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Case report

Concurrent Hydrocephalus and Ulcerative Colitis: Exploring the Role of IL18: A Case Report

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ABSTRACT

The coexistence of fetal hydrocephalus (HC) and ulcerative colitis (UC) within a single patient is exceptionally rare. This paper presents the case of a 4-year-old girl initially diagnosed with congenital hydrocephalus via in-utero ultrasonography at 20 weeks of gestation. Subsequent ventriculoperitoneal (VP) shunt placement was performed, and 3 years later, the patient was histologically and serologically diagnosed with ulcerative colitis. The synchronization of these distinct medical events in the same individual, particularly the interval between the treatments, represents an unprecedented occurrence not previously documented. The report details the patient's recent presentation of recurrent bloody diarrhea and failure to thrive, which was effectively managed with oral prednisolone and sulfasalazine. Notably, the simultaneous manifestation of these conditions prompts consideration of potential contributing factors, including genetic markers such as interleukin 18 (IL 18), which have been linked to both disorders in existing literature. This case underscores the need for further research to elucidate the genetic and pathological markers, as well as predictors, which may underlie the concurrent occurrence of hydrocephalus and ulcerative colitis. Understanding these complexities could offer valuable insights into the intricate interplay of genetic and environmental factors in the development of such unique medical co-morbidities.

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INTRODUCTION

Congenital hydrocephalus (HC) arises from an imbalance in cerebrospinal fluid (CSF) dynamics, resulting in increased CSF volume, influenced by ventricle and subarachnoid space dimensions [1]. Common causes of infant hydrocephaly encompass congenital malformations, intraventricular hemorrhages, neoplasms, infections, and age-specific factors [2]. At present, diagnosing fetal hydrocephalus involves intrauterine ultrasound, genetic testing, or postnatal assessment based on clinical signs, utilizing sonography, computed tomography (CT) scan, and/or magnetic resonance imaging (MRI). CT and MRI become crucial for evaluating disease progression and management efficacy, as prenatal ultrasound cannot gauge intracranial pressure [1, 2, 3]. While hydrocephalus as a standalone condition is common, its co-occurrence

with ulcerative colitis is exceptionally rare, warranting specialized attention due to the potential shared pathophysiology between the two conditions.

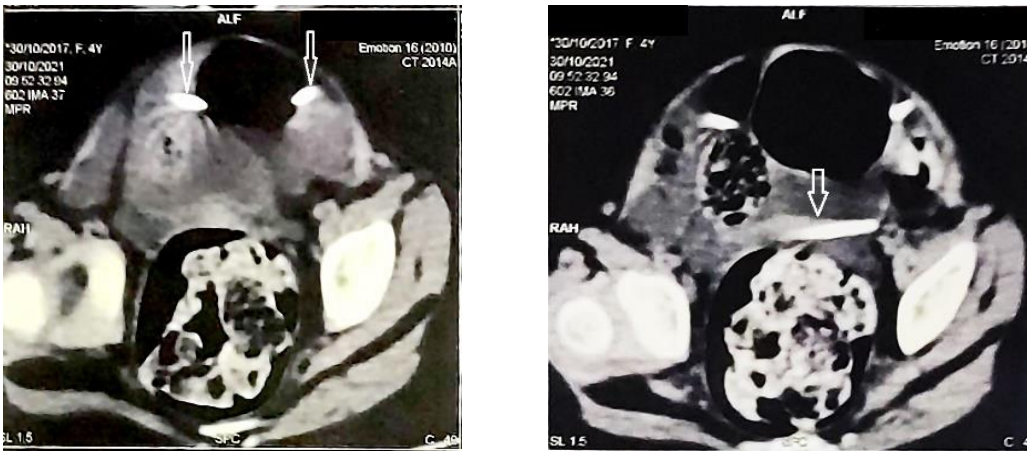
Inflammatory bowel disease (IBD) encompasses Crohn's disease and ulcerative colitis, constituting a recurrent inflammatory autoimmune disorder affecting the gastrointestinal mucosa [4]. The incidence of pediatric ulcerative colitis is estimated at 2 to 11 per 100,000 children per year, with a median age of diagnosis at 10 years [5, 6]. The disease etiology is considered multifactorial, involving immunity, probiotics, and genetic and environmental influences [6]. Bloody diarrhea, the initial symptom in our case, is commonly associated with various causes, including infectious enteritis, anal fissures, and IBD [7]. Thorough initial evaluation, beyond colonoscopy, is essential, particularly when hypoalbuminemia and anemia coexist, serving as predictors of subsequent changes in diagnosis [8, 9]. Pediatric UC poses challenges to growth, nutritional status, and psychosocial development, necessitating therapies for remission induction and maintenance, cancer prevention, and improved quality of life [10].

