Case Report

Urinary findings in a 12-year-old child, a rare case of Follicular Cystitis

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Abstract

Follicular cystitis (FC) is a chronic form of cystitis with uncertain etiology, characterized by the presence of lymphoid follicles in the bladder mucosa as a result of chronic irritation. This can be caused by various factors such as prolonged catheterization, lithiasis, recurrent urinary tract infections or neoplastic bladder pathology. Although it is a rare pathology, it is mainly seen in women over 50 years of age and manifests with nonspecific urinary symptoms such as dysuria, pollakiuria, haematuria and suprapubic pain. We describe a case of a 12-year-old boy with dysuria, haematuria and hypogastric pain. Despite the absence of a history of lithiasis or trauma, and no bacteria found in urinalysis, erythrocytes and leukocytes were found, along with reactivated and degenerated urothelial cells accompanied by heterogeneous-sized cells with a high nucleus/cytoplasm ratio. Ultrasonography showed no abnormalities, but cystoscopy revealed irregularities in the trigone of the bladder and biopsy confirmed the presence of lymphoid follicles, characteristic of FC. This case underscores the relevance of considering FC in patients with persistent bladder irritation and recurrent haematuria. Cystoscopy and histologic evaluation are crucial for an accurate diagnosis, although the role of the clinical laboratory is limited, an experienced specialist can facilitate a proper diagnosis.

Introduction

Follicular cystitis (FC) or cystitis follicularis is a type of chronic cystitis of uncertain etiology, characterized by the presence in the submucosal connective tissue of large numbers of plasma cells and lymphocytes that organize themselves to form lymphoid follicles with germination centers inside. This pathology develops from a chronic irritation of the bladder mucosa that will later give rise to histopathological lesions that characterize it [1, 2].

Chronic irritation of the bladder mucosa may be due to various factors such as prolonged bladder catheterization, lithiasis, repeated urinary tract infections (UTI) or neoplastic bladder pathology. In response to these stimuli, the bladder mucosa responds by the formation of lymphoid follicles characteristic of this pathology. In addition, it has been suggested that the bladder mucosa of patients with FC may have the capacity to

secrete immunoglobulins [1, 2].

The frequency of this pathology is very low, which is evidenced by the few cases that have been published. In these reports, there is a predominance of the female sex and a higher occurrence in those over 50 years of age [1-3].

FC leads to nonspecific symptoms in the urinary tract. It usually presents with dysuria, polyuria, haematuria (microscopic or macroscopic) or suprapubic pain in the lower urinary system [1-3].

Case report

A 12-year-old boy with dysuria, haematuria and pain in the hypogastrium. There was no history of trauma and no family history of urinary lithiasis. On physical examination the patient's vital signs were stable. The abdomen was not distended. In the anamnesis, the patient refers to having few urinary voidings per day and heat stroke every summer.

On suspicion of a UTI, a urine study and urine culture was requested. The dipstick detected the presence of protein in the urine, which was quantified by turbidimetry, erythrocytes and leukocytes (Table 1). The urinary sediment showed microhaematuria (28 erythrocytes/µL), leukocyturia (222 leukocytes/µL), absence of bacteriuria which was later confirmed by urinary culture and, in addition, the presence of urothelial cells with reactive and degenerative changes (Figure 1) accompanied by heterogeneous-sized cells with a high nucleus/cytoplasm ratio (Figure 2), whose morphology was verified with another sample the following day.

Table 1: Laboratory test results.

Laboratory test	Results
Dipstick	
pH	5.0
Glucose	0 (Normal)
Proteins	100 mg/dL
Erythrocytes (hemoglobin/myoglobin)	20/µL
Ketone Bodies	Negative
Bilirubin	Negative
Urobilinogen	Negative
Nitrites	Negative
Leukocytes (leukocyte esterases)	25/µL
Density	1.023
Urinary sediment	
Erythrocytes	28 erythrocytes/µL
Leukocytes	222 leukocytes/µL
Bacteria	Absence
Urothelial cells	Abundant
Urine culture	Negative
Protein/creatinine (Cr) ratio	956.1 mg/g Cr

Figure 1: Urothelial cells with reactive and degenerative changes (phase contrast, x400).

