Joint Bone Spine xxx (2014) xxx–xxx

Available online at
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Case report

Rationale and efficacy of CD52 targeting in HTLV-1-associated myositis

Delphine Cochereau[a,*], Sophie Georgin-Lavialle[b], Thierry Maisonobe[c], Odile Dubourg[c], Sara Melboucy-Belkhir[d], Olivier Hermine[a], Achille Aouba[a,e]

[a] Service d'Hématologie Adultes, Université Paris Descartes, Paris Sorbonne Cité, Institut Imagine, Faculté de Médecine, AP–HP, Necker–Enfants-Malades, 149, rue des Sèvres, 75743 Paris cedex 15, France
[b] Service de Médecine Interne, Hôpital Tenon, Université Pierre-et-Marie-Curie, AP–HP, 4, rue de la Chine, 75020 Paris, France
[c] Laboratoire de Neuropathologie, Hôpital Pitié-Salpêtrière, Université Pierre-et-Marie-Curie, 47, boulevard de l'Hôpital, 75651 Paris cedex 13, France
[d] Service de Médecine Interne, Hôpital Jean-Verdier, avenue du 14-Juillet, 93140 Bondy, France
[e] Service de Médecine Interne, Hôpital Antoine-Béclère, Université Paris XI, AP–HP, 157, rue de la Porte-de-Trivaux, 92140 Clamart, France

ARTICLE INFO

Article history:
Accepted 28 January 2014
Available online xxx

Keywords:
Myositis
HTLV-1
Alemtuzumab
Anti-CD52
Crohn-like disease
Myelopathy/tropical spastic paraparesis

ABSTRACT

We retrospectively analysed two selected patients, referred to our Haematology Department for refractory HTLV-1 associated myositis with circulating pathologic T-cell population with ATL phenotype. They respectively presented also HTLV-1 associated Crohn-like disease and myelopathy. Muscle biopsy of both patients was analysed to determine the pathologic infiltrate. Alemtuzumab was proposed as salvage therapy. Targeting CD52 with alemtuzumab showed good efficacy on myopathy of both patients for respectively 11 and 10 months. Interestingly, this treatment showed also efficacy on circulating pathologic T-cell population and on concomitant digestive and neurological diseases. The double infected cells ablation and immunosuppressive propriety of alemtuzumab probably explains its interest in this infectious and dysimmunitary disorder. Even though alemtuzumab probably remains a suspensive treatment, its place should be assessed in controlled trial in this difficult to treat rare disease.

© 2014 Société française de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

Idiopathic inflammatory myopathies are rare and clinically characterized by proximal skeletal muscle weakness, most often symmetric. They can also be associated with extramuscular manifestations, such as dysphagia, dyspnea, arthralgia, fever and also cutaneous signs in cases of dermatomyositis. The diagnosis is then suggested by elevated serum muscle enzyme concentrations, such as creatine kinase (CK) and confirmed by electromyography (EMG) and muscle biopsy showing large panel of inflammatory cells in muscle tissue, including B-, T-cells, macrophages and dendritic cells. Based on differences in clinical and histopathological findings, separate myositis subtypes have been identified, essentially classified into polymyositis, dermatomyositis, sporadic inclusion body myositis and cancer associated myositis [1]. A viral etiology has been reported in some myositis cases, including Chikungunya virus, A and B Influenza viruses, Cytomegalovirus (CMV), Epstein–Barr virus (EBV), the Human Immunodeficiency Virus (HIV), and the Human T-cell Leukaemia Virus type 1 (HTLV-1) [1].

HTLV-1 is a human retrovirus infecting 20 million people worldwide, with focal endemic areas of high prevalence (Japan, Africa, Caribbean islands, and Central and South America). Although 90% infected individuals remain lifelong asymptomatic carriers, HTLV-1 may be associated with severe diseases [2]. These last can be subdivided into three categories: neoplastic diseases, such as adult T-cell leukaemia (ATL)/lymphoma, opportunistic infections and inflammatory syndromes, such as HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), uveitis, arthritis, autoimmune thyroiditis, infective dermatitis, colitis and myositis [2,3]. Physiopathological features of HTLV-1 associated myositis (HAMy) are still not very known. However, data suggest that HAMy would not be due to direct, persistent infection of muscle fibers by the virus, but to a process induced by HTLV-1-infected mononuclear cells that infiltrate the muscle [4]. HAMy treatment currently remains disappointing, including traditional non-specific therapies for myositis, such as glucocorticoids, intravenous immunoglobulins and several immunosuppressive drugs.

Alemtuzumab is a humanized anti-CD52 monoclonal antibody (IgG1 subtype) that binds to the cell membrane in more than 95% of human B- and T-lymphocytes, monocytes, macrophages and eosinophils. Therefore, it is already widely used in some relapsed/refractory lymphoproliferative disorders and more recently also in relapsing inflammatory or autoimmune diseases, including arthritis, multiple sclerosis, vasculitis and autoimmune cytopenias with encouraging results [5–7]. Since muscle tissues of HAMy are invaded by inflammatory infiltrate

* Corresponding author.Tel: +33 1 44 49 52 83; fax: +33 1 44 49 52 80.
E-mail address: delphine_cochereau@hotmail.fr (D. Cochereau).

1297-319X/$ – see front matter © 2014 Société française de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.jbspin.2014.01.019

Please cite this article in press as: Cochereau D, et al. Rationale and efficacy of CD52 targeting in HTLV-1-associated myositis. Joint Bone Spine (2014), doi:10.1016/j.jbspin.2014.01.019

of macrophages, CD4- and CD8 T-cells expressing CD52 [8], we therefore wondered whether alemtuzumab could be efficient in refractory/relapsing HAMy.