Interleukin 18 (IL-18), previously identified as an interferon-gamma-inducing factor (IGIF), is related to the IL-1 family. Its function is related to IL-12, as it induces the production of T helper 1 (Th1) cytokines and participates in cell-mediated immune cytotoxicity [11]. Our report emphasizes the pressing need for further research, particularly exploring the potential role of interleukin 18, a cytokine previously implicated in both hydrocephalus and UC.

We present a unique case involving a 4-year-old girl with an uncommon coexistence of hydrocephalus and ulcerative colitis. This case stands out, as there has been only one prior report documenting the simultaneous occurrence of these conditions, and that was in a 21-year-old male. This case highlights the importance of vigilant monitoring for the emergence of UC in patients with a history of HC.

Case report

The patient had been diagnosed with a case of fetal hydrocephalus at 20 weeks of the pregnancy using ultrasonography, she was born at 37 weeks gestation with average birth parameters including weight and height at Tripoli University Hospital after a C-section because of the infant condition. A computer tomography (CT) scan revealed that there was dilatation of lateral, third, and fourth ventricles with rounding of frontal horns. Ventriculoperitoneal (VP) shunt placement was performed one month after her delivery and replaced two years later. CT image of the patient is shown in Figure 1.



(**a**) (**b**)

Figure 1. CT scans (a & b) of the abdominopelvic demonstrates the VP shunt catheter (open arrows) in place with pelvic effusion blade in sight.

After three years, the patient presented with a complaint of bloody diarrhea as many as seven bowel movements a day, and loose slimy stools mixed with blood and mucus; otherwise, she reported no other complaints for one month that deteriorated her condition. She had no food allergies. The patient presented with a three-day history of vomiting, mild to moderate dehydration, decreased oral intake, and persistent symptoms of a congested throat. No family history of hydrocephalus nor IBD was found among family members. Upon admission, the patient was conscious, and afebrile, with signs of mild to moderate dehydration, including sunken eyes and dry lips. Her vitals at the time of presentation showed a blood pressure of 100/60 mmHg, pulse rate of 120/min, and oxygen saturation (PO2) of 97%. Laboratory tests were performed in an outpatient setting: CBC (complete blood count) showed white blood cell count (WBC) of 20 x

10^9/L, hemoglobin (HB) of 8.6 g/dL, platelet count (PLT) of 787 x 10^9/L. Other laboratory results were: CRP (C-reactive protein) of 5 mg/dL, ESR (erythrocyte sedimentation rate) of 33 mm/h, and Ferritin of 3 ng/ml. Stool analysis revealed significant bacterial flora, elevated RBC count (10-15), and numerous pus cells. The case has been referred to a gastroenterologist at Tripoli University Hospital for further evaluation. On the day of arrival, the specialist recommended an endoscopy to be done for her. During this admission, a colonoscopy and intestinal biopsy were performed which revealed that the patient had a friable and granular mucosa, multiple pseudo-polyps and the lumen was narrow. There were inflamed and edematous colonic mucosa with multiple bleeding ulcers and bloody exudate beginning at the rectum and extending proximally to the hepatic flexure. The colonoscopy image of the child is shown in figure 2.

