MEDDOCS Open Access Publisher

ISSN: 2637-9627

Annals of Pediatrics

Open Access | Case report

Cystic Fibrosis Presenting as a Chief Complaint of Recurrent Arthritis: An Atypical Presentation of a Common Disorder

El-Baba FM, MD[1]*; Adams M, MD[2]; Srivastava R, MD[3]

[1]Department of Internal Medicine and Pediatrics, Wayne State University, USA.

[2]Department of Pediatric Rheumatology, Wayne State University, USA.

[3]Department of Pediatric Pulmonology, Central Michigan University, USA.

***Corresponding Author(s): Firas El-Baba**

Department of Internal Medicine and Pediatrics, Wayne State University, 4201 St Antoine st Suite 6a, Detroit MI 48201, USA

Tel: 248-953-0796; Mail: felbaba@med.wayne.edu

Received: Sep 10, 2020

Accepted: Oct 07, 2020

Published Online: Oct 09, 2020

Journal: Annals of Pediatrics

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Cystic Fibrosis; Recurrent arthritis; Cystic fibrosis-related arthritis.

Abbreviations: CF: Cystic Fibrosis; CFTR: Cystic Fibrosis Transmembrane conductance Regulator; CFA: Cystic Fibrosis associated Arthritis; CBC: Complete Blood Count; ANCA: Anti-Neutrophil Cytoplasmic Antibody; TBNK: T and B lymphocyte and Natural Killer cell profile; FVC: Functional Vital Capacity; FEV1: Forced Expiratory Volume in one second; BMI: Body Mass Index.

Abstract

Arthritis is an uncommon complication of poorly controlled cystic fibrosis. Our patient is a 13-year-old Caucasian female who presented to the Children's Hospital of Michigan's Pediatric Rheumatology clinic with a primary complaint of relapsing and recurring monoarticular arthritis of the ankle over a 2-3-year long period. When reviewing her history, it is noted that she had chronic sinus congestion and a nasal polyp. On physical exam, she had significant clubbing of her fingers and toes. Her sweat test was positive and genetic testing confirmed the clinical diagnosis. Of note, aside from congestion she had minimal respiratory complaints. She was initiated on standard CF therapy and her arthritis resolved; therefore, confirming the diagnosis of CF associated arthritis.

Cite this article: El-Baba F, Adams M, Srivastava R. Cystic Fibrosis Presenting as a Chief Complaint of Recurrent Arthritis: An Atypical Presentation of a Common Disorder. Ann Pediatr. 2020; 3(1): 1034.

Introduction

Cystic Fibrosis (CF) is a genetic disease caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. The CFTR protein is expressed in multiple organ systems including the lungs, liver, pancreas, intestines and sweat glands, and plays a pivotal role in mucous production. One of the rarer complications of CF is inflammatory arthritis known as Cystic Fibrosis Associated arthritis (CFA) [1].

Two theories exist to explain the pathogenesis of CFA. First is that mutated and unfolded CFTR cannot be inserted into the cell surface, resulting in cellular stress and inducing upregulation of pro-inflammatory cytokines via inflammasome activation [2]. Second, early and sustained lung inflammation associated with CF is postulated to cause a rise in systemic cytokines such as tumor necrosis factor-alpha and interleukin 17 with subsequent "sympathetic" inflammatory arthritis [3].

The presentation of CFA is variable but it has been reported to present as oligoarthritis involving 2-4 joints or polyarthritic. It is often remitting and relapsing; however, with time may become chronic [4]. It has also been noted that a link exists between pulmonary exacerbations and joint flares [5]. Nonetheless, this appears to be a late and rare complication of CF. To our knowledge, this is the first reported case of CF presenting as arthritis in a teenager.

Case description

The patient is a 13 year-old Caucasian female with a past medical history of joint pain and swelling, chronic congestion and a nasal polyp who presented to the pediatric rheumatology clinic at the Children's hospital of Michigan for evaluation of swollen ankles. Family reported that for 2-3 years, the patient had noted intermittent, transient and migratory episodes of ankle swelling, erythema, warmth and pain. The pain was significant enough that she could not bear weight. These episodes would always be monoarticular but affected both the right and left side at different times. These symptoms would last for 3-4 days and frequency had increased over the last month prompting her to seek medical attention. She denies any traumatic incidents with these swelling episodes.

On review of symptoms, she was noted to have an intermittent cough, worsening over the last 6 months and now productive of a greenish sputum. It occurs predominantly during the day; however, she is now having occasional nighttime cough. She was previously referred to an allergist who prescribed an albuterol inhaler, which she had not used. Otherwise, the patient denies unexplained weight loss, recurrent infections, fever, headache, vision changes, eye redness/discharge, ear pain, nasal/oral ulcers, cavities, difficulty in breathing, chest pain, abdominal pain, nausea, vomiting, constipation, diarrhea, greasy stools, dysuria, hematuria, frothy urine, neck pain, back pain, or any other pain/redness/swelling of any other joints other than her ankles. She also denies any history of pneumonia, bronchitis or hospitalizations.

Her past medical history was notable for history of chronic congestion for which she followed with an otolaryngologist. They performed a head computed tomography scan of her sinuses, which showed opacification of her left sided sinus with a nasal polyp.

On physical exam, her vitals were within normal limits including a normal hemoglobin saturation. Physical exam was also within normal limits except the patient was noted to have significant clubbing of her fingers and toes. Her ankles were without warmth or swelling.