In the present study, we briefly describe two refractory HAMy patients with other HTLV-1 associated diseases and report the results of alemtuzumab salvage therapy.

2. Case reports

Two patients were referred to our Haematology Department for refractory HAMy. Approvals from institutional medical-pharmaceutical committees or reviews boards were obtained and patient's consent was obtained after information on alemtuzumab.

Subcutaneous alemtuzumab regimen consisted in an attack treatment with 10 mg per week for 3 months and then a maintenance treatment with 10 mg per month for 6 months, in association with oral sulfamethoxazole–trimethoprim and valacyclovir for infection prophylaxis. Before alemtuzumab treatment, parasitological stools exam was performed and ivermectin was systematically administrated whatever the result to treat occult anguillulosis.

Follow-up consisted in monthly clinical evaluation, including manual muscular testing (scale 0 to 5) and CK levels monitoring, EMG control at 3 months, circulating pathologic T-cell population immunophenotyping control at 3 and 6 months and finally blood viral load monitoring (Table 1).

2.1. Patient 1

A 58-year-old woman born in French Antilles with no medical history had a severe HAMy associated with an ulcerative colitis diagnosed in 2001 presumed related to HTLV-1 infection because of concomitant evolution and in the absence of other retrieved cause (Table 1). Indeed, she presented muscle painfulness and weakness in thighs and both shoulder and pelvic girdles for 2 years associated with chronic diarrhea, abdominal pain and weight loss (10 kg in 2 years). In 2001, CK level was high (4330 IU/L); both blood HTLV-1 serology and polymerase chain reaction (PCR) were positive, whereas HIV, Hepatitis C (HCV) and B virus (HBV) serologies were negative. Hemogram and all usual blood tests were normal. Blood T- and B-cell immunophenotyping exhibited a small T-cell (3%) CD3+, CD4+, CD7−, CD25+ and DR+ population. HTLV-1 proviral load was 20,978 copies for 150,000 T-cells, i.e. 4.32 log. Thigh magnetic resonance imaging (MRI) was compatible with inflammatory myopathy diagnosis.

Quadricipital muscle biopsy revealed inflammatory myopathy pattern with necrotizing myositis, small perivascular infiltrate CD8 T-cell (Fig. 1). Testing for all myositis-specific autoantibodies (including anti-Jo1, anti-PL12, PL-7, anti-SRP, anti MI2) and anti-*Saccharomyces cerevisiae* (ASCA) were negative, whereas antinuclear antibodies were positive to 1/80 without specificity, anti-DNA antibodies being negative. EMG showed myopathic features especially in anterior tibial and right deltoid muscles, without neuropathy. Gastroscopy was normal and colonoscopy found ulcero-inflammatory lesions in the right colon. Colic biopsies showed an unspecific ulcerative colitis aspect in the terminal ileum and did not reveal any granuloma neither microbial nor EBV and CMV.

Several lines of treatment variously associating corticosteroids, methotrexate, plasmapheresis, mycophenolate mofetil, daclizumab (anti-interleukin-2), lenalidomide, intravenous human immunoglobulin, rituximab (anti-CD20), anakinra

Table 1
Comparative synopsis of the main features of the 2 patients suffering from HTLV-1 associated myositis treated with alemtuzumab.

	Patient 1	Patient 2
Patients characteristics		
Origin	French Antilles	Haïti
Sex	Female	Female
Age at diagnosis	58	54
Clinical data		
Disease associated with HAMy	Crohn-like colic involvement	Tropical spastic paraparesis
Laboratory data before treatment		
CK (IU/L)	4330	1076
Hemogram	Normal	Normal
Pathologic population on blood T- and B-cell immunophenotyping	3% T-cell CD3+ CD4+ CD7− CD25+ DR+	10% T-cell CD3+ CD4+ CD7− CD25+ DR+
HTLV-1 serology	Positive	Positive
HTLV-1 blood proviral load[a]		
Copies for 150,000 T-cells	20,978	28,092
Log10	4.32	5.45
Antinuclear antibodies	Positive to 1/400	Positive to 1/160
Myositis-specific autoantibodies	Negative	–
Other paraclinical data at diagnosis		
Muscle biopsy	Necrotizing myositis with endomysial infiltrates	Necrosis and regenerative features and endomysial inflammatory infiltrates
EMG	Myopathic features	Pseudo-myotonic salvia in the calves
Thigh MRI	Compatible with polymyositis	Not done
Results during and after treatment with Alemtuzumab		
Motor deficit	Decreased (scale from 1/5 to 3,5/5)	Decreased
Pathologic blood T-cell population	Disappeared	Disappeared
EMG	Normalized	Normalized
HTLV-1 PCR[a] at 3 months treatment		
Copies for 150,000 T-cells	5870	2226
Log10	3.77	3.34
HTLV-1 PCR[a] 14 months after treatment discontinuation		
Copies for 150,000 T-cells	6,345	–
Log10	3.80	–

CK: Creatine kinase; EMG: Electromyography; HAMy: HTLV-1 associated myositis; MRI: magnetic resonance imaging.
[a] HTLV-1 quantification (real-time quantitative PCR on T-cells; amplification of Tax region, research technic of Hôpital Saint-Louis, Paris, France).

Please cite this article in press as: Cochereau D, et al. Rationale and efficacy of CD52 targeting in HTLV-1-associated myositis. Joint Bone Spine (2014), doi:10.1016/j.jbspin.2014.01.019

Download English Version:

https://daneshyari.com/en/article/6118993

Download Persian Version:

https://daneshyari.com/article/6118993

Daneshyari.com