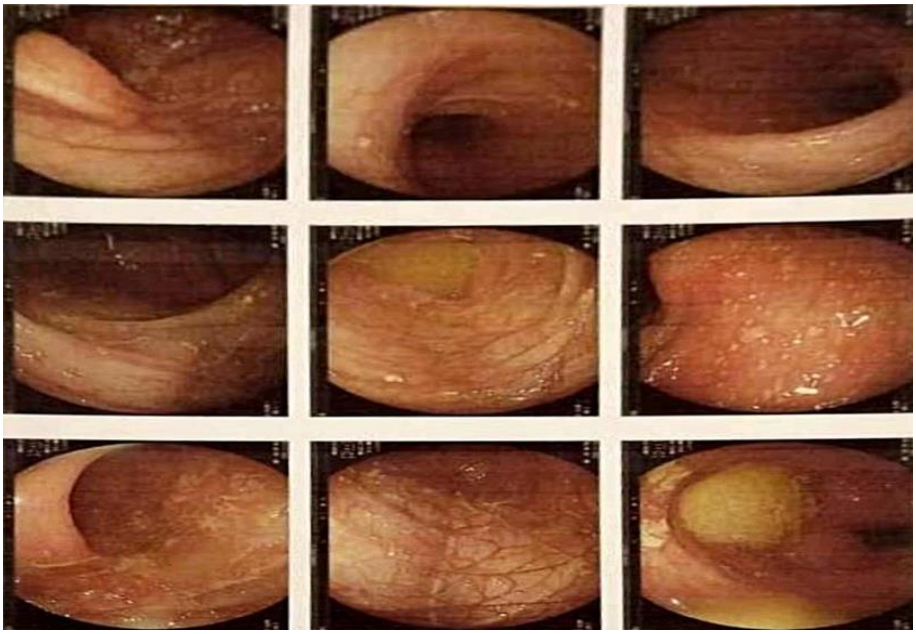
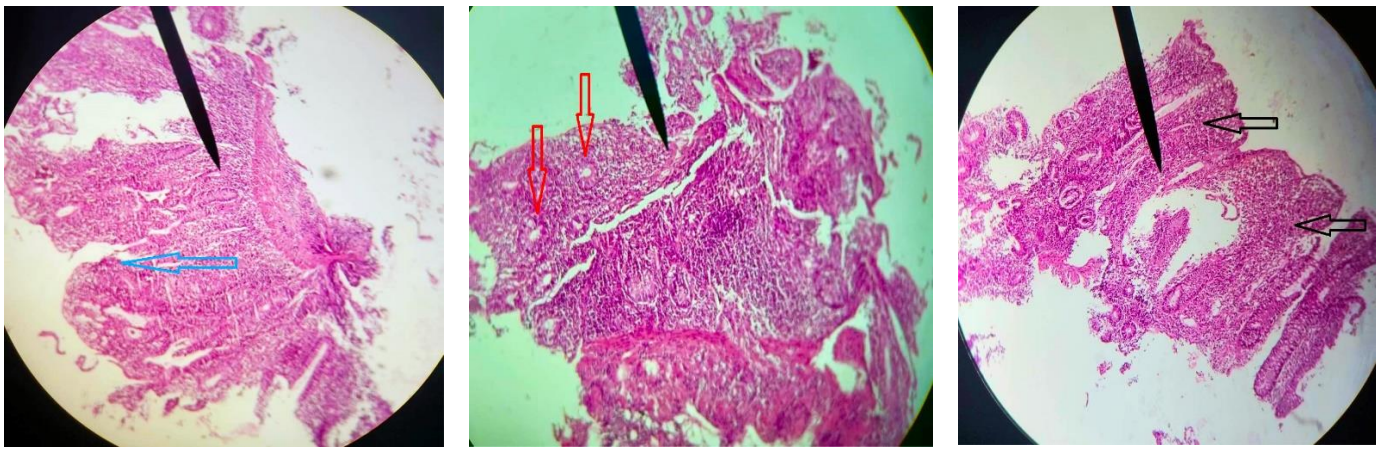


Figure 2. Endoscopic features of UC: diffuse erythema, submucosal hemorrhage, friability, granularity, crypt abscess and superficial ulcerations

The histopathological report showed evidence of focal active colitis with crypt abscess. Besides this, there was evidence of mixed inflammatory infiltrates composed of lymphocytes, plasma cells, neutrophils, and eosinophils in the lamina propria. These findings are shown in Figure 3. Active ulcerative colitis was the final diagnosis. Prednisolone was given intravenously to the patient.

Additionally, ceftriaxone and metronidazole were administered, together with an elimination diet along with Lacteol Fort sachets. A few days later, the frequency of diarrhea reduced, and no more blood came out, she had gained weight. The patient's general condition was good, and she was discharged home with a recommendation to continue oral treatment with Glucocorticosteroids, Mesalazine, and multivitamins and to use an elimination diet with regular follow-up at the Outpatient Clinic. Currently, the child is in clinical remission and is receiving only Mesalazine.



(**a**) (**b**) (**c**)

Figure 3. Histopathology of the colon using a hematoxylin-and-eosin-stained light microscope (a-d), showed flattening of mucosal surface epithelium, focal ulceration (blue arrows), irregular crypt, cryptitis, crypt abscess, crypt destruction and distoration (red arrows) mixed inflammatory infiltrate of lymphocytes, plasma cells, eosinophils, and neutrophils (black arrows).

DISCUSSION

In this report, we described a case of congenital hydrocephalus with coexistent ulcerative colitis that has responded well to Ventriculoperitoneal (VP) shunt placement, initiation of steroids, and immunosuppressive medications respectively. The findings presented highlight the intricate interplay between hydrocephalus (HC) and inflammatory bowel disease (IBD), particularly ulcerative colitis (UC). Our case report of a 4-year-old girl diagnosed with congenital hydrocephalus and later developing UC sheds light on the potential commonalities in the pathophysiology of these seemingly unrelated conditions.

Hydrocephalus is characterized by an imbalance in cerebrospinal fluid (CSF) homeostasis, resulting in the enlargement of cerebral ventricles [1, 12]. The condition may stem from disruptions in CSF circulation, such as increased secretion, flow obstruction, or decreased drainage to the venous system. Osmotic gradients, influenced by macromolecules in ventricular fluid, contribute to HC, defining it as a disorder of macromolecular clearance [12]. While HC can manifest at any age, it is most common in infants and the elderly. In infants, causes include intrauterine conditions, congenital malformations, infections, or intraventricular hemorrhage (IVH) [13].

