Case Report

Disseminated Strongyloidiasis in a Patient with Membranoproliferative Glomerulonephritis- Case Report

*Taheerh MALAKOUTIAN 1, Ronak MOHAMMADI 1, Mojgan ASGARI 2, Atefeh AMOUZEGAR 1

1. Division of Nephrology, Department of Internal Medicine, Hospital Management and Research Center (HMRC), Iran University of Medical Science, Tehran, Iran
2. Department of Pathology, Hospital Management and Research Center (HMRC), Iran University of Medical Science, Tehran, Iran

Received 10 May 2014
Accepted 21 Oct 2014

Abstract

Strongyloides stercoralis (SS) is a unique nematode with an auto infective cycle, so that it completes its life cycle within the human host and can live there for many years. In immunocompromised patients, infection can cause Strongyloides hyperinfection syndrome (S.H.S) that is associated with serious morbidity and mortality. As various infections are one of the leading causes of membranoproliferative glomerulonephritis (MPGN), we should consider subclinical strongyloidiasis as a possible underlying disease, especially in endemic areas. Here we describe a case of strongyloidiasis following immunosuppressive therapy for MPGN, the diagnosis of which was made, only a few hours before death, by stomach biopsy.

Keywords: Strongyloides stercoralis, Hyperinfection, Immunosuppression, Membranoproliferative glomerulonephritis

*Correspondence Email: malakoutian@ams.ac.ir

Introduction

Strongyloidiasis results from infection with Strongyloides Stercoralis (SS). The parasite can affect gastrointestinal, pulmonary, and dermatologic systems. Manifestations of the infection can range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease when immunosuppression is implemented. There are several case reports of disseminated strongyloidiasis among patients who
were receiving corticosteroid due to membranoproliferative glomerulonephritis (MPGN) or other pathologies of nephrotic syndrome (1-5).

Here we report a patient with *Strongyloides* hyperinfection syndrome (SHS) after a few months of immunosuppressive therapy for MPGN disease.

**Case presentation**

A 64 yr old man presented with vomiting and fever, from 2 weeks before admission to Hasheminejad Kidney Center (HKC) in Tehran, Iran in 2008. He was well until 6 months before admission, when he was referred from a southern province of Iran (Khuzestan) to another nephrology center due to nephrotic range proteinuria. Kidney biopsy had been performed at that time and glomerular membranoproliferative pattern was seen with crescent formation in 5 out of 13 glomeruli. Two glomeruli also showed fibrinoid necrosis. Tubular atrophy and proportional interstitial fibrosis was seen in 20% of submitted tissue surface. The diagnosis of diffuse proliferative and necrotizing glomerulonephritis with crescent formation was made with a suggestion of the background disease of Membranoproliferative Glomerulonephritis (Fig.1).

He was treated with prednisolone, 60 mg daily that was gradually tapered to 15 mg per day, and cyclophosphamide 75 mg daily. He was receiving both drugs when he was admitted to HKC. He was originally a resident of Khuzestan Province. In his past medical history, there was no positive finding of respiratory or gastrointestinal diseases.

On his first physical examination, the patient showed no abnormal finding except for a low-grade fever (37.8 °C). He appeared ill but had no respiratory distress, skin rash or lymphadenopathy.

Laboratory data and imaging studies are presented in Table 1.

**Table 1: Laboratory data of the patient**

|                      | CBC                        |
|----------------------|----------------------------|
|                      | WBC (eosinophil count:2%)  |
|                      | 2*10^3/μl                  |
|                      | Hg                         | 8 g/dl                      |
|                      | PLT                        | 75*10^3/μl                  |
| Blood Biochemistry   | BUN                        | 109 mg/dl                   |
|                      | Cr                         | 6.5 mg/dl                   |
|                      | K                          | 6.7 mmol/L                  |
|                      | Na                         | 136 mmol/L                  |
| Liver Enzymes        | SGOT                       | Normal                      |
|                      | SGPT                       | Normal                      |
| U/A                  | blood                      | 1+                          |
|                      | protein                    | 1+                          |
|                      | WBC                        | 2-3                         |
| Serologic Tests      | ANA                        | Normal                      |
|                      | ANCA                       | Negative                    |
|                      | Complements(C3,C4,CH50)    | Normal                      |
| Viral Markers        | HBS Ag                     | Negative                    |
|                      | HCV Ab                     | Negative                    |
| Imaging              | Chest X Ray                | Normal                      |
|                      | Abdominopelvic sonography  | Normal                      |
Fig. 1: Cellular crescent with endocapillary proliferation of the glomeurlus under light microscopy in favor of MPGN pattern, core biopsy of the patient's kidney. This sample was obtained in Khuzestan and the blocks were reviewed in Pathology Unit, Hashemi-nejad Kidney Center (Jones staining). Original picture.

