location in acute myeloid leukemia. Leuk Res 2003;27:363-6.
7. Manabe M, Nakamura K, Inaba A, et al. A rare t(4;12)(q12;p13) in an adolescent patient with acute myeloid leukemia. Cancer Genet Cytogenet 2010;200:70-2.
8. Al-Kali A, Cherry M, Kimmell K, et al. A case of acute myeloid leukemia initially treated as chronic lymphocytic leukemia: what do we know about t(4;12)(q12;p13)? Cancer Genet Cytogenet 2010;203:348-51.
9. van der Plas DC, Dekker I, Hagemeijer A, Hooijkaas H, Hählen K. 12p chromosomal aberrations in precursor B childhood acute lymphoblastic leukemia predict an increased risk of relapse in the central nervous system and are associated with typical blast cell morphology. Leukemia 1994;8:2041-6.
10. Ohyashiki K. Nonrandom cytogenetic changes in human acute leukemia and their clinical implications. Cancer Genet Cytogenet 1984;11:453-71.
11. Berger R, Flandrin G, Bernheim A, et al. Cytogenetic studies on 519 consecutive de novo acute nonlymphocytic leukemias. Cancer Genet Cytogenet 1987;29:9-21.
12. Matutes E, Foroni L, Amin S, et al. 'Pseudo-lymphoid' leukaemia with unusual features: ultrastructural, immunological, cytogenetic and molecular studies. Eur J Haematol 1987;38:303-9.
13. den Nijs van Weert JI, Beverstock GC, Kievits T, Haak HL, Havik-Bogaard FC, Leeksma CH. der(1)t(1;9): a specific chromosome abnormality in polycythemia vera? Cytogenetic and in situ hybridization studies. Cancer Genet Cytogenet 1989;40:121-7.
14. Pui CH, Raimondi SC, Head DR, et al. Characterization of childhood acute leukemia with multiple myeloid and lymphoid markers at diagnosis and at relapse. Blood 1991;78:1327-37.
15. Translocations involving 12p in acute myeloid leukemia: association with prior myelodysplasia and exposure to mutagenic agents. United Kingdom Cancer Cytogenetics Group (UKCCG). Genes Chromosomes Cancer 1992;5:252-4.

Primary acquired chronic pure red cell aplasia refractory to standard treatments: remission with rituximab

TO THE EDITOR: Pure red cell aplasia (PRCA) is a rare syndrome caused by erythropoietic hypoplasia in the absence of leukocytopenia and thrombocytopenia. It is characterized by severe normocytic and reticulocytopenic anemia, with a normally cellular bone marrow (BM) but devoid of erythroblasts [1]. The acquired form of PRCA is a chronic illness that is often diagnosed in conjunction with a variety of diseases [1], such as lymphoproliferative disorders [2], viral infections, autoimmune hemolytic anemia (AIHA) [3], rheumatologic disorders [4], and allogeneic stem cell transplantation [5]. However, this disorder is rarely diagnosed as an idiopathic condition. Acquired PRCA is managed as an immunologically mediated disease, using immunosuppressive therapy (IST) with corticosteroids and cyclosporine A (CSA) as the treatments of first choice [1]. As alternative and salvage treatment, rituximab has been reported to be highly effective [2-5]; however, to the best of our knowledge, no case of idiopathic PRCA managed with this agent has been reported. A 63-year-old woman was diagnosed in June 2003 as having PRCA after the discovery of isolated normocytic and reticulocytopenic anemia, the course of which had been insidious and progressive. All other possible underlying causes of erythroblastopenia were ruled out by appropriate investigations (Table 1); other laboratory and radiological evaluations revealed no abnormal findings. The patient had required transfusions of almost 2 units of packed red blood cells (RBC) every 2 to 3 weeks. Once the diagnosis was made, she was started on CSA plus corticosteroids, and soon achieved full recovery from BM erythropoiesis and attained normalization of peripheral blood counts. The patient no longer required transfusions. This was considered complete remission (CR) of PRCA. Therefore, the dosage of CSA was gradually reduced and discontinued. However, there was a progressive loss of response, and CSA was resumed in February 2007 due to a full relapse. The patient achieved a second CR, and the dosage of CSA was carefully tapered. However, the patient experienced progressive chronic renal failure (CRF) in January 2011, which fully resolved after discontinuation of CSA. PRCA recurred soon after, and the patient again required frequent RBC transfusions. When she required approximately 4 RBC units per month, steroids were retried, but without any benefit. Azathioprine was tried without any response. By May 2013, the need for transfusions had reached about 6 RBC units/month, and direct and indirect Coombs blood compatibility

Table 1. Laboratory findings at the PRCA diagnosis.

	Results
Hemoglobin	4.4 g/dL
WBC	4,770/μL
Platelets	227×10^3/μL
MCV	93 fL
MCH	33.2 pg
Reticulocyte	0.04%
Albumin	4.8 g/dL
ALT	31 U/L
AST	35 U/L
Total bilirubin	1.1 mg/dL
Direct bilirubin	0.5 mg/dL
Azotemia	25 mg/dL
Creatinine	0.9 mg/dL
Glucose	92 mg/dL
LDH	195 U/L
PT	13 sec (12.6–15.7)
aPTT	28 sec (26–35)
Fibrinogen	350 mg/mL (220–498)
Direct and indirect antiglobulin tests	Negative

Abbreviations: WBC, white blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenases; PT, prothrombin time; aPTT, activated partial thromboplastin time.

