Case Report

Acute Thrombocytopenia, Leucopenia, and Multiorgan Dysfunction: The First Case of SFTS Bunyavirus outside China?

Srdjan Denic, 1 Joumana Janbeih, 2 Suresh Nair, 2 Walter Conca, 1 Waheed Uz Zaman Tariq, 3 and Suhail Al-Salam 4

1 Department of Internal Medicine, Faculty of Medicine and Health Sciences, UAE University, P.O. Box 17666, Al Ain, UAE
2 Department of Medicine, P.O. Box 1006, Al Ain Hospital, Al Ain, UAE
3 Department of Pathology, Tawam Hospital, P.O. Box 15258, Al Ain, UAE
4 Department of Pathology, Faculty of Medicine and Health Sciences, UAE University, Al Ain, UAE

Correspondence should be addressed to Srdjan Denic, s.denic@uaeu.ac.ae

Received 15 June 2011; Accepted 9 August 2011

Academic Editors: T. Shibata, E. M. Stringer, W. I. van der Meijden, and K. Yeboah-Antwi

Copyright © 2011 Srdjan Denic et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

We report a 57-year-old man with acute thrombocytopenia, leucopenia, and multiorgan dysfunction. Patient was from North Korea and was temporarily working in Dubai, United Arab Emirates, when he fell ill in March 2009. At the same time and unknown to us, many patients with similar clinical manifestations were admitted to hospitals in China. The Chinese cases—identified between March and July 2009—were recently reported to have been infected with a tick-born strain of bunyavirus, a new disease. The virus infection was documented in patients from central China and the region that shares the border with North Korea. The clinical manifestations, the time of disease onset, and geographical link of the patient with the region in which the disease is endemic suggest that the patient had SFTS bunyavirus infection.

1. Introduction

Severe fever and thrombocytopenia syndrome (SFTS) is a newly identified disease in China that is caused by a strain of bunyavirus. The disease is characterized by fever, thrombocytopenia, leucopenia, bleeding, and multiorgan dysfunction and has 30% mortality rate. It is transmitted by a tick and has not been reported outside China. The clinical and epidemiological description of the disease in English literature is sparse [1].

2. Case Presentation

A previously healthy 57-year-old North Korean male working in Dubai, United Arab Emirates (UAE), developed an acute hemorrhagic stroke in March 2009. There was no history of trauma, abuse of tobacco or alcohol, exposure to toxic fumes or dust, or traveling outside UAE during the last 12 months. On physical examination he was drowsy and moving all four extremities. Temperature was normal, blood pressure 220/116 mmHg, and heart rate 98 per minute. CT scan of the brain showed thalamic hemorrhage with blood extension into the ventricular system and CT angiography showed no evidence of an aneurysm. The patient was intubated, chest tube was placed because of a left pneumothorax at the time of intubation. Blood pressure required control with labetolol only for initial few days. On admission, hemoglobin was 16.6 g/dL, neutrophils $8.9 \times 10^9/L$, lymphocytes $0.8 \times 10^9/L$ and platelets $130 \times 10^9/L$. Within 48 h, patient developed fever, severe neutropenia, thrombocytopenia, and a more profound lymphocytopenia (Figure 1) and skin and lung bleeding. Coagulation tests were normal. Bone marrow examination findings are shown in Figure 2. Toxic screen was negative. The flow cytometry disclosed normal CD8 and low CD3, CD4, and CD19 cell counts; IgG level was decreased. Pneumonia and K. pneumoniae sepsis developed but there was no evidence of disseminated intravascular coagulation, hemolysis or renal impairment. Treatment with Tazocine, immunoglobulins, granulocyte-colony stimulating factor, steroids, and interleukin-11 was commenced. CT scan of the chest showed bilateral pneumothorax, lung bullae, and consolidation; however, blood oxygenation of
Clinical manifestations of SFTS is not well documented in English language literature. Cerebral hemorrhage in the patient could have been due to a virus-induced vasculitis [4–6]. Vasculitis associated with ANCA autoantibodies was excluded with negative tests [7]. CT angiography may not detect small vasculitic changes and the absence of aneurysm does not exclude vasculitis. Hypertension in our patient is an unlikely cause of cerebral hemorrhage and more likely an immediate reaction to an increased intracerebral pressure from bleeding; patient subsequently neither had hypertension nor the signs of its preexistence. Transient thrombocytopenia, neutropenia, and lymphocytopenia were most likely the consequence of virus infection as well because evidence does not support other possible causes: multisystem diseases, drugs, and toxins [8]. Bone marrow findings are also consistent with viral infection (Figure 2). Several viral infections could produce lymphocytopenia and low IgG level via “cytokine storm” that is also associated with a depression of granulocyte and monocyte counts, both decreased in our patient [9–14]. Bacterial sepsis in the patient could produce neutropenia and thrombocytopenia but this is excluded by the presence of cytopenias prior to the development of bacterial infection. Similarly, stroke-induced immunosuppression may produce neutropenia but thrombocytopenia, myositis, hepatitis and Guillain–Barre neuropathy are not part of this syndrome [15]. Acute hepatitis and myositis could be caused by several types of viruses but repeated tests for those agents were negative. The type and doses of medications which were given to the patient are not strongly associated with the development of hepatitis, and myositis. Similarly, K. pneumoniae infection is unlikely a cause of myositis [16–18]. Further, there was no evidence of primary multisystem diseases that could cause hepatitis and myositis. Consequently, unidentified