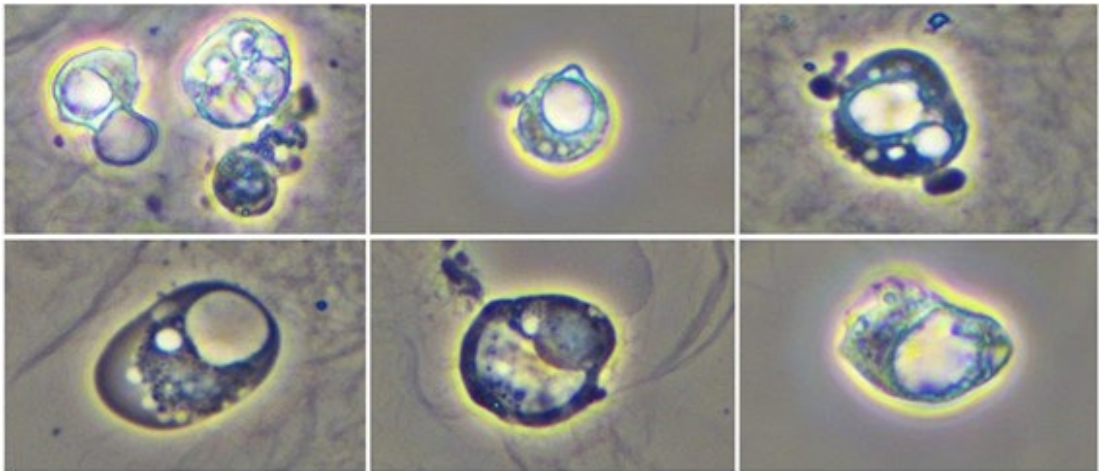
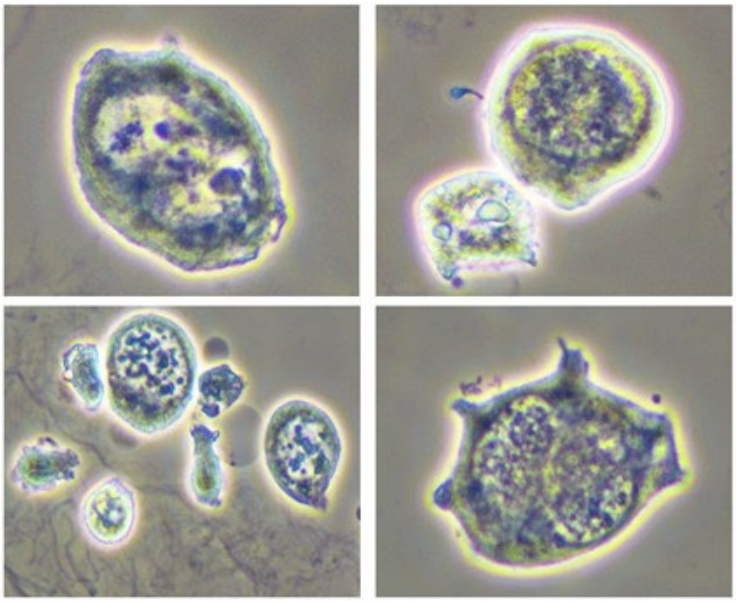


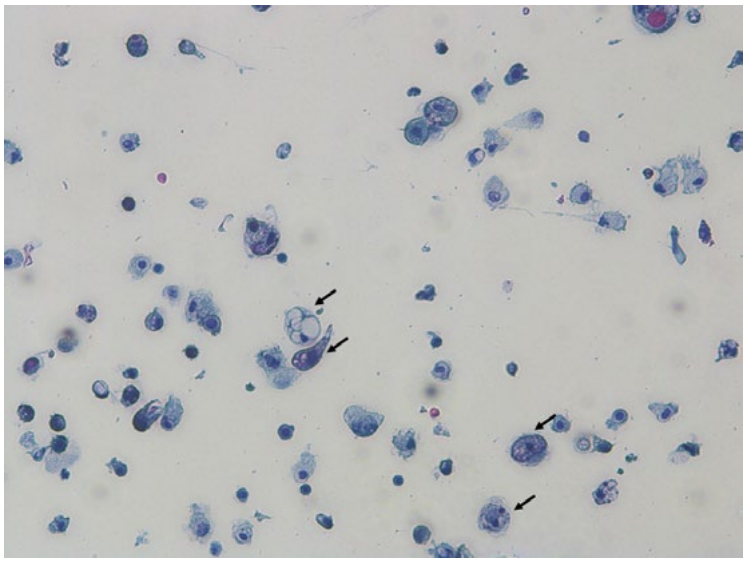
Figure 2: Heterogeneous-sized cells with a high nucleus/cytoplasm ratio (phase contrast, x400).



