

## Case Report

# Granulomatous vulvitis and Guillain-Barre syndrome in pediatric Crohn's disease: a case report

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## ABSTRACT

Granulomatous vulvitis/cheilitis may occur rarely as an extraintestinal manifestation of Crohn's disease (CD) and may precede the development of gastrointestinal symptoms. Guillain-Barre syndrome (GBS) is associated with a wide variety of illnesses including inflammatory bowel disease. Though the immunologic abnormalities in inflammatory bowel disease may encompass both granulomatous inflammation as well as autoimmune components, the combination of CD, GBS and granulomatous vulvitis/cheilitis in the same patient has not been described in literature. We hereby reported a 14 year old girl with granulomatous vulvitis/cheilitis for 4 years preceding the development of gastrointestinal manifestations of CD, who also had GBS during the course of hospitalization.

**Keywords:** Crohn's, Inflammatory bowel disease, Granulomatous vulvitis, Guillain Barre syndrome

## INTRODUCTION

Pediatric Inflammatory bowel disease (IBD) is a complex disease presenting in children and young adolescents with a significant impact on growth velocity, puberty and quality of life including psychosocial concerns. Though there remains a paucity of Indian data on pediatric IBD, there has been a gradual influx of information on the two broad phenotypes of ulcerative colitis (UC) and CD in recent times.<sup>1</sup> CD most commonly presents with gastrointestinal (GI) symptoms with pointers towards diagnosis being abdominal pain, chronic diarrhea, weight loss and anorexia. We hereby reported a case of CD presenting with chronic granulomatous vulval edema and growth failure apart from GI manifestations, with GBS during the course of treatment.

## CASE REPORT

A 14 year old girl was brought with complaints of swelling of left labia minora and vulva associated with

itching for over 4 years, having been labelled as chronic granulomatous inflammation of vulva at 10 years of age via excision biopsy. The swelling gradually progressed to involve bilateral labia causing pressure effects in form of ulceration of the adjacent skin folds and thighs (Figure 1).

On presentation to us, she also complained of loose stools with an intermittent per rectal mucoid discharge (2 months prior to presentation). On arrival her vitals were stable but her examination otherwise revealed her to be cachexic with dry scaly skin, periorbital puffiness, multiple oral ulcers, angular stomatitis and cheilitis. On local examination of genitalia gross vulval edema involving labia majora and minora with perianal tags was noted. Her lab parameters are as mentioned in the Table 1.

A possibility of CD was suspected considering the isolated chronic granulomatous vulvitis with persistent GI symptoms and oral ulcers and signs of chronic malnutrition. Upper GI endoscopy showed erythematous

mucosa in stomach with normal esophagus and duodenum suggestive of gastritis, while colonoscopy showed serpiginous ulcers with skip areas throughout

large intestines (ceacum, colon, rectum) with ulcers (Figure 2) and large opening in anal canal with loss of anal sphincter tone.



**Figure 1: Chronic vulval edema due to granulomatous vulvitis.**



**Figure 2: Colonoscopy showing serpiginous ulcers with skip areas.**

**Table 1: Investigations.**

Investigations	Reports
<b>USG abdomen+pelvis</b>	Circumferential symmetrical long segment wall thickening from distal part of transverse colon to the rectum, suggestive of inflammatory etiology.
<b>MRI pelvis</b>	Mild inflammatory tissue in the posterior perineum posterior to the anal canal and anal verge in the midline in the lower inter-gluteal cleft; no obvious localized collection and fistulous tract is visualized; no obvious macroscopic fistulous communication between the anorectum, vagina and urinary bladder; long segment circumferential wall thickening in the rectum, sigmoid colon and visualized descending colon; possibility of inflammatory bowel disease; uterus is small for the age.
<b>CT abdomen plain</b>	Diffuse sigmoid and rectal wall thickening with fat stranding is consistent with IBS; bilateral medullary nephro-calcinosis; diffuse fatty infiltration of liver.
<b>Left labial mass HPE</b>	Chronic granulomatous inflammation of labia, no definite features of Koch or malignancy.
<b>Small specimen HPE</b>	Chronic granulomatous colitis with active ulcerative lesions suggestive of CD.
<b>Stool examination</b>	Normal
<b>Fecal calprotectin</b>	>1800 mcg/g
<b>Haemogram</b>	Hb-7.0 gm%, TLC-20400/cumm, neutrophils-81%, lymphocytes-7%, platelet count-17.40 lakh/cumm
<b>LFT</b>	Serum bilirubin (direct)-0.10 mg/dl; serum bilirubin-0.10 mg/dl (indirect); serum bilirubin (total)-0.20 mg/dl; SGOT-10 IU/l; SGPT-11 IU/l; serum proteins (total)-4.29 g/dl; serum albumin-1.80 g/dl; serum proteins (globulin)-2.49 g/dl; AG ratio-0.72; serum alkaline phosphatase-232 IU/l.
<b>CRP quantitative</b>	57 mg/l.
<b>ESR</b>	86 mm.
<b>Free T3/T4/TSH</b>	T3-2.72 pg /ml T4-0.90 ng/dl TSH-1.22 micro IU/MI