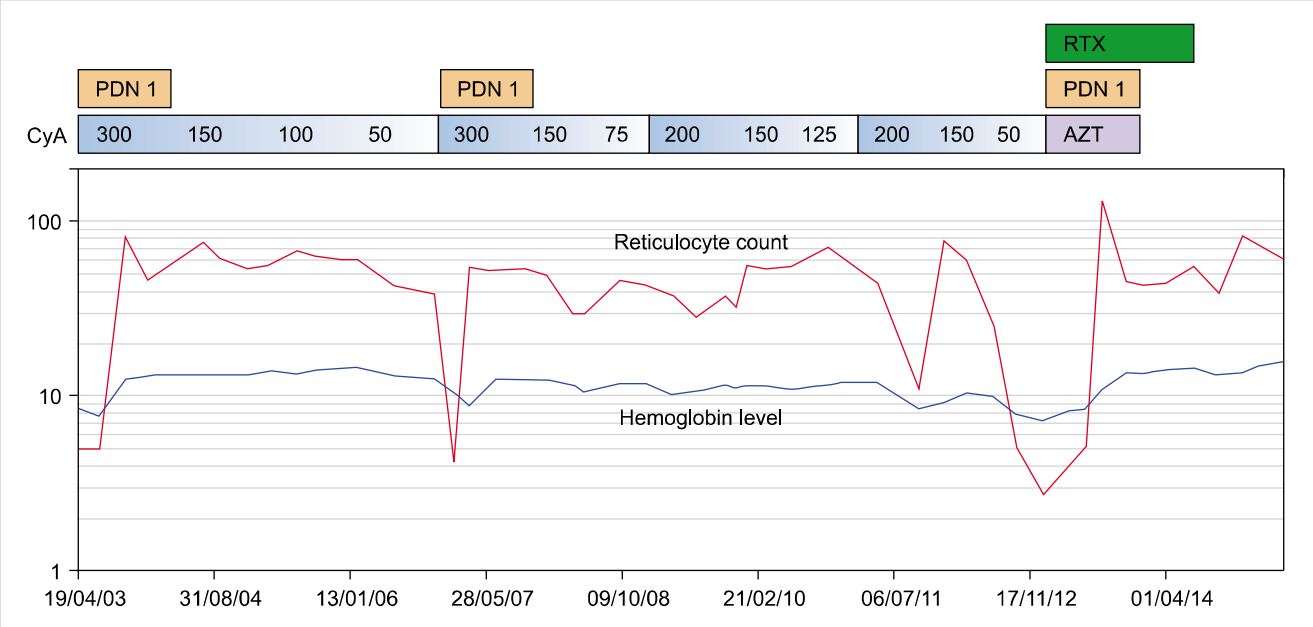

Fig. 1. Treatments and their effects on the patient's hemoglobin (Hb) level and reticulocyte count.
Abbreviations: CyA, oral cyclosporine A (mg/day); RTX, rituximab; PDN 1, oral prednisone 1 mg/m^2/day; AZT, oral azathioprine.

tests became positive with the appearance of anti-IgG autoantibody; therefore, the availability of required transfusions became a concern due the difficulty of finding compatible RBC units. In view of this life-threatening complication and a severe hematological condition refractory to all standard treatments for PRCA [1], rituximab was started as a salvage measure at a dose of 375 mg/m^2/week for a total of 4 cycles, after the patient gave properly informed consent. Given the lack of experience with rituximab in the setting of primary PRCA, this treatment schedule was derived from that reported as safe and effective in patients with PRCA secondary to lymphoproliferative disorders [2]. After the second dose of rituximab, she exhibited a striking rise in her reticulocyte count and an increase in hemoglobin level. Thus, a third CR was achieved and was maintained during the subsequent 24 months (Fig. 1). In conclusion, the present letter describes a case of acquired chronic primary PRCA of idiopathic origin, refractory to standard measures, with remission on rituximab salvage treatment. To the best of our knowledge, this is the first report of idiopathic PRCA managed with rituximab. In our experience, this agent provided important clinical benefits in an elderly patient with a 12-year PRCA history, during which she had become intolerant/unresponsive to the majority of immunosuppressive agents used in this difficult-to-treat disorder. The course of disease and repeated responses to IST pointed to a possible underlying autoimmune pathogenesis. Although this hypothesis has not been proven by extensive clinical and laboratory evaluations; for this case, rituximab was highly effective in inducing long-lasting remission without any adverse effects.

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No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Sawada K, Fujishima N, Hirokawa M. Acquired pure red cell aplasia: updated review of treatment. Br J Haematol 2008;142:505-14.
2. D'Arena G, Vigliotti ML, Dell'Olio M, et al. Rituximab to treat chronic lymphoproliferative disorder-associated pure red cell aplasia. Eur J Haematol 2009;82:235-9.
3. Scaramucci L, Niscola P, Ales M, et al. Pure red cell aplasia associated with hemolytic anemia refractory to standard measures and resolved by rituximab in an elderly patient. Int J Hematol 2008;88:343-4.
4. Gupta RK, Ezeonyeji AN, Thomas AS, Scully MA, Ehrenstein MR, Isenberg DA. A case of pure red cell aplasia and immune thrombocytopenia complicating systemic lupus erythematosus: response to rituximab and cyclophosphamide. Lupus 2011;20:1547-50.
5. Jung SH, Ahn JS, Yang DH, et al. Successful treatment of pure red cell aplasia with rituximab in patients after abo-compatible allogeneic hematopoietic stem cell transplantation. Case Rep Oncol 2012;5:110-3.