CASE REPORT

Durvalumab-Induced Secondary Pure Red Cell Aplasia Successfully Treated With Cyclosporin

Kageaki Watanabe, MD,* Rui Kitadai, MD, Shingo Kitagawa, MD, Takashi Toya, MD, Yukio Hosomi, MD, PhD

Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan

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Introduction

Immune checkpoint inhibitors, such as anti–programmed cell death protein-1 (anti–PD-1) and anti–programmed death-ligand 1 (anti–PD-L1) antibodies, have beneficial effects on many cancers, including lung cancer. Pure red cell aplasia (PRCA) is a rare syndrome defined by a normocytic normochromic anemia with severe reticulocytopenia and marked reduction or absence of erythroid precursors from the bone marrow.[1] We present a case of durvalumab-induced secondary PRCA successfully treated with cyclosporin.

Case Presentation

A 70-year-old Japanese man without anemia was diagnosed as having stage IIIB lung squamous cell carcinoma and had received four cycles of cisplatin and vinorelbine chemotherapy concurrently with definitive radiotherapy (60 Gy). As partial response was maintained, we started durvalumab, a human IgG1 monoclonal antibody. Two weeks after five cycles of durvalumab, a steroid was started for grade 2 radiation pneumonitis. Chest radiograph result revealed improved pneumonitis but worsened dyspnea.

Blood testing result revealed normocytic normochromic anemia (hemoglobin, 7.8 g/dL), and reticulocytes were markedly reduced at +12 weeks (Fig. 1), although white blood cell and platelet counts were normal. Durvalumab was discontinued and red blood cell transfusions were continued for 3 weeks, but his anemia worsened (hemoglobin, 6.0 g/dL) at +15 weeks, and there was no elevation of reticulocytes. Bone marrow testing result revealed normocellular marrow with decreased erythroid cells and no dysplasia. Erythropoietin level was high (3410 IU/L). Without parvovirus B19 infection or newly initiated drugs except for durvalumab, we diagnosed him as having PRCA as a durvalumab-induced immune-related adverse event (irAE).

We continued red blood cell transfusions for 1 month, but the anemia did not improve. We started prednisone (1 mg/kg/day) at +21 weeks, without any improvement. Cyclosporin (target trough levels of 150–250 ng/mL) was added at +23 weeks. His reticulocytes were elevated for 1 week, and his anemia quickly improved and became transfusion independent. The cyclosporin dose was adjusted, and the corticosteroid was reduced accordingly. There was no recurrence of anemia, but recurrence of bone and liver metastases was recognized on subsequent computed tomography.

Discussion

The frequency of hematologic irAEs with PD-1 or PD-L1 is only 0.5%.[2] The frequency of PRCA is reportedly 3% of hematologic irAEs.[2] There are a few reports of PRCA as irAEs after administration of PD-1 and

*Corresponding author.

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Address for correspondence: Kageaki Watanabe, MD, Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, 3-18-22, Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan. E-mail: kageakiwatanabe@cick.jp

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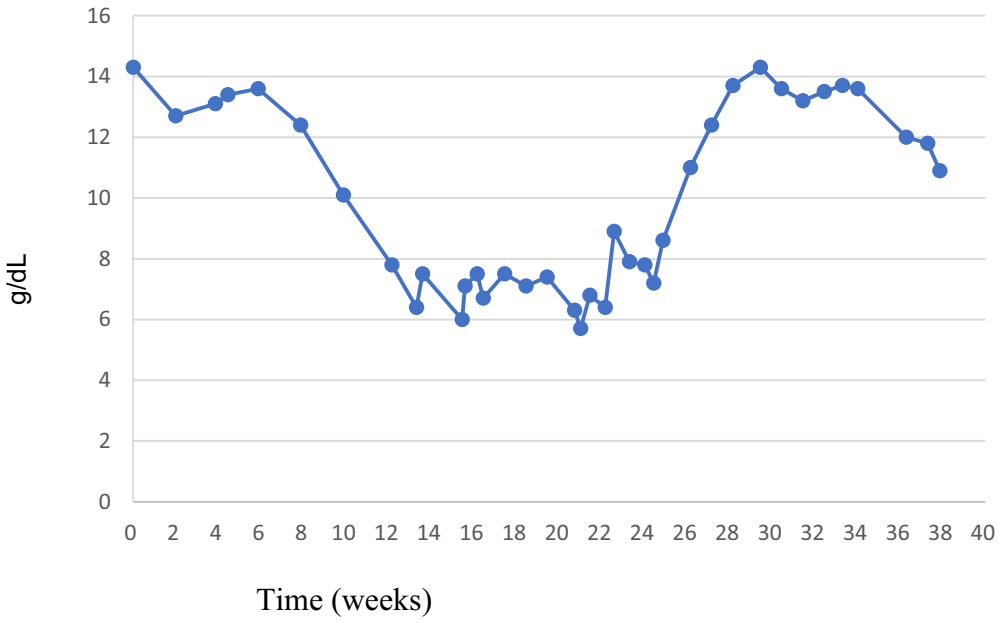

Figure 1. Hemoglobin level during and after treatment with durvalumab.

CTLA-4 antibodies to treat melanomas.[3,4] There are no reports of PRCA as an irAE in lung cancer and none about PRCA as an irAE associated with the PD-L1 antibody. If symptoms caused by irAE cannot be controlled by steroids, infliximab, cyclophosphamide, intravenous immunoglobulin, or mycophenolate mofetil are added as immunosuppressants.

Earlier, when PRCA as an irAE was not improved by steroids, immunosuppressants were often added.[3,4] For idiopathic PRCA, cyclosporine is highly effective.[1] In our case, cyclosporine quickly improved the anemia.

Cyclosporine for PRCA as an irAE has not been previously reported. It is unclear whether PRCA caused by an immune checkpoint inhibitor and idiopathic PRCA develop by the same mechanism. In our case, cyclosporine improved PRCA. Addition of cyclosporine to reduce the durvalumab effect may be considered. There is no clear consensus on the management of immunosuppressive agents for irAE. More information is needed regarding optimal treatment.

References

1. Means RT Jr. Pure red cell aplasia. *Hematology Am Soc Hematol Educ Program*. 2016;2016:51–56.
2. Delanoy N, Michot JM, Comont T, et al. Haematological immune-related adverse events induced by anti-PD-1 or anti-PD-L1 immunotherapy: a descriptive observational study. *Lancet Haematol*. 2019;6:e48–e57.
3. Nair R, Gheith S, Nair SG. Immunotherapy-associated hemolytic anemia with pure red-cell aplasia. *N Engl J Med*. 2016;374:1096–1097.
4. Gordon IO, Wade T, Chin K, Dickstein J, Gajewski TF. Immune-mediated red cell aplasia after anti-CTLA-4 immunotherapy for metastatic melanoma. *Cancer Immunol Immunother*. 2009;58:1351–1353.