Surgical interventions, particularly ventriculoperitoneal (V-P) shunt placement, are often necessary for long-term management [14]. High-pressure HC is linked to microglial activation and white matter damage, with evidence supporting the role of chronic inflammation in its pathogenesis [15]. Elevated CSF interleukin-18 (IL-18) and interferon-gamma (IFN γ) concentrations are associated with white matter damage, suggesting a potential for early anti-inflammatory treatment [15, 16]. IL-18, secreted by immune and nonimmune cells, along with other cytokines, emerges as a potential biomarker for HC, providing insights for targeted therapeutic interventions [14, 16].

Ulcerative colitis and Crohn's disease (CD) are part of the inflammatory bowel disease spectrum. While their pathogenesis is multifactorial, involving abnormal immune responses, mucosal protection, and regeneration, the intricate network of bioactive substances plays a crucial role [17]. Management strategies for UC and CD include anti-inflammatory medications, corticosteroids, thiopurine immunomodulators, and advanced therapies like infliximab [10]. Cytokines, particularly IL-18, contribute to immune modulation, and their systemic levels serve as indicators of gut inflammation in UC. Regular follow-up is essential due to long-term complications, including the risk of colon cancer, highlighting the importance of surveillance colonoscopy [5]. The intricate network of bioactive substances and the role of cytokines, including IL-18, in the pathophysiology of IBD draw intriguing parallels with the immunological aspects implicated in hydrocephalus.

We propose that investigating cytokines, including IL-18, as potential biomarkers in hydrocephalus could offer valuable insights. The shared inflammatory pathways might extend beyond UC, encompassing other conditions like HC. This proposition gains strength from the rarity of the coexistence of hydrocephalus and UC, warranting a closer examination of the potential genetic markers that could serve as predictors for evaluating and monitoring these patients.

CONCLUSION

From this case description, it can be concluded that hydrocephalus and ulcerative colitis can coexist, though rarely as suggested by the previous case reports. Therefore, in HC patients with GI manifestation, the remote possibility of UC must be considered. As reported previously, serum interleukin 18 has been elevated in both disorders. Further research and studies should be employed for using it as a biomarker, monitor, and predictor for both diseases and the possibility of the therapeutic role of IL-18BPa in the management of hydrocephalus and inflammatory bowel disease in general.

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Conflicts of Interest

We declare no financial, personal, or professional conflicts of interest.

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استسقاء الرأس والتهاب القولون التقرحي المتزامن: استكشاف دور IL18 : تقرير حالة

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المستخلص

يعد التعايش بين استسقاء الرأس الجنيني والتهاب القولون التقرحي داخل مريض واحد أمرًا نادرًا للغاية. تعرض هذه الورقة حالة فتاة تبلغ من العمر 4 سنوات تم تشخيص إصابتها باستسقاء الرأس الخلقي في البداية عن طريق التصوير بالموجات فوق الصوتية داخل الرحم في الأسبوع 20 من الحمل. تم إجراء تحويلة البطين الصفاقي اللاحقة، وبعد 3 سنوات، تم تشخيص المريض تشريحيًا ومصليًا بأنه مصاب بالتهاب القولون التقرحي. إن تزامن هذه الأحداث الطبية المتميزة في نفس الشخص، وخاصة الفترة الفاصلة بين العلاجات، يمثل حدثًا غير مسبوق لم يتم توثيقه من قبل. ويورد التقرير تفاصيل معاناة المريض الأخيرة من الإسهال الدموي المتكرر والفشل في النمو، والتي تمت إدارتها بفعالية باستخدام البريدنيزولون والسلفاسالازين عن طريق الفم. ومن الجدير بالذكر أن المظهر المتزامن لهذه الحالات يدفع إلى النظر في العوامل المساهمة المحتملة، بما في ذلك العلامات الجينية مثل إنترلوكين 18، والتي تم ربطها بكلا الاضطرابين في الأدبيات الموجودة. تؤكد هذه الحالة على الحاجة إلى مزيد من البحث لتوضيح العلامات الوراثية والمرضية، وكذلك المتنبئات، التي قد تكمن وراء حدوث استسقاء الرأس والتهاب القولون التقرحي بشكل متزامن. إن فهم هذه التعقيدات يمكن أن يقدم رؤى قيمة حول التفاعل المعقد بين العوامل الوراثية والبيئية في تطور مثل هذه الأمراض الطبية الفريدة.

الكلمات الدالة. استسقاء الرأس الخلقي، التهاب القولون التقرحي، التعايش، الإسهال الدموي، الكورتيكوستيرويدات.