To summarize the case, this is a 13-year-old Caucasian female with a history of chronic sinusitis, left sided nasal polyp, and clubbing of her fingers and toes who presented to pediatric rheumatology clinic for evaluation of recurrent arthritis. The history and physical exam were suggestive of CFA and Pulmonology was consulted. The differential also included chronic granulomatous disease, common variable immunodeficiency, granulomatosis with polyangiitis (Wegener's Granulomatosis), and less likely juvenile idiopathic arthritis, systemic lupus erythematosus or mixed connective tissue disease.

Diagnostic assessment

Laboratory evaluations included complete blood count (CBC) with differential, anti-neutrophil cytoplasmic antibody (ANCA), complement components C3, C4, immunoglobulin A, E, G and M, oxidative burst, T and B lymphocyte and natural killer cell profile (TBNK), as well as x-rays of the ankles. Her CBC showed elevated white count and her C-reactive protein was also elevated, but all other lab results were normal.

Chest radiograph was obtained that read "bilateral increased perihilar markings with peribronchial cuffing and hyperinflation on the lateral radiograph." Sweat testing was abnormal, with a chloride of 97 and 100 mMol/L on the right and left forearms respectively with an adequate sweat volume of 40 µL, leading to a diagnosis of CF which was further confirmed with genetic testing which showed two CF causing mutations, i.e. the *phe508del* and the *c.2052dupA* mutations.

Follow-up/outcomes

Once the diagnosis of CF was confirmed, the patient established care with our CF center and was seen by all the members of the CF team, including the dietician, respiratory therapist and CF nurse. We ordered respiratory cultures to assess for resistant organisms and ordered a fecal elastase test to assess for pancreatic insufficiency. The patient was started on dornase alfa 2.5mg daily to augment airway clearance. Spirometry at presentation showed mild obstruction as follows: functional vital capacity (FVC) of 3.22L (99% predicted) and 3.29L (101% predicted) post-bronchodilator and a mildly reduced forced expiratory volume in one second (FEV_1) of 2.22 (78% predicted) and 2.42L (85% predicted) post-bronchodilator, and a low FEV_1/FVC of 69% predicted.

Her respiratory cultures did grow *pseudomonas aeruginosa* (mucoid and non-mucoid strains) treated with oral ciprofloxacin 500 mg twice a day for 14 days and inhaled tobramycin 300mg twice daily for 28 days. Her fecal elastase came back low at <50 µg elastase/g, confirmed on repeat testing and the patient was started on pancrealipase (Creon) 36,000 units/cap 2 caps prior to meals and 1 cap prior to snacks. She was also started on 7% hypertonic saline twice daily as maintenance therapy.

At her follow-up appointment, her spirometry was improved with normal lung function as follows: her FVC was 3.60L (107% predicted), FEV1 was 3.01L (102% predicted) and FEV1/FVC was 84%. Her body mass index (BMI) had also improved to the 50th-75th percentile at follow-up.

She then followed with the rheumatology clinic. She stated at that follow-up that her arthritis had resolved since initiating CF therapy. Therefore, they concluded that her arthritis

was secondary to uncontrolled/undiagnosed CF. She no longer needed follow up with rheumatology and was discharged from their clinic, only to follow up in symptoms recur.

One year later, the patient did have a recurrence of her left lower extremity swelling that required admission to the hospital. She was evaluated by rheumatology, orthopedics and infectious disease. After discussing with the family, the patient had not been adherent to her pulmonary treatments because of stress at school. Once treatments were re-initiated, her arthritic symptoms resolved. She has been adherent to her CF regimen since and her arthritis has not recurred.

Discussion

As discussed in the introduction, CFA is a relatively rare and underappreciated complication of CF. In addition, according to the literature, CFA tends to be a late complication of CF when it is very poorly controlled. What makes this case unique is that this patient presented with predominantly CFA symptoms with limited respiratory complaints. Despite being undiagnosed for her entire 13 years of life, her spirometry only showed mild obstruction. The severity of her arthritis therefore was disproportionate to her respiratory disease; however, there has been a correlation between chest disease exacerbations and worsening of the arthritis. The major limitation to this case is the time since diagnosis has been made. The patient was diagnosed in May of 2018 and has been following with our clinic since then, and we believe the source of her arthritis is CFA; however, it is unclear at this time whether an additional etiology could be the source of her arthritis. Only further time will tell.

References

1. Pertuiset E, Menkes CJ, Lenoir G, Jehanne M, Douchain F, et al. Cystic fibrosis arthritis. A report of five cases. Br J Rheumatol. 1992; 31: 535-538.
2. Cohen-Cymberknoh M, Kerem E, Ferkol T, Elizur A. Airway inflammation in cystic fibrosis: molecular mechanisms and clinical implications. Thorax. 2013; 68: 1157-1162.
3. Courtney JM, Ennis M, Elborn JS. Cytokines and inflammatory mediators in cystic fibrosis. J Cyst Fibros. 2004; 3: 223-231.
4. Clarke EA, Watson P, Freeston JE, Peckham DG, Jones AM, et al. Assessing arthritis in the context of cystic fibrosis. Pediatr Pulmonol. 2019: 770-777.
5. Dixey J, Redington AN, Butler RC, Smith MJ, Batchelor JR, et al. The arthropathy of cystic fibrosis. Ann Rheum Dis. 1988; 47: 218-223.