Urology Case Reports 48 (2023) 102409

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Pediatrics

Unexpected cystoscopic images in a patient with Chronic Granulomatous Disease

Kinga Kowalczyk [a,*], Edyta Heropolitańska–Pliszka [b]

[a] Department of Pediatric Urology, Children's Memorial Health Institute, Al. Dzieci Polskich 20, Warsaw, 04-730, Poland
[b] Department of Immunology, Children's Memorial Health Institute, Al. Dzieci Polskich 20, Warsaw, 04-730, Poland

ARTICLE INFO

Keywords:
Cystoscopic images
Bladder vessels in granulomatous disease
Chronic granulomatous disease
Bladder granulomas

ABSTRACT

Chronic Granulomatous Disease is a primary immunodeficiency syndrome caused by a phagocytic defect, characterized by recurrent, life-threatening bacterial and fungal infections and an excessive inflammatory response. We present the case of a boy with disease's symptoms mainly from the genitourinary tract. We describe diagnostic difficulties and atypical cystoscopic images, which showed bright morphotic elements of unclear etiology moving in the vessels of the bladder mucosa. These lesions were retrospectively interpreted as clusters of white blood cells (granulomas). Due to the lack of description of a similar phenomenon in the literature, we would like to make the recorded endoscopic images available.

1. Introduction

This article describes the diagnostic and therapeutic difficulties and unusual images obtained during cystoscopy in a patient with Chronic Granulomatous Disease (CGD).

2. Case presentation

A 3-year-old boy was admitted to the Department of Urology with urinary retention due to painful voiding. The medical history included information about myocarditis in the neonatal period and episodes of pneumonia. Urinalysis and urine culture were normal. Ultrasonography revealed two normal kidneys of the same size and a significant thickening of the bladder wall [Fig. 1]. The uroflows were dysfunctional. Treatment with doxazosin and amoxicillin with clavulanic acid was started, resulting in temporary relief of symptoms and improvement of flow curves. After seven months, the boy developed severe constipation, recurrent fever and abdominal pain. Ultrasound examination revealed the thickening of the bladder and ileum wall and enlargement of the abdominal lymph nodes. Neither biopsy of the gastrointestinal tract nor endoscopic examination showed any pathology. Treatment with metronidazole and macrogol was initiated, resulting in resolution of abdominal symptoms. After a few months, severe pain during micturition and defecation reappeared. Apart from microscopic hematuria, urine culture and urinalysis were normal. Renal ultrasound continued to show significant thickening of the bladder wall. Cystoscopy revealed cystitis cystica and an abnormal bladder mucosa. Flowing bright morphotic elements of unclear etiology were visualized in the vessels of the bladder mucosa. [Fig. 2, video]. A mucosal biopsy was performed, which showed only nonspecific inflammatory changes. The patient developed recurrent gingivitis, bilateral inguinal lymphadenitis and bronchitis in the following two years. He was treated in various departments of the Children's Memorial Health Institute. After two years, the boy was readmitted to the Urology Department because of worsening urinary symptoms. On ultrasound, in addition to a thickened bladder wall, there were dilatation of the left ureter. CT urography showed thickening of the wall of the left ureter and bladder, delayed excretion of contrast agent from the left kidney, and abscesses in the liver. Renal isotope study showed reduced left kidney function (ERPF-23%) with complete block of contrast outflow. The consulting immunologist recommended testing and diagnostics for CGD. Nitroblue-tetrazolium test (NBT) was <1% (range 7–15%). Measurements of NADPH oxidase activity by flow cytometry with dihydrorhodamine (DHR) showed activity of 0.02% in the patient and 98.2% in the mother.

Abbreviations: CGD, Chronic Granulomatous Disease; CRP, C-reactive protein; CT urography, Computed Tomography urography; ERPF, Effective Renal Plasma Flow; GI, gastrointestinal; GU, genitourinary; GVHD, Graft-Versus-Host Disease; HSCT, Hematopoietic Stem Cell Transplantation; NADPH, Nicotinamide Adenine Dinucleotide; NBT, Nitroblue Tetrazolium Test; UTI, Urinary Tract Infection; US, Ultrasound examination.