In view of the laboratory findings, an ultrasound of the urinary system was performed, in which no abnormality was found, and urine cytology was requested.

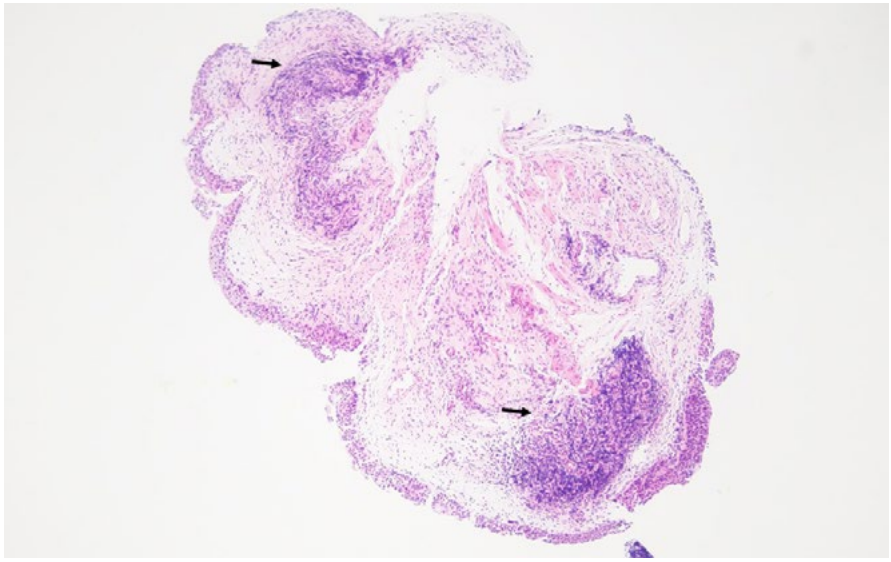
The cytology performed by the Pathology Department confirmed the presence of degenerated urothelial cells (Figure 3) and, in addition, the presence of some cells with anisokaryosis, nuclear atypia and nucleolus, for which a cystoscopy was recommended.

Figure 3: Cytology showing urothelial cells with reactive and degenerative changes (arrow) and other inflammatory cells in the background (Papanicolau stain, x200).



Cystoscopy revealed superficial irregularities in the trigone area and biopsies were taken from this area. The existence of lymphoid follicles with germinal center formation, which is pathognomonic for FC, was finally verified by the biopsy results (Figure 4).

Figure 4: Bladder biopsy showing two lymphoid follicles (arrow) with germinal centers in subepithelial area consisting of the majority of lymphocytes and plasma cells (Hematoxylin-eosin, x40).



Due to the lack of common risk factors, such as prolonged bladder catheterization, lithiasis, repeated UTI or neoplastic bladder pathology, this case report represents a rare case of FC. The patient's poor hydration and urinary habits may have contributed to the chronic bladder irritation that ultimately resulted in the development of FC.

In the treatment plan, the control of inflammation and cause-oriented therapy are the main goals. As a result, it was advised that the patient drink more water and void more frequently each day. The patient had a clinically significant improvement at the follow-up appointment showing a good health status and no recurrence of haematuria.

Discussion

FC usually presents with haematuria (microscopic or macroscopic) and dysuria [1-3]. These symptoms and findings, however, are nonspecific and just confirm the clinician's suspicions. While a patient's physical examination may

sometimes be normal, nonspecific bladder discomfort is rarely seen.

