H1N1 influenza outcome in rheumatic patients under biological therapy

Sirs,

Following the outbreak of the H1N1 influenza pandemic in 2009, fears were expressed regarding the impact of a potential H1N1 infection on rheumatic patients receiving immunosuppressive treatment and especially biologics. An increased susceptibility of this population to a severe or even fatal form of the infection came up as an issue of major concern. In addition, evidence for reduced humoral responses after influenza vaccination, in patients with autoimmune conditions treated with biologics, alone or in combination with DMARDs, further aggravated concern (1-3). Shale *et al*. analysed the data reported to the US Food and Drug Administration (FDA) during the 2003 to 2008 period and found 714 cases of seasonal influenza associated to anti-TNF-α therapy, including 7 deaths (4). However, a similar analysis regarding the H1N1 infection is lacking. Two years after the eruption of the pandemic, data in the literature regarding the severity and outcome of H1N1 infection in rheumatic patients under biological treatment remains scarce and conflicting, with only two case reports having been published to date. One refers to a patient receiving adalimumab for psoriatic arthritis, who fully recovered after developing the infection (5) and the other to a woman, who died of H1N1 related respiratory tract infection, after having received infliximab for psoriasis (6). In Greece, the H1N1 pandemic has accounted for 149 deaths during the 2009–2010 epidemiological surveillance period (7), while another 180 fatalities due to influenza have been reported in the post pandemic period, from 4.10.2010 until 12.5.2011 (8). During this time frame, nine patients from our rheumatology departments, receiving biological therapy, developed an H1N1 infection, detected by rapid antigen testing of pharyngeal swabs (Table I). In seven cases this was further confirmed by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR). Three among these patients were obese (BMI≥30). As far as immunisation status is concerned, previous vaccination against the H1N1strain was only reported by a 54-year-old rheumatoid arthritis patient under treatment with abatacept. Due to an increased awareness of the potential severity of H1N1 infection at that time and in the given population, treatment with oseltamivir (Tamiflu 75mg bid) and oral antibiotics was initiated within 48 hours of symptom onset, in all but one patient, a 59 year old woman with psoriatic arthritis. In this case oseltamivir was started four days after the onset of fever. Five out of nine patients needed hospitalisation, while the remaining four were treated on an outpatient basis. In eight cases the disease course was uncomplicated and within five days of antiviral treatment administration, fever and intense symptoms remitted leaving no sequelae. Only one patient, a 32-year-old woman receiving adalimumab and leflunomide for rheumatoid arthritis, developed radiographic evidence of pneumonia, requiring intubation and a 20-day hospitalisation in the intensive care unit. She too, however, had a full recovery. The clinical course and outcome of these nine cases supports the suggestion (5) that treatment with biologics may not predispose to a serious or lethal form of H1N1 infection, dramatically different from that expected in the general population. Our data are also consistent with the published experience of H1N1 infection in solid organ transplant recipients, who represent another specific population of immunocompromised patients (9). We believe that our experience significantly expands the published information on the outcome of H1N1 infection in patients with rheumatic diseases receiving biological treatment.

V.K. BOURNIA *MD*[1]
C. SFONTOURIS *MD*[2]
M. KONSTA *MD*[1]
A. ILIOPOULOS *MD*[1]

[1]Department of Rheumatology, Veterans Administration Hospital (NIMTS), Athens, Greece; [2]Department of Rheumatology, Evangelismos Hospital, Athens, Greece.

Address correspondence to:
Dr V.K. Bournia, Department of Rheumatology, Veterans Administration Hospital (NIMTS), Monis Petraki 10-12, 115 21, Athens, Greece.
E-mail: lily_bournia@hotmail.com

Competing interests: none declared.