* Corresponding author.
E-mail addresses: urologia@czd.pl (K. Kowalczyk), immuno@czd.pl (E. Heropolitańska–Pliszka).

https://doi.org/10.1016/j.eucr.2023.102409
Received 25 March 2023; Received in revised form 13 April 2023; Accepted 30 April 2023
Available online 1 May 2023

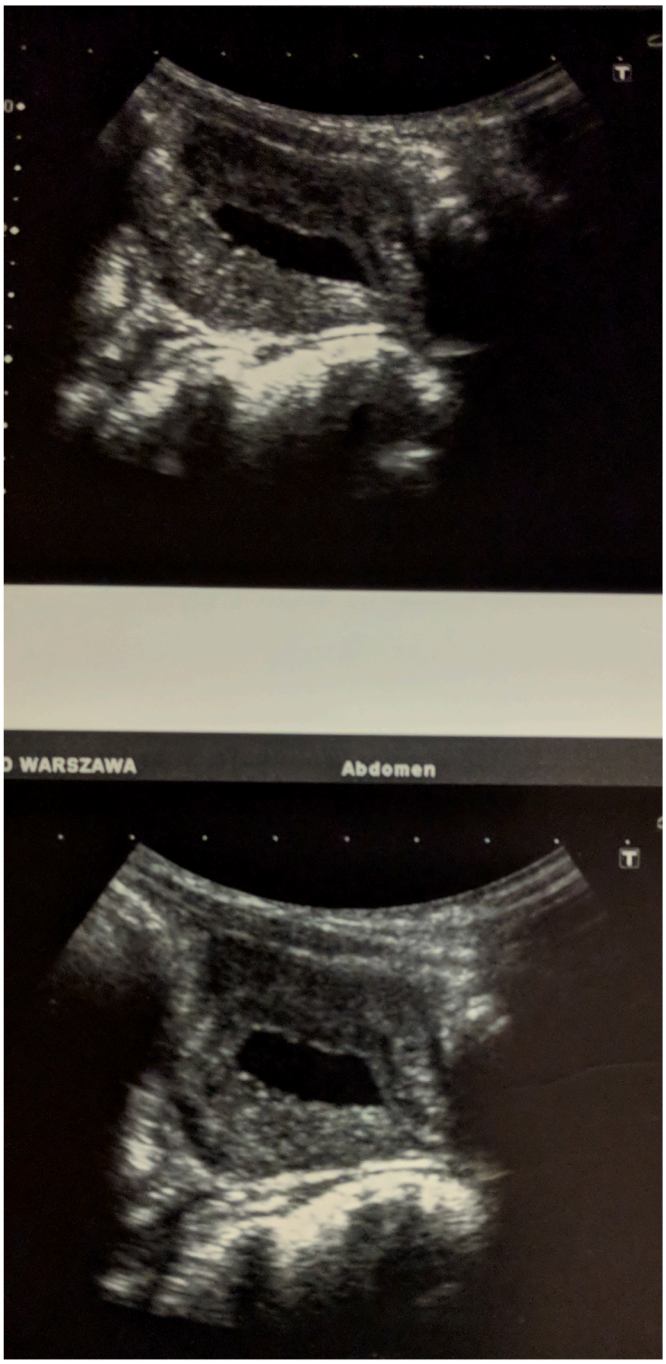

Fig. 1. Ultrasound examination scan: severe thickening of bladder wall.

CGD was diagnosed. Anti-staphylococcal and antifungal prophylaxis and corticosteroid therapy were instituted. The left kidney was decompressed with a D-J catheter. Circumcision was performed. After two months of targeted treatment, there was no dilatation of the urinary tract, the thickening of the bladder wall subsided, and the liver lesions had decreased. Left kidney function increased to 44% ERPF. After three months, the ureteral catheter was removed without additional problems from the upper urinary tract. The patient underwent a hematopoietic stem cell transplant from an unrelated donor at the age of five. NADPH activity is now 100%.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.eucr.2023.102409

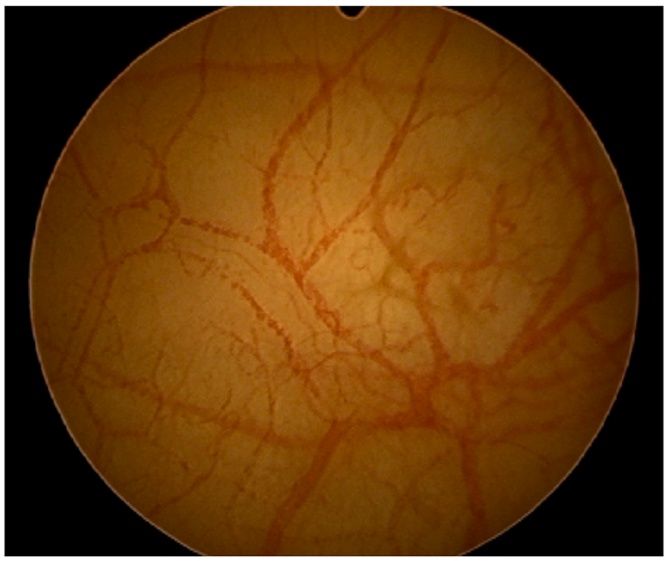

Fig. 2. Endoscopic view of bladder mucosa: visible vessels with granulocyte clusters.