Long segment circumferential wall thickening in the rectum, sigmoid colon and visualized descending colon suggested possibility of IBS. Histopathological examination of colonic biopsy showed features

suggestive of chronic granulomatous colitis with ulcerative lesions suggestive of CD. MRI pelvis showed mild inflammatory tissue in perineum posterior to the anal canal and anal verge in the midline in lower

intergluteal cleft. Fecal calprotectin was more than 1800 mcg/g. She was started on immune-modulation with oral prednisolone and azathioprine for 2 weeks and later shifted to mesalamine (5-aminosalicylic acid). Nutritional needs were addressed with specified feeding as well as calcium and multivitamin supplements. On day 15 of hospital stay, she developed new onset weakness of bilateral lower limbs associated with absent reflexes on examination. Nerve conduction studies showed findings suggestive of GBS for which she was given intravenous immunoglobulin therapy to which she responded well and her power gradually improved. Purge rate gradually decreased, oral ulcers subsided and she started gaining weight. She was discharged on oral mesalamine, metronidazole and tapering dose of steroids.

## DISCUSSION

The causes of chronic vulval edema include infectious (granulomatous and non-granulomatous), inflammatory, angioneurotic and malignant etiologies. Granulomatous causes like *Mycobacteria*, sarcoidosis, CD usually causes a painless swelling.<sup>2</sup> Granulomatous vulvitis may be associated with granulomatous cheilitis as well, though infrequently. Cutaneous Crohn's disease (CCD) is commonly known to present with skin colored, red, and violaceous papules, nodules and plaques containing noncaseating granulomas in the skin mostly in the anogenital region.<sup>3</sup> There may be a few years of delay between appearance of cutaneous manifestations like, granulomatous vulvitis/cheilitis and GI manifestations of CD.<sup>4</sup> However subclinical gastrointestinal involvement is known to occur with this association. Hence it is imperative to perform gastrointestinal workup for CD in any child who presents with the combination of granulomatous vulvitis/cheilitis even if there are no overt symptoms.

Granuloma formation is one of the microscopic hallmarks of CD. Chronic granulomatous disease causing inflammation of the bowel mimics CD pathologically.<sup>5</sup> Granulomatous vulvitis may be considered as an extraintestinal manifestation of CD, as part of the spectrum of a granulomatous inflammatory disorder. Though it is not proven that autoimmunity is directly involved in the pathogenesis, circulating auto-antibodies have been demonstrated in patients with IBD as well as increased risk of autoimmune diseases are found. Increased disease severity has been associated with an increased risk of autoimmune disease development.<sup>5</sup> GBS has been linked to remarkable variety of disorders including UC. A handful of case reports exist in association with CD as well.<sup>6,7</sup> The pathogenesis of injury to the peripheral nervous system in inflammatory bowel disease has yet to be established, although it could possibly be related to immune mechanisms.<sup>8</sup> As part of a common immunologic basis, intestinal inflammation and breakdown as in CD might permit antigen presentation normally hidden from the immune system, predisposing to an immune response which in association with

molecular mimicry may lead to an autoimmune disease.<sup>6</sup> Peripheral neuropathy in IBD has also been attributed to iatrogenic-related disorders associated with the drugs used in treating these conditions and also to the micronutrient deficiencies secondary to malabsorption-related disorders.<sup>8</sup>

Thus, the spectrum of immunologic abnormalities in CD may encompass granulomatous inflammatory disorders like vulvitis, cheilitis as well as associations of autoimmune disorders like GBS, though a combination of all three manifestations in the same patient has not been reported before. Immune-mediated conditions have been known to co-occur in families, with individuals having one such condition having been shown to be at increased risk of developing additional disorders.<sup>9</sup> Studies have identified frequently recurring susceptibility loci in several immune-mediated diseases, suggesting that the etiologies of many of these conditions share a common genetic framework encompassing pleiotropic susceptibility genes.<sup>10</sup> Interestingly, anti-inflammatory therapy, as with long term use of aminosalicylates have shown a reduced risk of autoimmune disease development in adults with inflammatory bowel disease.<sup>11</sup>

## CONCLUSION

Awareness about precursor lesions like granulomatous vulvitis will lead to prompt evaluation for Crohn's disease. Also, children with IBD are at risk of developing other autoimmune conditions such as GBS due to mechanisms not well understood. Considering these factors, a keen follow-up of these patients and involvement of an experienced interdisciplinary team in the management of these complex multisystem disorders are paramount in improving their outcomes.

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