![Figure 1: Blood cell counts during hospitalization. Abbreviations: IL-11: interleukin-11; G-CSF: granulocyte-colony stimulating factor; Imm.Glob: human immunoglobulins.](image)

3.2. Clinical Manifestations. The full spectrum of clinical manifestations of SFTS is not well documented in English language literature. Cerebral hemorrhage in the patient could have been due to a virus-induced vasculitis [4–6]. Vasculitis associated with ANCA autoantibodies was excluded with negative tests [7]. CT angiography may not detect small vasculitic changes and the absence of aneurysm does not exclude vasculitis. Hypertension in our patient is an unlikely cause of cerebral hemorrhage and more likely an immediate reaction to an increased intracerebral pressure from bleeding; patient subsequently neither had hypertension nor the signs of its preexistence. Transient thrombocytopenia, neutropenia, and lymphocytopenia were most likely the consequence of virus infection as well because evidence does not support other possible causes: multisystem diseases, drugs, and toxins [8]. Bone marrow findings are also consistent with viral infection (Figure 2). Several viral infections could produce lymphocytopenia and low IgG level via “cytokine storm” that is also associated with a depression of granulocyte and monocyte counts, both decreased in our patient [9–14]. Bacterial sepsis in the patient could produce neutropenia and thrombocytopenia but this is excluded by the presence of cytopenias prior to the development of bacterial infection. Similarly, stroke-induced immunosuppression may produce neutropenia but thrombocytopenia, myositis, hepatitis and Guillain–Barre neuropathy are not part of this syndrome [15]. Acute hepatitis and myositis could be caused by several types of viruses but repeated tests for those agents were negative. The type and doses of medications which were given to the patient are not strongly associated with the development of hepatitis, and myositis. Similarly, K. pneumoniae infection is unlikely a cause of myositis [16–18]. Further, there was no evidence of primary multisystem diseases that could cause hepatitis and myositis. Consequently, unidentified
Figure 2: Bone marrow study: (a) mild hypocellularity. (b) Positive histiocytes stain for CD68 marker. (c) Myeloid cell line composed mostly of promyelocytes with prominent Golgi apparatus and absent neutrophils and metamyelocytes (maturation arrest). (d) Histiocytes and promyelocyte (center) with a rare histiocyte showing hemophagocytosis.

virus becomes the most likely etiology of hepatitis and myositis. Acute motor axonal neuropathy type of Guillain-Barré syndrome was present in our patient and was related in the past to several bacterial and viral infections. However, none of our repeated tests were positive for these infections. Further, Guillain-Barré syndrome was reported in patient with suppressed immune function by drugs, HIV, and CMV but those causes were excluded in our transiently immunocompromised patient [19].

In summary, clinical manifestations in our patient are best explained by systemic viral infection. We did not find in literature such a combination of manifestations in a single patient. The presence of acute thrombocytopenia, neutropenia, lymphocytopenia, bleeding, and multiorgan dysfunction was all reported in patients with SFTS bunyavirus infection [1]. The absence of high fever on admission argues against SFTS in our patient. However, temperature increased once thrombocytopenia and leucopenia developed despite administration of steroids.

4. Conclusion

Clinical manifestations and spatiotemporal epidemiology of the disease suggest diagnosis of SFTS bunyavirus infection.