Laboratory findings have limited value in the diagnosis of FC, unless the urine analysis shows characteristic urothelial cells with reactive and degenerative changes as well as increased number of lymphocytes varied in maturation with a predominance of small mature lymphocytes accompanied by immature (follicular center) lymphocytes including tingible body macrophages and follicular dendritic cells [3, 4]. Furthermore, this characteristic pleomorphism of the lymphoid population sets it apart from both the majority of cases of non-Hodgkins lymphomatous UT involvement, where the dispersed atypical lymphoid cells are relatively uniform, and chronic cystitis with increased lymphocytosis, where there is a dispersion of mature lymphocytes and other chronic inflammatory cells in the background [5].

Imaging methods provide a little role in the diagnosis of FC. However, ultrasonography may be useful in some cases of follicular cystitis with the appearance of a papillary-type pseudoneoplastic mass [6]. Thus, imaging methods may aid in the differential diagnosis rather than in the diagnosis of the patient.

The differential diagnosis of cytologic material should consider other pathologies. These include granulomatous cystitis, interstitial cystitis, lymphoma, high-grade urothelial carcinoma and lymphoepithelial carcinoma. These pathologies can present cytologic patterns that vary significantly.

In granulomatous cystitis, loose clusters of epithelioid histiocytes with elongated nuclei are observed [7] and in interstitial cystitis, the presence of inflammatory cells, mainly neutrophils and occasionally eosinophils, is common [8].

In lymphoma, the cell population is discohesive and monomorphic, composed of large, atypical lymphocytes with a high nucleus/cytoplasm ratio, irregular nuclear borders and prominent nucleoli [9].

Finally, in lymphoepithelial carcinoma and high-grade urothelial carcinoma, a heterogeneous population of lymphoid cells is observed in the background along with carcinomatous cells exhibiting a high nucleus/cytoplasm ratio, irregular nuclear membranes, and coarse chromatin [10].

Cystoscopic findings can be detected, mainly the presence of nodules with erythematous surface and trigonal location. Cystoscopy followed by histological examination is currently the gold standard for diagnosis of FC [2-4]. The presence of lymphoid follicles in the bladder wall with germinal center formation is pathognomonic for FC.

There is no identified specific treatment; generally treatment is targeted at the cause and suppression of the inflammation. In addition, anti-inflammatory drugs are also routinely used to reduce the inflammatory reaction. Prednisone treatment and vitamin A supplementation are other conservative treatment options for the reduction of inflammation.

Lessons learnt

- This article highlights the importance of urinalysis performed by a skilled clinical laboratory specialist. Urinalysis is normally used to detect different pathologies, such as UTI, crystalluria, monitor chronic kidney disease, evaluate tubular disorders, but it can also contribute to the diagnosis of less frequent pathologies, such as FC.
- FC is a rare condition mainly described in adult women, but it should be considered in any patient, regardless of age of sex, who presents with persistent bladder irritation, recurrent haematuria and urothelial cells with reactive and degenerative changes in the urinary sediment, especially after ruling out more common pathologies.
- The guideline for diagnosing FC involves a comprehensive approach starting with a thorough patient history and physical examination to identify symptoms such as dysuria, hematuria, and bladder pain, alongside risk factors like poor hydration and urinary habits. Key laboratory tests include urinalysis to detect proteinuria, hematuria, and leukocyturia, and urine culture to rule out bacterial infections. Urine cytology is crucial for identifying urothelial cells with reactive and degenerative changes. Imaging studies, such as ultrasound, are used to exclude other abnormalities. If FC is suspected, cystoscopy is performed to inspect for bladder irregularities, particularly in the trigone area, followed by biopsies of suspicious areas. The definitive diagnosis is confirmed through histological examination of biopsy samples, identifying lymphoid follicles with germinal centers, which are pathognomonic for FC.
- There is no specific treatment identified for follicular cystitis; generally, treatment focuses on addressing the underlying cause and suppressing inflammation. Additionally, anti-inflammatory drugs are routinely used to mitigate the inflammatory response.

Author Contributions

All authors confirmed they have contributed to the intelectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

Authors' Disclosures or Potential Conflicts of Interest

No authors declared any potential conflicts of interest.

Consent

Informed and written consent was obtained from parent.

Ethical approval

Not applicable.

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