Case Report

An unusual case of cystic fibrosis with pancytopenia due to copper deficiency and blindness caused by vitamin A deficiency: A case-report

Hesamedin Nabavizadeh a, b, Leila Johari a, *, Rafat Noeiaghdam a, Soheila Alyasin a, b, Hossein Esmaeilzadeh a, b, Zahra Kanannejad b, Maryam Emaminia a

a Department of Allergy and Clinical Immunology, Nemazee Teaching Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
b Allergy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

ARTICLE INFO

Keywords:
Cystic fibrosis
Blindness
Pancytopenia

ABSTRACT

Cystic fibrosis (CF) is a multi-systemic autosomal recessive disease which mostly involves the respiratory, digestive, and reproductive systems, but it can present with various clinical presentations, especially in adulthood. We describe a 19-year-old boy, a known case of CF who presented with less known clinical presentations of CF, blindness, liver cirrhosis, vitamin A deficiency, and pancytopenia.

1. Introduction

Cystic fibrosis (CF) is caused by a mutation in the CF (CFTR) regulatory gene and is a common autosomal recessive genetic disease [1]. It is more common in northern European people than in Africans, the Americans, and Asians. In the Middle East, various incidence rates of CF have been reported, ranging from 1 in 2560 to 1 in 15,876 [2].

The incidence of CF varies among different geographical isolates of Iran. For example, while no confirmed cases of CF have been reported in southern Iran, the prevalence rate of CF reported from northwestern Iran is 7.98 per 100,000 in a 5-year period (2004–2008) [3]. Typical CF symptoms often involve several systems, particularly the lungs, pancreas, gastrointestinal tract, and genitals in men [4].

2. Case presentation

A 19-year-old Iranian boy, a known case of cystic fibrosis (CF) and liver cirrhosis, presented with ascites one month ago. Patient had been diagnosed with CF at the age of four years which later had become complicated by liver cirrhosis, splenomegaly, and pulmonary disorders. Moreover, patient past medical history was significant for corneal perforation and blindness due to xerophthalmia as a result of vitamin A deficiency at the age of eight years. Medications at the time of presentation included vitamin A, vitamin K, vitamin D, vitamin E, calcium D, folic acid, capsule Creon, ursobil, spironolacton, Gentamycin with nebulizer, spray fluticasone, and azithromycin. Patient had no history of tobacco, cigarette, or alcohol consumption. In the physical exam, patient had abdominal distention, icteric sclera, extremity edema, moderate ascites, and non-tender splenomegaly. Other examinations were unremarkable. An abdominal tap was done 3 times due to ascites and evidence of infection was seen, so vancomycin, meropenem, and ciprofloxacin were prescribed for him. Patient’s chest CT scan (Fig. 1) and lab data were in favor of aspergillosis; the pleural tab was exudative, so...

* Corresponding author.
E-mail address: leilajohari1986@gmail.com (L. Johari).

https://doi.org/10.1016/j.rmcr.2022.101774
Received 6 August 2022; Accepted 6 November 2022
Available online 7 November 2022
2213-0071/© 2022 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
we added itraconazole and prednisolone to his medications. On admission into the hospital, patient's hematological values which showed pancytopenia were as follows: red blood cell count (RBC) 2.6 × 10 12/l; hemoglobin (Hb) 8.1 g/dl; hematocrit (HCT) 26.7%; mean cell volume (MCV) 101.5 µ3; white blood cell count (WBC) 3.4 × 10 9/l with neutrophils 88%, lymphocytes 9% and eosinophils' 1%; and platelet count 46 × 10 9/l. Initial evaluation included negative coombs and anti-neutrophil antibody with normal folate, vitamin B12, vitamin E, iron studies, and soluble transferrin receptor. A peripheral smear revealed no morphologic abnormalities. Patient's bone marrow aspiration and biopsy was normal. Due to the possibility of copper deficiency in CF patients as a result of poor absorption, we measured serum copper (20 mcg/dl) in the patient; the results showed that it was under the limit of the normal range (normal range of serum copper: 80 -155mcg/dl). Informed consent was obtained from patient in this study.

3. Discussions

Cystic fibrosis (CF) is a multi-systemic autosomal recessive disease that mostly presents with recurrent respiratory infections and pancreatic insufficiency, but it has various clinical presentations [5]. As many CF patients survive to adulthood nowadays, it is of great importance that we become familiar with other less common presentations in order to better diagnose and control the complications [6]. This is the reported case of a 19-year-old Iranian boy who presented with xerophthalmia and pancytopenia due to vitamin A and copper deficiency, respectively. Both of his symptoms are among the less common presentations of CF.

