



CASE REPORT

Immune Thrombocytopenia as a Primary Sign of Relapse in Hodgkin Lymphoma: A Case Report

Hossein Karami¹, Mohammad Naderisorki^{1*}, Maryam Ghasemi², Sayed Mohammad Sakhaei³

¹Thalassemia Research Center, Department of Pediatrics Hematology and Oncology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

²Associate Professor of Pathology, Immunogenetics Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

³Assistant Professor of Interventional Radiology, Department of Radiology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

ARTICLE INFO

Article History:

Received: 25.01.2019

Accepted: 28.03.2019

Keywords:

Hodgkin lymphoma

Immune thrombocytopenia

Relapse

Autoimmunity

*Corresponding author:

Mohammad Naderisorki,
Bou Ali Sina Hospital, Mazandaran
University of Medical Sciences,
Pasdaran Boulevard, P.O. Box: 48158-
38477, Sari, Iran
Tel/Fax: +98 11 33342331
Email: dr.naderisorki@gmail.com

ABSTRACT

Hodgkin lymphoma (HL) as a malignant tumor presents with lymphadenopathy and systemic complaints. The origin of this tumor is mostly suggested to be B lymphocytes. There is a close relationship between autoimmunity and HL, but the mechanism of this immune syndromes is unclear. Immune thrombocytopenia (ITP) is the most common autoimmune syndrome which may present before, at the same time, and even after treatment of the HL. We present a case of ITP as a primary sign of relapse of HL in a 15-year-old boy after complete treatment of HL.

Please cite this article as: Karami H, Naderisorki M, Ghasemi M, Sakhaei SM. Immune Thrombocytopenia as a Primary Sign of Relapse in Hodgkin Lymphoma: A Case Report. IJBC 2019; 11(2): 72-74.

Introduction

Hodgkin lymphoma (HL) is a malignant tumor originated from B lymphocytes which is characterized by presence of giant multinucleated Reed-Sternberg (RS) cells.¹ The peak incidence of the disease in developing countries is before adolescence; whereas in industrialized countries has a unique bimodal age distribution, early peak occurs under 20s and the second one after the age of 50 years.²

Patients with HL present with lymphadenopathy and systemic complaints. The lymph node enlargement is usually painless, commonly is located in the neck and supraclavicular areas. Another common presentation of lymphadenopathy is enlargement of mediastinal lymph nodes.³

Unexplained fever, weight loss of 10% within 6 months and night sweats are three specific constitutional (B)

symptoms. Patients with these three symptoms usually have poor prognosis.⁴ In up to 40% patients with HL, we can find Epstein-Barr virus (EBV)-encoded RNA in RS cells.⁵ Also, there is a close relationship between autoimmune phenomena and HL but the mechanism is unclear due to its rarity.⁶

Despite new treatment strategies, approximately 25 % of patients may relapse and most of the relapses are detected during routine imaging follow up.⁷ We report a case of immune thrombocytopenia purpura (ITP) in a 15-year-old boy after remission of HL. In fact, ITP heralded relapse of HL in this teenager.

Case Presentation

The patient was a 15-year-old boy admitted with supraclavicular lymphadenopathies on both sides. He didn't show group B signs or symptoms. Physical

examination revealed multiple lymphadenopathy in right and left supraclavicular regions with maximum diameter of 3 cm. Hepatosplenomegaly was absent.

Laboratory data showed WBC $10.6 \times 10^3/\mu\text{L}$ Hemoglobin 13.3 g/dL, platelet $312 \times 10^3/\mu\text{L}$, neutrophils 65%, lymphocytes 33%, ESR 22 mm/h, C-reactive protein (CRP) 11.2 mg/L and LDH 322 U/L. Brucella wright and 2ME tests, Tuberculin skin test, Epstein–Barr virus (EBV) antibodies and serology for toxoplasmosis were negative.

Spiral computed tomography scan (CT scan) showed multiple adenopathies up to 35 mm in greater axis at left supraclavicular region, one lymph node up to 17 mm at right supraclavicular region and multiple adenopathies in upper anterior mediastinum.

Excisional biopsy of a left supraclavicular lymph node found classic Reed-Sternberg cells in favor of Hodgkin lymphoma.

