

Rituximab's cost for the treatment of primary cold agglutinin disease should not limit its use

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Primary cold agglutinin disease (CAD) is an infrequent lymphoproliferative disorder without any efficient conventional therapy. Its prevalence is comprised from 1/70000 to 1/350000.¹ It may give severe symptoms and reduced quality of life. Because of the haemagglutination most patients experience pallor, acrocyanosis and Raynaud's phenomenon during slight to moderate cold exposure.² It is a serious disease in the context of lymphoma. CAD is characterized by the clonal expansion of CD20+ B cells secreting monoclonal immunoglobulin M.³ Interestingly, thanks to the extent of biotherapies, monoclonal antibodies directed against CD20 antigen (rituximab) have been available for several years and have already been successfully included in the treatment of some hematological diseases, especially lymphomas. Moreover, despite a shortage of long patient follow up, adverse effects seem uncommon. Thus, the evaluation of anti CD 20 monoclonal antibodies in CAD among other autoimmune cytopenias was very attractive.⁴ However, the cost of managing such a therapy has not clearly been raised before and this has caused alarm with in our hospital pharmacies. Therefore, we report the case of a 74 year-old woman with a previous history of primary CAD diagnosed in 1997 with the presence of hemolytic anemia due to an IgM cold agglutinin. No lymphoma was associated at the first evaluation of the illness and during the 7 years of follow-up. Until 2004, red cell transfusions were occasionally infused. However, because of asthenia, dyspnea and symptomatic cerebral and lower limb atherosclerosis lesions, 24 courses of red cell transfusions were necessary in 2004. As the hemoglobin level was always under 10 g/dL with recurrent clinical symptoms, adjuvant infusions of immunoglobulins associated with erythropoietin were administrated but unsuccessfully. In December 2004, one course of rituximab was completed at a dose of 375 mg/m² as an intravenous infusion on days 1, 8, 15, 22 with good tolerance. One red cell transfusion was necessary after the fourth infusion of rituximab. During the nine months of follow-up after anti-CD20 monoclonal antibody treatment, the patient's hemoglobin level remained stable around 11g/dl with neither symptoms of anemia nor vascular disease. Despite a very cold winter in 2005 no red cell transfusion was needed.

The efficiency of rituximab in the treatment of CAD has been recently described among 27 patients.³ The expected duration of rituximab efficacy is about 12 months. Thus it is possible to predict that neither red-cell transfusion nor rituximab infusion will be necessary until the end of 2005 for this patient

Medical expenses are currently becoming a major pre-

occupation and this is affecting our practice of medicine. Consequently, we have tried to assess the cost of both rituximab and red cell transfusions in our patient over the years 2004 and 2005 in two different ways. Firstly, we simply compared the cost of rituximab versus red cell infusions. Secondly we compared the global expenses incurred by the hospital. In fact, the cost of an in-patient stay in hospital day is fixed in France whatever the price of the given drugs. Thus, it would be more relevant to compare the duration of hospitalization for the delivery of blood transfusions versus rituximab:

1-Without taking account the nursing time, the total cost of rituximab was 6316€ (1579€ at each infusion) while the total charge for blood transfusions was 4032€ (168€ for each red cell unit).

2-Two red cell units were provided during a one-day hospitalization each time, which represents 12 hospitalization days, while only 4 hospitalization days were necessary for rituximab. In this way, the red cell transfusion cost was 5556€ against 1852€ for rituximab. Moreover no additional hospitalization days were necessary during rituximab courses due to ischemic neurologic attacks.

Thus, in our patient, even if rituximab itself costed 57% more than red cell transfusions, the hospital and social security charges were 200% higher for red cell transfusions. Furthermore, even if formal assessments were not carried out, it is likely that quality of life was improved without any further symptoms of anemia and ischemic diseases.

From these calculations based on a single example within the French financial system, it is not possible to draw any internationally valid conclusion on cost savings. In addition, rituximab's long-term safety has to be carefully assessed. However, among persons with persistent CAD-associated anemia, rituximab may be an attractive and potentially cost saving option compared to conventional immunosuppressive therapy.

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