Ninety percent of CF patients suffer from pancreatic insufficiency which results in poor absorption of fat. Therefore, deficiency of fat-soluble vitamins like vitamin A can occur in them as these vitamins are co-absorbed with fat [7]. One of the major consequences of vitamin A deficiency is eye involvement like night blindness and conjunctival and corneal xerosis which had happened in our case [8]. If we screen patients with vitamin A deficiency earlier, we will be able to prevent permanent defects, and it is more significant in CF patients as deficiency of vitamin A in developed countries most commonly occurs with malabsorption states such as CF [9,10].

Other micronutrient deficiencies, such as minerals and trace elements can also occur in CF. One of these micronutrients is copper deficiency which occurs due to ineffective absorption from the diet, or excessive loss through bile [11]. Copper is essential for normal functions of the body; for example, it is important for growth, different cells maturation such as red and white blood cells, metabolism of cholesterol and glucose, bone mineralization, brain development, and proper defense mechanisms [11]. Because of the numerous actions of copper in the body, its deficiency causes different clinical presentations, but it mostly presents with anemia which is unresponsive to iron supplementation, neutropenia, and bone abnormalities. Less frequently, it may cause pancytopenia and features of myelodysplastic syndrome (MDS) [12]. Knowing about the possibility of micronutrient deficiencies in CF patients and checking them regularly would help us not only to prevent permanent defects, but also to choose proper treatments and reduce the costs and adverse effects.

4. Conclusion

CF has numerous clinical presentations, some of which are less common and atypical. Our case presented with two atypical presentations, blindness and pancytopenia. For reducing CF complications, we need to improve our knowledge about rare and atypical presentations. It is recommended that the patients should be observed and followed up closely and regularly.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

There is no conflict of interest between authors.
Acknowledgements

The authors would like to thank Shiraz University of Medical Sciences, Shiraz, Iran and also Center for Development of Clinical Research of Nemazee Hospital and Dr. Nasrin Shokrpour for editorial assistance.

References

[1] J.L. Taylor-Couzar, M.A. Mall, B.W. Ramsey, E.F. McKone, E. Tullis, G. Marigowda, et al., Clinical development of triple-combination CFTR modulators for cystic fibrosis patients with one or two F508del alleles, ERJ Open Res 5 (2) (2019) 00082-2019.
[2] E.F. Okonji, O.C. Okonji, Understanding varying COVID-19 mortality rates reported in Africa compared to Europe, Americas and Asia 26 (7) (2021) 716–719.
[3] L.R. Kalankesh, S. Dastgiri, M. Rafeey, N. Rasouli, L. Vahedi, Minimum data set for cystic fibrosis registry: a case study in Iran, Acta Inf. Med. 23 (1) (2015) 18.
[4] X. Guo, K. Liu, Y. Liu, Y. Situ, X. Tian, K.-F. Xu, et al., Clinical and genetic characteristics of cystic fibrosis in Chinese patients: a systemic review of reported cases, Orphanet J. Rare Dis. 13 (1) (2018) 1–10.
[5] D. Goetz, C.L. Ren, Review of cystic fibrosis, Pediatr. Ann. 48 (4) (2019) e154–e161.
[6] K. De Boeck, F. Vermeulen, L. Dupont, The diagnosis of cystic fibrosis, Presse medicale (Paris, France : 1983 46 (6 Pt 2) (2017) e97–e108.
[7] J.A. Dodge, D. Turck, Cystic fibrosis: nutritional consequences and management, Best Pract. Res. Clin. Gastroenterol. 20 (3) (2006) 531–546.
[8] C. Gilbert, The eye signs of vitamin A deficiency, Community Eye Health 26 (84) (2013) 66-67.
[9] R.J. Rayner, J.C. Tyrrell, E.J. Hiller, C. Marenah, M.A. Neugebauer, S.A. Vernon, et al., Night blindness and conjunctival xerosis caused by vitamin A deficiency in patients with cystic fibrosis, Arch. Dis. Child. 64 (8) (1989) 1151–1156.
[10] Y. Spits, J.J. De Laey, B.P. Leroy, Rapid recovery of night blindness due to obesity surgery after vitamin A repletion therapy, Br. J. Ophthalmol. 88 (4) (2004) 583-585.
[11] M.F. Escobedo-Monge, E. Barrado, C. Alonso Vicente, M.A. Escobedo-Monge, M.C. Torres-Hinojal, J.M. Marugán-Miguelsanz, et al., Copper and Copper/Zinc Ratio in a Series of Cystic Fibrosis Patients, vol. 12, 2020 11.
[12] D.M. Williams, Clinical syndromes of copper deficiency, Nutritional Anemia: Scientific Principles, Clinical Practice and Public Health 111 (2019).