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Case Report

Hodgkin Lymphoma on Hemodialysis Successfully Treated with Extended Courses of Brentuximab Vedotin

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Keywords
Castleman disease · Doxorubicin, bleomycin, vinblastine, and dacarbazine · Anti-CD30 therapy · Monomethyl auristatin E · End-stage renal disease

Abstract
Chemotherapy for hemodialysis (HD) patients is a challenging situation because HD patients are generally frail, and the pharmacokinetics and pharmacodynamics of most chemotherapeutics in HD patients are unknown. We report a classical Hodgkin lymphoma (cHL) patient successfully treated with 34 courses of brentuximab vedotin (BV) monotherapy, of which 30 courses were carried out during HD. Although grade 2 peripheral sensory neuropathy and one occasion of febrile neutropenia were observed, treatment was well-tolerated overall and effective. This is the first report of successful BV administration in a cHL patient on HD, and also the first to report efficacy and safety of extended courses of BV in an HD patient. Treatment options for cHL in the HD patient are limited, and extended courses of BV monotherapy may be an optimal treatment approach for some patients.

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Introduction

Chemotherapy for the hemodialysis (HD) patient is a challenging situation. We report a classical Hodgkin lymphoma (cHL) patient successfully treated with 34 courses of brentuximab vedotin (BV) monotherapy, of which 30 courses were carried out during HD. This is the first report of successful BV administration in a cHL patient on HD, and also the first to report efficacy and safety of extended courses of BV in an HD patient.

Case Presentation

A 69-year-old man with a history of chronic kidney disease was referred to our department for persisting fever, fatigue, and thoracic and abdominal lymph node swelling measuring 10–20 mm in size. Abdominal lymph node biopsy showed slightly regressed germinal centers, hypervascularization, and expanded interfollicular areas with plasmacytosis. HHV8 was negative. Blood tests showed low Hb of 9.9 g/dL, elevated CRP of 17.4 mg/dL, no active Epstein-Barr virus and HIV infections, no autoimmune disease, and elevated serum IL-6 of 109 pg/mL (normal range: <4.0 pg/mL). Pathological findings and clinical features were compatible with idiopathic multicentric Castleman disease, and tocilizumab administration was initiated and continued every 2 weeks from March 2014. Fever resided, and his general condition improved remarkably. However, fever recurred from January 2018, and fatigue and loss of appetite lead to hospitalization. Laboratory data showed Hb 7.8 g/dL, normal white blood cell and platelet counts, BUN 66 mg/dL, Cre 4.72 mg/dL, and CRP 10.58 mg/dL. CT scans revealed swelling of abdominal and inguinal lymph nodes, and biopsies from both sites revealed mixed cellularity cHL. His poor general status including impaired renal function led to the decision that standard doxorubicin, bleomycin, vinblastine, and dacarbazine therapy would be intolerable, and brentuximab vedotin (BV) monotherapy was initiated from April 2018 at 1.8 mg/kg every 3 weeks. In order to evade tumor lysis syndrome, course 1 of BV was divided and slowly infused at 0.9 mg/kg/24 h on days 1 and 2, and HD was initiated on days 3 and 4 and continued 3 days a week. Although he developed febrile neutropenia (FN) during course 1, his general condition improved remarkably and fever and high CRP levels resided, and he was able to withdraw from HD by course 2 of BV. Because he experienced FN during course 1, BV dose was reduced 50% to 0.9 mg/kg/30 min on day 1 only approximately every 3 weeks from course 2. Tocilizumab administration was soon terminated, but inflammatory symptoms did not relapse. CT evaluation after course 4 showed a partial response of cHL. However, at the same time, renal function again deteriorated and intermittent HD three times a week was reinitiated and continued thereafter. Because BV was well-tolerated in recent courses, BV dose was escalated to 1.8 mg/kg/30 min from course 8, but no exceptional adverse events besides grade 1 peripheral sensory neuropathy were observed. PET-CT after BV course 16 showed that he maintained a partial response, but the remaining multiple PET-positive lesions were assumed to be viable. Because of his state of HD, it was judged that continuation of BV was safer than exploring other treatment methods. Peripheral sensory neuropathy progressed to grade 2 after BV course 21, and treatment was suspended. However, 2 months later, fever and high CRP levels recurred, and CT scans revealed systemic exacerbation of lymphadenopathy. BV was reinitiated, and CT after course 24 again showed regression of lymphadenopathy. However, the cHL eventually progressed even under BV administration, BV was terminated after course 34, and the patient moved on to palliative care at another hospital.