Patient was treated with 6 courses of COPP/ABV Protocols for Pediatric Classical Hodgkin Lymphoma.⁸ After he completed chemotherapy, he received additional low-dose involved field radiation therapy. At the end of the treatment, spiral chest CT scan was normal and there was no evidence of remnant disease.

Three month later, fluoro-D-glucose-positron emission tomography (FDG-PET) was performed and there was no metabolically active lesion throughout the body, indicative of complete metabolic response to the treatment.

About two month later, patient admitted with abrupt onset of skin petechiae and ecchymoses. There were no fever and night sweats. Physical examination showed was unremarkable. Laboratory data showed: WBC $2.96 \times 10^3/\mu\text{L}$, lymphocytes 30%, neutrophils 50%, monocytes 10%, Eosinophils 10%, Hemoglobin 11.5 g/dL and platelet $5 \times 10^3/\mu\text{L}$. LDH was 366 U/L and ESR was 25 mm/h. Abdominopelvic ultrasound and Spiral CT scan of neck, chest, abdomen and pelvis were negative. The patient was diagnosed with a preliminary diagnosis of ITP. Bone Marrow aspiration showed increased megakaryocytes. Treatment was started with Intravenous immunoglobulin (IVIG) 1 g/kg/day for two days. Five days later platelet count was $5 \times 10^3/\mu\text{L}$. Prednisolone 2 mg/kg/day was started on day 6, one week later platelet count increased to $11 \times 10^3/\mu\text{L}$. One month after receiving methylprednisolone, platelet count raised to $90 \times 10^3/\mu\text{L}$.

About one month after presentation of ITP, while the platelet was $87 \times 10^3/\mu\text{L}$, the patient was admitted with cervical lymphadenopathy (3 x 4 cm in size). Spiral CT scan of neck, chest and abdomen showed multiple lymphadenopathies in left cervical and left supraclavicular regions. Excisional biopsy was scheduled. Pathology was indicative of recurrent HL (positive for CD15 and CD30). The patient was treated with gemcitabine and vinorelbine. So far, and after 4 courses, the disease is stable, there is no sign of thrombocytopenia and platelet count is $234 \times 10^3/\mu\text{L}$. Written informed consent was obtained from the patients' parents for publication of this case report.

Discussion

There is a clear association between autoimmune phenomena and lymphoproliferative disorders.⁶ In

addition, autoimmune hemolytic anemia, neutropenia and thrombocytopenia (ITP) have been reported in association with HL. ITP present in 1-2% of patients with HL before, simultaneously and even after treatment of the disease.⁸ On the other hand, an epidemiological study in Scandinavia showed an increased risk of HL in patients with previous history of ITP.⁹ The mechanism of this association is cross-reaction between platelet and tumor-associated antigens; another theory of this phenomenon is the presence of immune complex on platelet membranes.¹⁰ But the onset of thrombocytopenia as a paraneoplastic syndrome requires further investigation.¹¹

The presence of thrombocytopenia may make it difficult to diagnose HL. S. Marino et al. reported a 16-year-old boy with fever, petechiae and ecchymoses. Bone marrow aspiration was normal with increased megakaryocytes. The patient was treated with corticosteroids upon a diagnosis of ITP; however, further workup revealed multiple masses both in the chest and abdomen. Laparoscopic biopsy was performed which histologic pathology was regarded as HL.¹¹ There are other reports of the simultaneous occurrence of ITP and HL which have caused difficulties in diagnosis of the HL mainly due to receiving any kind of treatment before the correct diagnosis.^{12,13}

Treatment and response to treatment of ITP in patients with HL is similar to the other cases of ITP. In addition, ITP may occur after completion of therapy for HL, essentially without any association with relapse.⁸

In a study on 1029 patients with HL, 3 cases of ITP was found at the time of diagnosis of HL and 3 other cases after remission of the disease and during the follow up. None of the last three cases relapsed. They concluded that ITP after completion of treatment of HL is an independent process which does not increase the risk of relapse.¹⁴

Conclusion

There are few reports of the simultaneous onset of the ITP and HL. The occurrence of ITP after cure of HL seems an independent phenomenon which necessarily does not associate with relapse. However, according to this case, we need to follow cases of ITP following cure of HL more carefully in order to detect early relapse.