Cyclophosphamie was discontinued, broad-spectrum antibiotic therapy was started and hemodialysis was performed. One day after admission, upper gastrointestinal (GI) endoscopy was performed, because of intractable vomiting which showed severe erythematous lesions in stomach mucosa. On third hospital day, his general condition deteriorated rapidly and the patient developed dyspnea. A chest CT scan demonstrated diffuse alveolar infiltrates. He was intubated due to worsening of dyspnea and massive hemoptysis. Histological examination of gastric biopsy specimens revealed numerous cross-sections of eggs and rhabditiform larvae of SS (Fig. 2).

Treatment was started with ivermectin immediately, however the patient died soon after, with massive alveolar hemorrhage and respiratory failure, on the fifth hospital day and only 12 hours after the diagnosis of SHS.

Fig. 2: Gastric mucosa of the patient showing inflammatory infiltration of lamina propria and eggs (A) and rhabditiform larvae (B) of *Strongyloides stercoralis* in the glands under light microscopy in a biopsy made by endoscopic procedure (H&E staining). Original picture.

**Discussion**

*Strongyloides stercoralis* is an intestinal parasite affecting 100 million people worldwide. It is endemic in tropical and subtropical areas in the world (6-9). Diagnosis of latent infection is difficult due to limitations of current parasitological and serological methods (10-15). In Iran, it is an endemic parasite especially in southern and Northern provinces. Jalali et al. reported a prevalence of 1.4% in north of Iran, whereas Farahnak reported a prevalence of 6.9% in southern parts of Iran (6-7). In Kermanshah in 2004, out of 206 patients who were HIV positive, 2 (0.9%) had positive stool culture for SS (10).

In immunosuppressed hosts, SS may become invasive, causing SHS, which results from systemic dissemination of filariform larvae (8-9). Defects in cell-mediated immunity and corticosteroid use are considered the major risk factors for development of *Strongyloides* hyperinfection in immunocompromised hosts (17-18). Cruz and Rogers reported the first cases of SHS in 1966, as the occurrence of
fatal strongyloidiasis with immunosuppression (16-17). In Iran, there are few reports of SHS in patients who had acute or chronic lympho-blastic leukemia (26-27).

In a study, 103 previously described cases of presumed Strongyloides hyperinfection were reviewed. Among 89 patients, immunocompromised by therapy or disease, the mortality rate was 86% (18). In endemic areas, most cases are infected with this nematode a long time before manifestation of the hyperinfection syndrome (18).

In this case report, we present a case of steroid and cyclophosphamide resistant MPGN complicated by disseminated strongyloidiasis who died 7 months after beginning of proteinuria.

There are many reports of association of parasitic infections and glomerulonephritis, however Strongyloides associated glomerulonephritis has not been well-defined (19-21).

Although SS can involve any organ directly, there is evidence that suggest that immunological reactions can play a role in the pathogenesis of disease (22-24). Considering many reports of remission of nephrotic syndrome after treatment of Strongyloides infection with anthelmintic agents, the possibility of Strongyloides related glomerulopathy is strengthened.

Conclusion

Regarding long persistence of SS in the human host after initial exposure and its potential to progression to disseminated strongyloidiasis in immunosuppressed patient from one hand and its high mortality rate from another hand, patients with risk factors for SS who are candidate for immunosuppressive therapy should be screened for disease. We also recommend screening for SS in patients who have nephrotic syndrome and live in endemic areas.

Acknowledgements

The authors declare that there is no conflict of interests.