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Discussion

BV is an antibody-drug conjugate, consisting of a chimeric monoclonal anti-CD30 antibody covalently bonded to the microtubule-disrupting agent, monomethyl auristatin E. Clinical trials of BV monotherapy in relapsed/refractory cHL and systemic anaplastic large cell lymphoma (sALCL) patients have shown efficacy and safety when administered for a maximum of 16 courses [1, 2]. Two studies have shown clinical benefit and tolerability of retreatment or extended courses of BV. For patients with pretreated cHL or sALCL, Forero-Torres et al. [3] reported a median of 24 courses of BV (range: 17–42 courses) administered to 19 patients, and Fukuhara et al. [4] reported a median of 18 courses of BV (range: 5–46 courses) administered to 28 patients; both studies concluded that extended courses of BV may be an optimal treatment option for some patients [3, 4].

Zhao et al. [5] reported that treatment with 1.2 mg/kg of BV resulted in a 1.9-fold increase of monomethyl auristatin E exposure in patients with creatinine clearance <30 mL/min, and they rationalized that dose modifications may be considered for patients with severe renal dysfunction. However, pharmacokinetic studies of BV in HD patients are lacking, and thus the optimal dose and timing of BV administration in HD patients is unknown. Under these circumstances, reports of actual BV administration and treatment outcomes are extremely valuable for decision making, but only one report of BV administration in an HD patient exists [6]. Nanni et al. [7] reported successful treatment of an sALCL patient on HD with BV monotherapy every 3 weeks for 16 courses, and they reduced the dose of BV from the standard 1.8 mg/kg to 1.2 mg/kg according to the results reported by Zhao et al. [5]. However, we demonstrate through the presented case that an extended 34 courses of BV administration (30 courses administered under HD), mostly at a dose of 1.8 mg/kg, was both effective and feasible in an HD patient. Although the patient experienced FN during course 1 of BV, and progression of peripheral sensory neuropathy to grade 2 after course 21, no unexpected adverse events were observed. The patient was reintroduced to HD after course 4 of BV, but it was the opinion of the nephrology experts of our institution that the direct cause of need for maintenance HD was not due to BV administration, and that renal failure had already reached the point of no return before BV treatment. The optimal timing of BV administration in relation to HD sessions is also unknown, but Nanni et al. [7] administered BV 24 h before HD sessions, and we administered BV basically after HD or on non-HD days (except for course 1).

Castleman disease coexisting with cHL has been repeatedly reported in the literature, and some researchers consider it as a distinct entity [8]. Although Castleman disease and cHL were not diagnosed concomitantly in the presented case, we speculate that the presented case may have also been one of such cases.

In conclusion, we report the first case of cHL on HD treated with an extended 34 courses of BV monotherapy, and treatment was both effective and tolerable. Treatment options for cHL in the HD patient are limited, and extended courses of BV monotherapy may be an optimal treatment approach for some patients, but our findings need to be confirmed in a larger number of patients.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

Norio Komatsu received grants and honoraria from Takeda Pharmaceutical Company. All other authors have no conflicts of interest to declare.

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Author Contributions

Manuscript writing: Ayana Uchimura and Hajime Yasuda. Data collection and interpretation: Jun Ando, Yasunori Ota, Makoto Sasaki, Tomoiku Takaku, Yutaka Tsukune, Miyuki Tsutsui, Yoko Edahiro, Naoki Watanabe, and Tomonori Ochiai. Literature research: Ayana Uchimura, Hajime Yasuda, and Yasunori Ota. Manuscript revision: Norio Komatsu and Miki Ando.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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