of blood after defecation. He had a history of polypectomy. Seven days after polypectomy bleeding restarted with the same character. Patient had no history of fever, abdominal pain, joint pain, constipation, rash, abnormal bleeding tendency, visual disturbances. He had no family history of such type of illness. He was delivered by LUCS with birth weight of 5 kg. He had a history of delayed milestone of development. General physical examination revealed mild pallor, normal oral cavity. There was no jaundice, cyanosis, edema, thyromegaly, lymphadenopathy, clubbing, or scoliosis. Vitals within normal limit. Skin survey normal. Anthropometric examination revealed macrocephaly with head circumference of 59 cm (>97 percentile), height 139 cm (on 25th centile), weight 26 kg (between 5th & 3rd centile). Multiple subcutaneous masses were present on the left lower abdomen measuring about 11 cm × 9 cm, soft in consistency.

Colonoscopy revealed polyp in transverse colon (Figure 3) & histopathology showed cystically dilated glands with chronic inflammation, features were consistent with hamartomatous polyp (Figure 4). Patient also had intellectual impairment on WISK-R assessment. There is cryptorchidism on genitalia examination.
On the basis of clinical features of macrocephaly, lipomas, intellectual impairment, cryptorchidism and intestinal hamartomatous polyp; a diagnosis of Bannayan-Riley-Ruvalcaba Syndrome (BRRS) was made. PTEN gene mutation analysis could not be done.

**Discussion:**
Bannayan-Riley-Ruvalcaba syndrome (BRRS) is a rare hamartomatous polyposis syndrome. This syndrome was originally described separately by Riley and Smith, Bannayan and Zonana, and Ruvalcaba, Myher, and Smith. In 1990, Cohen used term BRRS to unify these as a single entity. DiLiberti proposed a new nomenclature of multiple syndromes that are caused by mutations in the PTEN gene. He proposed that it be called the PTEN MATCHS syndrome; MATCHS was derived from macrocephaly, autosomal dominant, thyroid disease, cancer, hamartomata, and skin abnormalities. Marsh et al. (1999) suggested that the spectrum of disorders maybe known as PTEN hamartoma tumor syndrome (PHTS).

It occurs both in an autosomal dominant and in a sporadic manner. It occurs through mutations in the phosphatase and the tensin homolog gene (PTEN) located on chromosome 10q23. Germline mutations of (PTEN) gene are found in approximately 60% of BRRs. This is a tumour suppressor gene that plays an important role in the pathway of cell proliferation, migration and apoptosis. PTEN mutations are responsible for PTEN hamartoma tumor syndromes (PHTS), a group of diseases including, Cowden syndrome (CS), BRRS, PTEN-related Proteus syndrome, Proteus-like syndrome. PHTS are significant because of their predisposition to cancer.

BRRS is characterized by macrocephaly, lipomas, hemangiomas, hamartomatous intestinal polyps and pigmented macules in the genital region. It is a rare disorder, several dozen case reports have been reported in medical literature. The symptoms can either be present at birth or shows up during early childhood. Symptoms generally vary from one patient to another. Males are affected more often than females. Majority of infants have increased birth.
weight and length and about half of affected infants
have macrocephaly without enlargement of
ventricles. Growth usually slows during childhood,
so affected adults are of normal height and body size.
There may be a delay. In developmental milestones
and low intelligence quotient. In our male
patient born with increased birth weight, also have
macrocephaly, low IQ & h/o of developmental delay.
Other reported abnormalities include ocular
abnormalities like strabismus, and deviation of one
eye away from mother (exotropia), widely spaced eyes,
visual impairment (amblyopia), abnormal elevation of
optic disc which appears edematous (pseudopapilledema).
Patients may have seizures & thyroid problem.
Skin abnormalities include presence of freckle-like pigmented
macules on the penis in males or vulva in females. Our patients may have coffee-
colored spots on the skin (café-au-lait spots) or
telangiectasias. In some cases, patients may present
with musculoskeletal abnormalities like hypotonia,
myopathy, hyperextensibility of joints, pectus
excavatum, scoliosis and high arched palate.
The penile macules may present as small pigmentary
changes that can be missed during a cursory
examination of the penis. It is more likely to occur in
later childhood, and its absence in infants and
toddlers should not exclude consideration of the
diagnosis of BRRS. Gontijo et al. 2013 reported BRRS
with deformng lipomatous hamartomas in infant.
Intestinal hamartomatous polyposis occurs in 35-45% of
BRRS cases. The polyps may be located along
the entire gastrointestinal tract, more frequently in the
colon and rectum. During infancy, they may present
with diarrhea, abdominal pain, painless rectal
bleeding, anemia, intussusception and
intestinal obstruction. Our patient present with
painless per rectal bleeding & during colonoscopy
polyp present in colon.
Marsh et al defined the clinical diagnosis of BRRS
as the presence of three out of four feature:
macrocephaly, lipomatosis, hemangiomas and
speckled pigmented maculae on the penis. Parisi
et al defined the syndrome as the presence of two of
the three feature: macrocephaly, hamartomas
(including at least one lipoma, hemangioma or
intestinal polyp) and maculae on the penis. In our
case BRRS was diagnosed with the observation
of two entities.

Patients with BRRS and Cowden have an increased
risk for benign and malignant tumor formation. So, individuals with BRRS and a germline
PTEN pathogenic variant should undergo the same
surveillance as individuals with Cowden syndrome.

Acknowledgements:
Dr. Bishnu Pada Dey, Medical Officer, Dept. of
Pathology, BSMMU, Dhaka who provide the histopathological report of the patient.

References:
1. Lynch NE, Lynch SA, McMenamin J, Webb D.
Bannayan-Riley-Ruvalcaba syndrome: a cause
of extrememacrocephaly and neuro-
developmental delay. Arch Dis Child. 2009;
94:553-4.
2. Blumenthal GM, Dennis PA. PTEN hamartoma
16:1289-300
3. Marsh DJ, Kum JB, Lunetta KL, Bennett MJ,
Gorlin RJ, Ahmed SF, et al. Mutation spectrum
and genotype phenotype analysis in Cowdens
disease and Bannyan-Zonana syndrome, two
hamartoma syndromes with germline PTEN
4. Bannayan G A. Lipomatosis, angiomatosis, and
macrencephalia. A previously undescribed
congenital syndrome. ArchPathol. 1971; 92:1-5
5. Orloff MS, Eng C. Genetic and phenotypic
heterogeneity in the PTEN hamartoma tumour
6. Latiff ZA, Atmawidiaja WR, Raje Lope JR, et
al. Bannayan Riley Ruvalcaba syndrome. Ann
7. Cohen M M. Mental deficiency, alterations in
performance and CNS abnormalities in
2003; 117 49-56
BA. Bannyan-Relay-Ruvalcaba syndrome. Am
9. Palencia R, Ardura J. Bannyan syndrome with
intracranial arteriovenous malformations. An
10. Dvir M, Beer S, Aladjem M. Heredofamilial
syndrome of mesodermal hemartomas,
macrocephaly and pseudopapilledema


