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Picture of the Month

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A 2-YEAR-OLD CHILD had a 4-month history of rectal bleeding with the passage of stool. His mother also had noted an asymptomatic, enlarging mass on his anterior abdominal wall for the same period of time. His medical history was notable for the transrectal removal of an intestinal polyp when the child was 15 months old. A large head size had been noted since birth. His development was delayed with motor and cognitive skills performance at 14 to 16 months at age 24 months.

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Prominent physical findings included macrocephaly, with a head circumference of 56 cm (6 SD higher than the mean for age), occipital prominence, and 3 firm, subcutaneous, bony projections from the skull. Examination of the skin revealed a 3-cm café au lait patch on the left leg, multiple pigmented macules on the penis (**Figure 1**), and a verrucous plaque, 5×3 cm, on the posterior thigh above the popliteal fossa. A 2.5×2.5-cm soft, nontender mass was palpable in the anterior abdominal wall tissues (**Figure 2**). The joints demonstrated hyperextensibility. Examination of the child's mother revealed no physical abnormalities. The father was reportedly healthy. Findings from a biopsy of the soft tissue abdominal wall mass were interpreted as a lipoma.

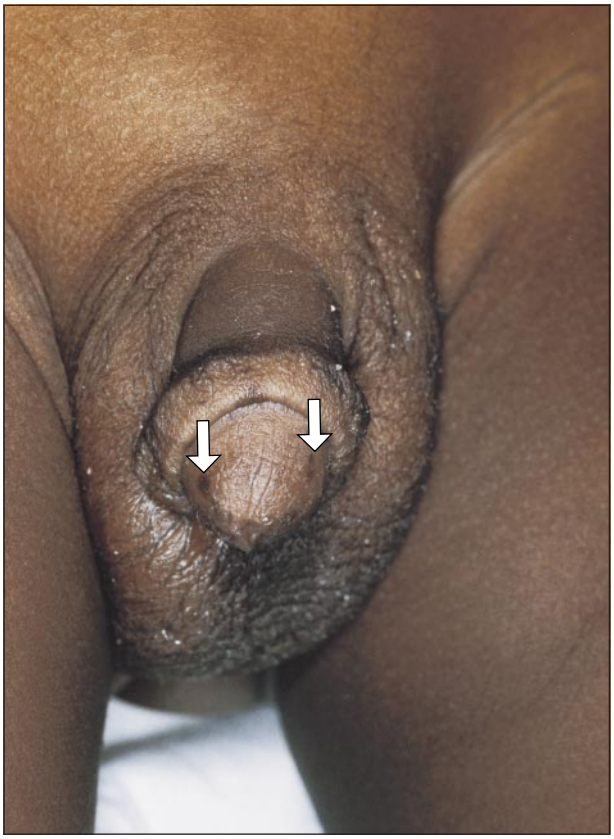

Figure 1.

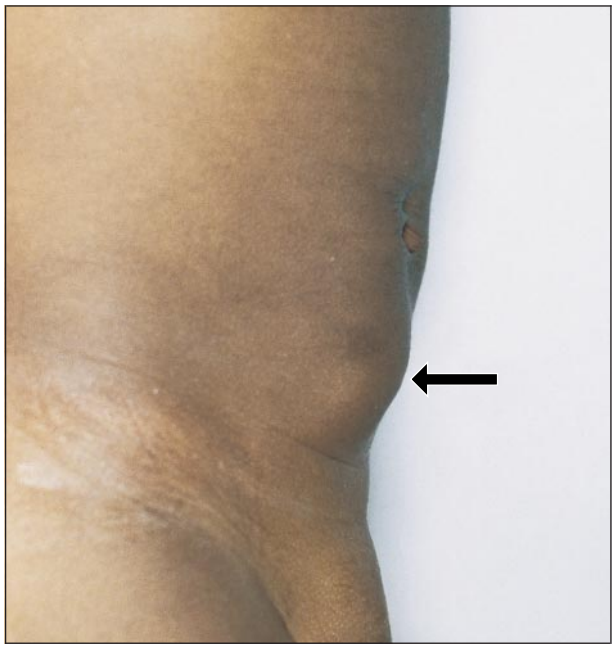

Figure 2.

Denouement and Discussion

Bannayan-Ruvalcaba-Riley Syndrome

Figure 1. *The skin of the penis is freckled.*

Figure 2. *A subcutaneous lipoma is present in the lower abdominal wall.*

The Bannayan-Ruvalcaba-Riley (BRR) syndrome had been thought to be 3 separate disorders until the overlapping findings were considered to represent one syndrome.[1] Bannayan[2] described a child with congenital macrocephaly and multiple lipomatosis and angiomatosis involving the skin and visceral tissues in 1971. Riley and Smith[3] reported a syndrome consisting of macrocephaly, multiple cutaneous hemangiomata, and pseudopapilledema, with an apparent autosomal dominant pattern of inheritance, in 1960. Ruvalcaba et al[4] noted the association of macrocephaly, intestinal polyposis, and pigmented penile lesions in 1980.

CLINICAL FEATURES

Macrocephaly is a prominent feature of BRR syndrome. The head circumference is at least 2.5 SD higher than the mean for age, and the brain has normal ventricular size. Down-slanting palpebral fissures and ocular hypertelorism may be present as well as pseudopapilledema and prominent corneal nerves.

Cutaneous abnormalities include lipomas and hemangiomas, as well as mixed vascular-lymphatic-adipose tumors. Although these tumors are most commonly discrete, intracranial, visceral, and osseous lesions have been described, which sometimes are infiltrative.[5] Pigmented macules, resembling freckles, on the skin of the shaft and glans penis are present in most males with this syndrome. Café au lait spots, acanthosis nigricans-like lesions, and wart-like lesions of the face have also been described. Almost 50% of patients with BRR syndrome develop hamartomatous polyps of the intestine, usually limited to the distal ileum and colon.[1] The polyps may be associated with rectal bleeding or intussusception.

Although infants with BRR syndrome appear large at birth, the head circumference appears to account for apparent increase in total body mass and length.[6] Approximately one half of the patients described have had mild to severe mental deficiency and/or speech delay, and 25% have had seizures.[1] Hypotonia is common and is associated with a lipid storage myopathic process of the proximal muscles in approximately 60% of patients.[1] Common skeletal system abnormalities include joint hyperextensibility, scoliosis, and pectus excavatum. Autoimmune thyroiditis seems to be part of the clinical spectrum of the disorder.[1]

MOLECULAR BIOLOGY

The inheritance of BRR is in an autosomal dominant pattern. Germline mutations in the PTEN (phosphatase and tensin homolog deleted on chromosome 10) locus mapped to chromosome 10q23.3 have been reported in patients with this syndrome.[6] It is interesting that the same germline mutation has been described in patients with Cowden disease, a disorder that shares some features of BRR syndrome.[6] The BRR syndrome and Cowden disease may represent variable manifestations of mutations of the same gene.[7] A proposal has been made to encompass these disorders under the acronym PTEN-MATCHS (macrocephaly and myopathy, thyroid disease, cancer, hamartomata, and skin abnormalities).[6]

TREATMENT AND PROGNOSIS

The treatment of patients with BRR is usually symptomatic. Gastrointestinal polyps may require removal, and surveillance of the gastrointestinal tract should be considered. There is a predisposition to cancer of the breast, prostate, and thyroid in Cowden disease. A similar predisposition for the development of malignant tumors in BRR syndrome during adulthood is possible, suggesting that affected children should have regular medical follow-up.

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Submissions

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