References

[1] X. J. Yu, M. F. Liang, S. Y. Zhang et al., “Fever with thrombocytopenia associated with a novel bunyavirus in China,” The New England Journal of Medicine, vol. 364, no. 16, pp. 1523–1532, 2011.
[2] O. Ergonul, “Crimean-Congo haemorrhagic fever,” The Lancet Infectious Diseases, vol. 6, no. 4, pp. 203–214, 2006.
[3] P. Brouqui, “Arthropod-borne diseases associated with political and social disorder,” Annual Review of Entomology, vol. 56, pp. 357–374, 2011.
[4] P. O’Charoen, J. R. Hesselink, and J. F. Healy, “Cerebral aneurysmal arteriopathy in an adult patient with acquired immunodeficiency syndrome,” American Journal of Neuroradiology, vol. 28, no. 5, pp. 938–939, 2007.
[5] J. J. Alexander, A. S. Lasky, and W. D. Graf, “Stroke associated with central nervous system vasculitis after West Nile virus infection,” Journal of Child Neurology, vol. 21, no. 7, pp. 623–625, 2006.
[6] C. C. Linnemann and M. M. Alvira, “Pathogenesis of varicella-zoster angiitis in the CNS,” Archives of Neurology, vol. 37, no. 4, pp. 239–240, 1980.
[7] C. G. M. Kallenberg, “Antineutrophil cytoplasmic autoantibody-associated small-vessel vasculitis,” Current Opinion in Rheumatology, vol. 19, no. 1, pp. 17–24, 2007.
[8] J. W. Williams, “Lymphocytopenia,” in Hematology, J. W. Williams, E. Beutler, J. A. Erslev, and A. M. Lichtman, Eds., pp. 964–966, McGraw-Hill, New York, NY, USA, 4th edition, 1990.

[9] A. Summerfield, M. Alves, N. Ruggli, M. G. M. De Bruin, and K. C. McCullough, “High IFN-α responses associated with depletion of lymphocytes and natural IFN-producing cells during classical swine fever,” Journal of Interferon and Cytokine Research, vol. 26, no. 4, pp. 248–255, 2006.

[10] A. R. Stacey, P. J. Norris, L. Qin et al., “Induction of a striking systemic cytokine cascade prior to peak viremia in acute human immunodeficiency virus type 1 infection, in contrast to more modest and delayed responses in acute hepatitis B and C virus infections,” Journal of Virology, vol. 83, no. 8, pp. 3719–3733, 2009.

[11] G. D. Barlow and M. W. McKendrick, “Parvovirus B19 causing leucopenia and neutropenia in a healthy adult,” Journal of Infection, vol. 40, no. 2, pp. 192–195, 2000.

[12] R. T. Schooley, P. Densen, and D. Harmon, “Antineutrophil antibodies in infectious mononucleosis,” American Journal of Medicine, vol. 76, no. 1, pp. 85–90, 1984.

[13] P. Colson, C. Foucault, M. Mokhtari, and C. Tamalet, “Severe transient neutropenia associated with acute human immunodeficiency virus type 1 infection,” European Journal of Internal Medicine, vol. 16, no. 2, pp. 120–122, 2005.

[14] E. Dalpa, E. Kourepini, H. Papadaki, G. D. Elioopoulos, D. A. Spandidos, and G. Sourvinos, “Cytomegalovirus as a potential cause in the pathogenesis of chronic idiopathic neutropenia,” Journal of Clinical Virology, vol. 36, supplement 2, p. S14, 2006.

[15] U. Dirnagl, J. Klehmet, J. S. Braun et al., “Stroke-induced immunodepression: experimental evidence and clinical relevance,” Stroke, vol. 38, no. 2, pp. 770–773, 2007.

[16] T. Klopstock, “Drug-induced myopathies,” Current Opinion in Neurology, vol. 21, no. 5, pp. 590–595, 2008.

[17] N. F. Crum-Cianflone, “Bacterial, fungal, parasitic, and viral myositis,” Clinical Microbiology Reviews, vol. 21, no. 3, pp. 473–494, 2008.

[18] T. Karpathios, M. Kostaki, S. Drakonaki et al., “An epidemic with influenza B virus causing benign acute myositis in ten boys and two girls [4],” European Journal of Pediatrics, vol. 154, no. 4, pp. 334–336, 1995.

[19] R. A. Hughes and D. R. Cornblath, “Guillain-Barré syndrome,” The Lancet, vol. 366, no. 9497, pp. 1653–1666, 2005.