3. Discussion

Chronic granulomatous disease is a rare primary immunodeficiency disease caused by a defect in the phagocytic NADPH oxidase. The most common molecular defect in CGD is the mutation of the gene located on the X chromosome (X-CGD). Other forms of CGD with mutations in other genes are inherited in an autosomal recessive pattern.[1] Recent evidence suggests that the severity of CGD depends on the amount of residual NADPH oxidase activity, regardless of the mode of inheritance. CGD is characterized by severe recurrent bacterial and fungal infections, with catalase-positive organisms as the main cause.[2] Phagocytes properly ingest bacteria, but cannot kill them[2,3]. Intracellular survival of ingested bacteria leads to the development of granulomas. Infections usually occur in lymph nodes, skin, lungs, small and large intestine, liver and bones.[1,4] Gastrointestinal (GI) and urogenital (GU) tracts are less frequently affected by the disease process.[2,4] The onset of CGD can occur anytime from infancy to late adulthood. However, the vast majority of those affected are diagnosed before the age of five. In cases of ureteral obstruction due to the presence of large granulomas, surgical treatment is the option of choice. In the most severe cases, a stent can be placed, or a nephrostomy or nephrectomy can be performed.[4] In 1992, Walther et al. reported that 23 (38%) of 60 patients with CGD had urological symptoms. Seven patients had ureteral strictures due to granulomas. Three patients had granulomas within the bladder, one had urethral stricture. Twelve patients had concomitant urinary tract infections and seven developed kidney damage.[5] Nobody to date mentioned or described any endoscopic images of bladder mucosa vessels in patients with CGD. The appearance of symptoms in various organs made it difficult to make a correct diagnosis in the described case. Initially, the cystoscopy image obtained during the exacerbation of the disease was incomprehensible. We have not found a description of a similar phenomenon in the medical literature. The cystoscopy technique does not allow visualization of individual morphotic elements in the blood. Only the suggestion of the immunologist and the diagnosis of CGD resulted in re-analysis of the endoscopic image. It seems that the only logical conclusion is to interpret the changes as conglomerates of white blood cells forming granulomas. Unfortunately, due to the age of the patient and the size of the biopsy forceps, it was not possible to confirm the suspicion histopathologically. The cause of kidney damage remains unclear. It is likely that the inflammatory swelling of the ureteral wall impaired its motility. Treatment with steroids turned out to be crucial for reducing the inflammation of the ureters, the DJ catheter secured the

proper outflow of urine.

4. Conclusions

There was no histopathological evidence that the elements in the video were granulomas. However, it is highly probable. Due to the rarity of the disease and the lack of description of a similar phenomenon in the literature, we would like to share recorded endoscopic images. We would like to encourage others to a more accurate endoscopic assessment of bladder vessels and intestinal mucosa in the diagnosis of inflammatory diseases of unclear etiology, multi-organ location and thickening of the bladder or intestine wall.

Funding source

No funding was secured for this study.

Financial disclosure

All authors have no financial relationships relevant to this article to disclose.

Conflict of interest disclosures

All authors (Kinga Kowalczyk and Edyta Heropolitańska-Pliszka) have indicated they have no conflicts of interest relevant to this article to disclose.

Support

The authors (Kinga Kowalczyk and Edyta Heropolitańska-Pliszka) have not received any specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Contributors' statement page

Dr. Kinga Kowalczyk is responsible for substantial contribution to conception and design, acquisition of data, or analysis and interpretation of data and drafting the article or revising it critically for important intellectual content and final approval of the version to be published. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolve.

Dr. Edyta Heropolitańska–Pliszka is responsible for substantial contribution to conception and design, acquisition of data, or analysis and interpretation of data and drafting the article or revising it critically for important intellectual content and final approval of the version to be published. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolve.

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