References

1. Hsieh YP, Wen YK, Chen ML. Minimal change nephrotic syndrome in association with strongyloidiasis. Clin Nephrol. 2006;66:459–63.
2. Morimoto J, Kaneoka H, Sasatomi Y, Sato YN, Murata T, Ogahara S. Disseminated strongyloidiasis in nephrotic syndrome. Clin Nephrol. 2002;57:398–401.
3. Sathe PA, Madivale CV. Strongyloides hyperinfection in a Patient with membranoproliferative glomerulonephritis. J Postgrad Med. 2006;52:221–2.
4. Paul B. Keiser, Thomas B. Nutman Strongyloides stercoralis in the. Immunocompromised Population. Clin Microbiol Rev. 2004, 17(1):208.
5. Miyazaki M, Tamura M, Kabashima N, et al. Minimal change nephrotic syndrome in a patient with strongyloidiasis. Clin Exp Nephrol. 2010,14:367–71.
6. Jalali M, Rezaian M, Rokni MB. Relationship between serum IgE level and intestinal parasites. Iran J Public Health. 2004;33:28–32.
7. Farahnak A. Survey on prevalence of parasites in the central area of Khuzestan. Medical Journal of Tabriz University of Medical Sciences,2001;49:57–62.
8. Husni RN, Gordon SM, Longworth DL, Adal KA. Disseminated Strongyloides Stercoralis infection in an immunocompetent patient. Clin Infect Dis.1996, 23:663–4
9. Tanton DD, Durning S, Chambers S. Pulmonary hyperinfection with Strongyloides Stercoralis in an immunocompetent patient. J Gen Intern. Med.2002, 17:72–73.
10. Buchwald D, Lam M, Hooton TM. Prevalence of intestinal parasites and association with symptoms in Southeast Asian refugees. J Clin Pharm Ther. 1995; 20:271–5.
11. Genta RM. Dysregulation of strongyloidiasis: a new hypothesis. Clin Microbiol Rev. 1992. 5:345–355.
12. Siddiqui AA, Berk SL. Diagnosis of Strongyloides Stercoralis infection. Clin Infect Dis. 2001. 33:1040–1047.
13. Olsen A, van Lieshout L, Marti H, et al. Strongyloidiasis—the most neglected of the neglected tropical diseases? Trans R Soc Trop Med Hyg. 2009;103(10):967-72.

Available at: http://ijpa.tums.ac.ir
14. Gill GV, Beeching NJ, Khoo S, et al. A British Second World War veteran with disseminated strongyloidiasis. Trans R Soc Trop Med Hyg. 2004; 98:382–6.
15. H Moghaddassani, Mirhendi H, Hosseini M, Rokni MB, Mowlavi Gh, Kia Eb. Molecular Diagnosis of Strongyloides Stercoralis Infection by PCR Detection of Specific DNA in Human Stool Samples. Iran J Parasitol. 2011; 6: 23-30.
16. Cruz T, Reboucas G, Rocha H. Fatal strongyloidiasis in patients receiving corticosteroids. N Engl J Med. 1966;275:1093–6.
17. Rogers WA, Jr, Nelson B. Strongyloidiasis and malignant lymphoma: “Opportunistic infection” by a nematode. JAMA. 1966;195:685–7.
18. Igra-Siegman Y, Kapila R, Sen P et al. Louria Syndrome of Hyperinfection with Strongyloides Stercoralis. Oxford J Med Clin Infec Dis.1981, 3:397-407.
19. Boonpucknavig V, Soontorniyomkij V. Pathology of renal diseases in the tropics. Semin Nephrol. 2003;23:88–106.
20. Seet RC, Lau LG, Tambyah PA. Strongyloides hyperinfection and hypogammaglobulinemia. Clin Diagn Lab Immunol. 2005;12:680–2.
21. Copelovitch L, Sam OI O, Taraquinio S, Chanpheaktra N. Childhood nephrotic syndrome in Cambodia: an association with gastrointestinal parasites. J Pediatr. 2010; 156:76–81.
22. Gill DS, Fonseca VA, Barradas MA, Ballioud R, Moorhead JF, Dandona P. Plasma histamine in patients with chronic renal failure and nephrotic syndrome. J Clin Pathol. 1991;44:243–5.
23. Bheekha-Escuna R, MacGlashan DW, Langdon JM, MacDonald SM. Human recombinant histamine-releasing factor activates human eosinophils and the eosinophilic cell line, AML14–3D10. Blood. 2000;96:2191–8.
24. Toyabe S, Kaneko U, Hara M, Uchiyama M. Expression of immunoglobulin E-dependent histamine-releasing factor in idiopathic nephrotic syndrome of childhood. Clin Exp Immunol. 2005;142:162–6.
25. Zali M R, Jafari Mehr A, Rezaian M, Meamar A R, Vaziri S, Mohraz M. Prevalence of Intestinal Parasitic Pathogens among HIV-Positive Individuals in Iran. Jpn J Infect Dis. 2004, 57: 268-270.
26. Kia EB, Rahimi H, Mirhendi H, et al. A case of fatal strongyloidiasis in a patient with chronic lymphocytic leukemia and molecular characterization of the isolate. Korean J Parasitol. 2008,46: 261-263
27. Mahmoodi Nesheli H, Galini Moghadam T, Zahedpasha Y, et al. Acute Lymphoblastic Leukemia with Eosinophilia and Strongyloides Stercoralis Hyperinfection. Iran J Pediatr. 2011, 21: 549-552.