Successful treatment of adalimumab in a child with Vogt-Koyanagi-Harada: which is the best available systemic treatment?

Sirs,

Vogt-Koyanagi-Harada (VKH) disease, most frequent in Asiatic, Hispanic, and Amerindian populations, is a rare multi-system autoimmune disorder with a prevalent ocular, auditory, neurologic and dermatologic involvement (1). Herein we report a paediatric case of VKH successfully treated with adalimumab (ADA) as first not steroid drug.

An 8-year-old boy was admitted to our hospital for red eyes and visual impairment from 15 days. He was the second child of non-consanguineous Egyptian parents, with silent family history. He had no relevant past medical history including ocular trauma or surgery.

On first examination, visual acuity (VA) was 1.6 logMAR and intraocular pressure (IOP) was normal bilaterally. The patient showed bilateral conjunctival congestion with perikeratic hyperaemia, anterior uveitis (cells 1+, flare 1+), and posterior synechiae. Fundus revealed severe vitreitis, swollen and hyperaemic optic disc, and serous retinal detachment in posterior and inferior retina. Optical coherence tomography confirmed bilateral serous detachment of neuroepithelium of posterior and inferior retina. The retinography highlighted a diffuse pigmentary dystrophy bilaterally. The patient did not complain of systemic symptoms, and physical examination was normal.

Anti-nuclear antibodies, anti-saccharomyces cerevisiae antibodies and antineutrophil cytoplasmic antibodies were negative. Angiotensin converting enzyme was in the normal range. Human leukocytes antigen B27 and B51 were absent. A comprehensive infectious work-up excluded any acute infection. Chest x-ray was normal. Brain and orbital MRI with contrast showed bilateral chorioretinitis and posterior retinal detachment. Since no history of ocular trauma, the bilateral ocular involvement, no evidence of infections and/or systemic rheumatic diseases, and the signs of choroiditis and exudative retinal detachment, patient fulfilled the diagnostic criteria for the definite diagnosis of VKH Disease (1). Intravenous methylprednisolone (30 mg/kg/daily) was started for 3 days, followed by oral corticosteroids. In order to control ocular inflammation, ADA (40 mg/2 weeks) was started and corticosteroids progressively tapered. VA progressively improved. After 8 months, uveitis and retinal detachment was completely recovered. The VA was bilaterally 0 logMAR, and the IOP was 15 mmHg. The patient did not experience adverse events.

Paediatric VKH presents a more aggressive course and worse visual outcomes com-

Table I. Summary about the available papers on the different treatments other than corticosteroids for paediatric VKH. All patients reported receiving systemic corticosteroid.

References	Ethnicity	n. of patients	M:F	Age range	Treatment carried out (n. of patients)	Effectiveness of treatment (n of patients)	Initial VA (logMAR)			Final VA (logMAR)		
							<0.3	0.3-0.99	≥1	<0.3	0.3-0.99	≥1
Farah 2002 (4)	White Brazilian	1	0:1	9	CsA, None	1 (100%)				1 (100%)		
Al Hemidan 2006 (5)	Saudi Arabian	1	0:1	3	tCCS+CsA	sCC+tCCS+CsA (100%)		1 (>0.3)	(100%)		1 (>0.3)	
Soheilian 2006 (12)	Iranian	10	2:8	4-14	tCCS (10) iCCS (10) MTX (6)	tCCS (10) iCCS (10) sCCS (10) MTX (6)		3 (30%)	7 (70%)	1 (10%)	6 (60%)	3 (30%)
Kahn 2006 (6)		2	0:2	11-18	tCCS (2) tacrolimus CSA MMF AZA MTX IFX (2)	IFX (2)	1 (50%)	1 (50%)	1 (50%)		1 (50%)	
Berker 2007 (7)	Turkish	1	0:1	9	tCCS CSA MTX	None		1 (100%)			1 (100%)	
Perente 2007 (8)	Turkish	1	0:1	13	CsA sCCS+CsA		1 (100%)	1 (100%)				
Khalifa 2010 (14)	Hispanic, American Japanese	2	0:2	10-12	CYC (1) IFX+MTX (2) iCCS (1)	CYC (1), sCCS+ IFX+MTX (1)			2 (100%)	1 (50%)	1 (50%)	
Ojaimi 2012 (9)	Philippine-English	1	1:0	11	tCCS MTX iCCS CsA	sCCS	1 (100%)			1 (100%)		
Jeroudi 2014 (15)	Hispanic	1	0:1	15	iCCS tCCS ADA+MTX	ADA		1 (100%)	1 (100%)			
Umran 2015 (16)	Arab	1	0:1	10	tCCS, MTX IFN-α RTX	RTX		1 (100%)		1 (100%)		
Caso 2015 (10)	NA	1	0:1	17	iCCS CsA RTX	RTX NA	NA	NA	NA	NA	NA	
Couto 2018 (2)	Argentinian	3	2:1	3	AZA (3) ADA (3)	ADA (3)	1 (33%)	1 (33%)	1 (33%)	2 (66%)		1 (33%)
Budmann 2018 (3)	Hispanic	1	0:1	9	MTX+IFX	sCCS, IFX	1 (100%)			1 (100%)		
Su 2019 (11)	Chinese American	1	0:1	12	tCCS iCCS ADA MMF	sCCS, ADA			1 (100%)	1 (100%)		
AlQahtani DS 2019 (13)	Arab	1	1:0	4	tCCS, iCCS, MTX+ADA	tCCS+MTX+ADA			1 (100%)		1 (100%)	