References

1. KAPETANOVIC MC, SAXNE T, NILSSON J-Å, GEBOREK P: Influenza vaccination as model for testing immune modulation induced by anti-TNF and methotrexate therapy in rheumatoid arthritis patients. *Rheumatology* 2007; 46: 608-11.
2. GELINCK LBS, VAN DER BIJL AE, BEYER WEP *et al*.: The effect of anti-tumour necrosis factor α treat-

Table I. Demographics, underlying rheumatic condition and treatment with DMARDs and biologics of the nine patients that developed H1N1 influenza infection. Risk factors for H1N1 and the need for hospitalisation following infection are also presented. (M: male, F: female, DMARD: disease-modifying anti-rheumatic drug, COPD: chronic obstructive pulmonary disease, MTX: methotrexate, ICU: intensive care unit).

Patient	Age	Sex	Underlying rheumatic disease	Biologic factor	Duration of biologic therapy (months)	DMARD-corticosteroids	Risk factors	Need for Hospitalisation	Pneumonia
1	54	M	Rheumatoid arthritis	Abatacept 750mg/month	21	Prednisolone 5mg qd	COPD-pulmonary fibrosis	Yes	No
2	39	F	Rheumatoid arthritis	Abatacept 750mg/month	46	Leflunomide 20mg qd, MTX 10mg/wk	–	No	No
3	36	M	Psoriatic arthritis	Adalimumab 40mg/14days	58	MTX 15mg/wk	–	Yes	No
4	59	F	Psoriatic arthritis	Adalimumab 40mg/14days	37	MTX 15mg/wk	Obesity	No	No
5	58	F	Rheumatoid arthritis	Etanercept 50mg/week	71	Prednisolone 5mg qd MTX 12.5mg/wk	Diabetes, obesity	Yes	No
6	32	F	Rheumatoid arthritis	Adalimumab 40mg/14 days	10	Leflunomide 20mg qd	–	ICU	Yes
7	56	M	Psoriatic arthritis	Infliximab 350mg/50 days	39	MTX 10mg/wk	–	No	No
8	28	F	Rheumatoid arthritis	Etanercept 50mg/week	36	Prednisolone 5mg qd MTX 15mg/wk	–	No	No
9	59	F	Wegener's vasculitis	Rituximab 1000mg/15 days (every 6 months)	6	Prednisolone 20mg qd	Obesity	Yes	No

ment on the antibody response to influenza vaccination. *Ann Rheum Dis* 2008; 67: 713-6.
3. GABAY C, BEL M, COMBESCURE C *et al*.: Impact of synthetic and biological disease modifying antirheumatic drugs on antibody responses to the ASO3-adjuvanted pandemic influenza vaccine: a prospective, open-label, parallel-cohort, single-center study. *Arthritis Rheum* 2011; 63: 1486-96.
4. SHALE M, CZUB M, KAPLAN GG, PANACCIONE R, GHOSH S: Anti-tumor necrosis factor therapy and influenza: keeping it in perspective. *Therap Adv Gastroenterol* 2010; 3: 173-7.
5. SERRATO VA, AZEVEDO VF, SABATOSKI V, GONCALVES BP, MACHADO DM: Influenza H1N1 infection in a patient with psoriatic arthritis in treatment with Adalimumab: a case report. *Clin Rheumatol* 2010 Mar 5 [Epub].
6. KLING MC, LARIAN AA, SCORDI-BELLO I, EMER J, LEBWOHL MG: Fatal influenza A(H1N1) respiratory tract infection in a patient having psoriasis treated with infliximab. *Arch Dermatol* 2010; 146: 651-4.
7. Weekly Report on Epidemiologic Monitoring of Influenza (26 May 2010). Athens, Greece, Hellenic Centre for Diseases Control and Prevention-Ministry of Health and Social Solidarity; 2010.
8. Weekly Report on Epidemiologic Monitoring of Influenza week 18/2011 (02-08 May 2011). Athens, Greece, Hellenic Centre for Diseases Control and Prevention, Ministry of Health and Social Solidarity; 2011.
9. KUMAR D, MICHAELS MG, MORRIS MI *et al*.: Outcomes from pandemic influenza A H1N1 infection in recipients of solid-organ transplants: a multicentre cohort study. *Lancet Infect Dis* 2010; 10: 521-6.j