Conflict of Interest: None declared.

References

1. Bräuninger A, Schmitz R, Bechtel D, Renné C, Hansmann ML, Küppers R. Molecular biology of Hodgkin's and Reed/Sternberg cells in Hodgkin's lymphoma. *Int J Cancer*. 2006; 118(8):1853-61. doi:10.1002/ijc.21716. PubMed PMID: 16385563.
2. Hjalgrim H, Engels EA. Infectious aetiology of Hodgkin and non-Hodgkin lymphomas: a review of the epidemiological evidence. *J Intern Med*. 2008; 264(6):537-48. doi: 10.1111/j.1365-2796.2008.02031.x. PubMed PMID: 19017178.
3. Ekstrand BC, Horning SJ. Hodgkin's disease. *Blood Rev*. 2002; 16(2):111-7. PubMed PMID: 12127954.
4. Gobbi PG, Cavalli C, Gendarini A, Crema A,

- Ricevuti G, Federico M, et al. Reevaluation of prognostic significance of symptoms in Hodgkin's disease. *Cancer*. 1985;56(12):2874–80. PubMed PMID: 4052959.
5. Weiss LM. Epstein-Barr virus and Hodgkin's disease. *Curr Oncol Rep*. 2000; 2(2):199–204. PubMed PMID: 11122844.
 6. Ehrenfeld M, Abu-Shakra M, Buskila D, Shoenfeld Y. The dual association between lymphoma Blood Cells Mol Dis. 2001; 27(4):750–6. doi: 10.1006/bcmd.2001.0442. PubMed PMID: 11778659.
 7. Evens AM, Hutchings M, Diehl V. Treatment of Hodgkin lymphoma: the past, present, and future. *Nat Clin Pract Oncol*. 2008; 5:543–56. PubMed PMID: 18679394.
 8. Pizzo PA, Poplack DG, Adamson PC, Blaney SM, Helman L. *Principles and Practice of Pediatric Oncology*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health. 2016.
 9. Landgren O, Engels EA, Pfeiffer RM, Gridley G, Mellemkjaer L, Olsen JH, et al. Autoimmunity and susceptibility to Hodgkin lymphoma: a population-based case-control study in Scandinavia. *J Natl Cancer Inst*. 2006; 98(18):1321–30. doi: 10.1093/jnci/djj361. PubMed PMID: 16985251.
 10. Bellone JD, Kunicki TJ, Aster RH. Immune thrombocytopenia associated with carcinoma. *Ann Intern Med*. 1983; 99(4):470–2. doi: 10.7326/0003-4819-99-4-470. PubMed PMID: 6625379.
 11. Marino S, Di Cataldo A, Magro G, D'Amico S, La Spina M, Di Benedetto V, et al. A difficult diagnosis of Hodgkin lymphoma due to immune thrombocytopenia. *Clin Case Rep*. 2015; 3(3):179–82. doi: 10.1002/ccr3.176. PubMed PMID: 25838909. PubMed Central PMCID: PMC4377251.
 12. Ertem M, Uysal Z, Yavuz G, Gözdaşoğlu S. Immune thrombocytopenia and hemolytic anemia as a presenting manifestation of Hodgkin disease. *Pediatr Hematol Oncol*. 2000; 17(2):181–5. doi: 10.1080/088800100276550. PubMed PMID: 10734662.
 13. Shah SJ, Warriar RP, Ode DL, Lele HE, Yu LC.. Immune thrombocytopenia and hemolytic anemia associated with Hodgkin disease. *J Pediatr Hematol Oncol*. 1996; 18(2):227–9. doi: 10.1097/00043426-199605000-00029. PubMed PMID: 8846146.
 14. Dimou M, Angelopoulou MK, Pangalis GA, Georgiou G, Kalpadakis C, Pappi V, et al. Autoimmune hemolytic anemia and autoimmune thrombocytopenia at diagnosis and during follow-up of Hodgkin lymphoma. *Leuk Lymphoma*. 2012; 53(8):1481–7. doi: 10.3109/10428194.2012.660628. PubMed PMID: 22280533.