sCCS: systemic corticosteroids; tCCS: topical corticosteroids; iCCS: intraocular corticosteroids; MTX: methotrexate; CsA: cyclosporin A; AZA: azathioprine; CYC: cyclophosphamide; RTX: rituximab; IFN-α: interferon-α; ADA: adalimumab; IFX: infliximab; MMF: mycophenolate mofetil.
Efficacious treatment was intended as the reduction of ocular inflammation according to the Standardization of Uveitis Nomenclature (SUN) working group criteria (*Am J Ophthalmol* 2005; 140: 509-16).

pared to adults, therefore a prompt diagnosis and aggressive treatment result mandatory (2). Systemic corticosteroids is the mainstay of initial treatment, but its prolonged use results in relevant side effects. Thus, a quick steroid tapering is of utmost importance and an immunosuppressant approach is necessary.

We performed a systematic literature review (time period 1990 – 10th November 2020) to evaluate different reported treatments other than corticosteroids in paediatric VKH. Articles were eligible if in English and reported inflammatory eye outcomes. Overall, we found 28 additional children with VKH (Table I). Among the common disease-modifying anti-rheumatic drugs (DMARDs), 7 children received cyclosporine A, 4 azathioprine, 2 mycophenolate mofetil and 15 methotrexate (MTX) reporting the treatment as efficacy in 2/7 (28.6%), 0/4, 0/2, and 6/15 (40%) in monotherapy respectively (2-16).

Among biologic drugs, 4 patients received infliximab with concomitant MTX describing an ocular response in 3/4 (75%) patients (3, 6, 14). Rituximab was administered in 2 patients with resolution of ocular inflammation in both patients (10, 16). Six patients received ADA, in 2 cases associated with MTX, resulting efficacious in all patients (2, 11, 13, 15).

In accordance with the literature data, our patient showed a complete resolution of ocular inflammation and complete recovery of VA after ADA starting. Conversely what previously reported, we promptly administered ADA soon after the steroid induction, without use of traditional DMARDs.

Although the small number of described cases, biologic therapies seem to provide a better efficacy compared to classic immunosuppressants in paediatric VKH. Considering the aggressive course and potentially invalidating complications these treatments should be considered in association to corticosteroids as first-line therapy in selected cases.

I. MACCORA[1,2], *MD* *
V. MANISCALCO[1], *MD* *
E. MARRANI[1], *MD*
C. DE LIBERO[3], *MD*
I. PAGNINI[1], *MD*
M.V. MASTROLIA[1,2], *MD*
G. SIMONINI[1,2], *MD*

**These authors contributed equally.*

[1]Rheumatology Unit, Meyer Children's University Hospital, Florence;
[2]Neurofarba Department, University of Florence;
[3]Ophthalmology Unit, Meyer Children's University Hospital, Florence, Italy.

Please address correspondence to:
Ilaria Maccora,
U.O. di Reumatologia,
Azienda Ospedaliero-universitaria Meyer,
Viale Pieraccini 24,
50139 Firenze, Italy.
E-mail: ilamaccora@gmail.com

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