Cardiomyopathy Caused by Longterm Treatment with Chloroquine: A Rare Disease, or a Rare Diagnosis?

To the Editor:

Chloroquine (CQ) has been used for the treatment and prophylaxis of malaria since World War II. Ten years later, the administration of CQ and hydroxychloroquine (HCQ) was introduced for the longterm therapy of rheumatic diseases. Although no reliable statistical data are available, HCQ, which differs from CQ only in a hydroxyl group at the end of the side chain, but not in pharmacokinetics or metabolism, is described in the literature as less toxic and has been staging a comeback, particularly in the treatment of systemic lupus erythematosus (SLE)¹.

CQ and HCQ induce a dysfunction of the lysosomal enzymes, leading to the impairment of intracellular degradation processes in conjunction with the accumulation of pathological metabolic products (glycogen and phospholipids). These appear histologically as granulovacuolar cell mutations and ultrastructurally as lamellar inclusion bodies ("myeloid bodies") and as "curvilinear bodies" in cytoplasm (remnants of poorly digested membranes)^{2,3}. Their pharmacokinetics are characterized by a long half-life and a high volume of distribution; they follow a multicompartment model with very slow distribution between plasma and tissue, leading to sustained organ sequestration and sometimes irreversible organ damage⁴.

Severe toxicity in the form of irreversible retinopathy⁵ is well known under longterm treatment with these substances. In contrast, neuromyopathy⁶ and especially cardiac damage⁷ receive scant mention in the literature. Cardiac complications comprise conduction disturbances [bundle-branch block, atrioventricular (AV) block] and cardiomyopathy — often with hypertrophy, restrictive physiology, and congestive heart failure (literature reviews are found in Nord, *et al*⁸ and Costedoat-Chalumeau, *et al*⁹).

Because the clinical features of cardiotoxicity are unspecific, the followup of potentially affected patients is of utmost importance.

We report a case of a patient with rheumatoid arthritis (RA) and heart disease who was treated with CQ.

A 65-year-old woman was admitted for rehabilitation after having undergone surgery for lumbar spinal stenosis in April 2007. Electrocardiography revealed an atypical bundle-branch block. She reported mild dyspnea and angina pectoris (New York Heart Association Class II) for many years without progression. A diagnosis of hypertensive heart disease was rendered in 2001. In October 2006 she experienced syncope with subsequent resuscitation. The electrocardiogram showed a complete AV block, and a dual-chamber pacemaker was implanted. There were no indications

of myocarditis or variation in her medications preceding the syncope. CQ medication was continued; she recovered completely.

Her history revealed that she had been diagnosed with RA 43 years before. It was treated with corticosteroids, nonsteroidal antiinflammatory drugs, and CQ. Azathioprine, methotrexate, gold compounds, and leflunomide were discontinued because of side effects. CQ had been administered for 35 years (250 mg daily), and the cumulative dose was 3195 g CQ phosphate. Except for a slow, continuous deterioration of her vision, she noted no other side effects.

Her medications upon admission included CQ phosphate 250 mg, naproxen 500 mg (twice daily), prednisolone 15 mg, oxycodone 40 mg, nebivolol 2.5 mg, torsemide 10 mg, and pantoprazole 40 mg.

On examination she appeared to be in good general condition, with blood pressure 140/80 mm Hg and heart rate 84/min. Mild synovitis of the finger joints and severe polyarthropathic deformities due to longstanding RA were noted. There was no evidence of muscular weakness, no impairment of sensation, and no diminished stretch reflexes. Heart and lungs were without pathological findings. There was no distension of the jugular veins, no edema, and vascular status was normal.

Laboratory findings showed elevation of enzyme levels (lactate dehydrogenase 426 U/l, reference –247; creatine kinase 259 U/l, ref. –145; creatine kinase-MB/mass 11.7 μ g/l, ref. –3.6; troponin I 0.26 ng/ml, ref. –0.1) and rheumatoid factor (160 IU/ml, ref. –15). The remaining laboratory results were normal.

Under Holter monitoring no arrhythmia was detected; regular function of the pacemaker was noted. Transthoracic echocardiography showed normal-size atria and ventricles, borderline hypertrophy (1.2 cm), hypokinesis of the posterior and lateral wall, mitral insufficiency I-II°, diastolic dysfunction II°, and no signs of restrictive physiology.

Chest radiography found the ventricular pacemaker lead in the coronary sinus, while the heart and lungs were normal. Magnetic resonance imaging (MRI) revealed left ventricular (LV) hypertrophy (lateral wall 1.9 cm) and LV ejection fraction 53%, caused by hypokinesis of the apical anterior and the basal inferolateral wall. The delayed gadolinium enhancement sequence (Figure 1) showed decreased viability in a nonvascular pattern, but no myocardial edema to suggest myocarditis.

Left heart catheterization revealed a LV end-diastolic pressure of 10 mm Hg; no coronary artery disease was found. Five endomyocardial biopsies were obtained from the lateral wall, guided by the delayed enhancement pattern in MR imaging.

Pathological examination (Figure 2) showed extensive cytoplasmic

Figure 1. Magnetic resonance imaging shows decreased viability of the left ventricle in a nonvascular pattern (arrows indicate delayed gadolinium enhancement). Left panel: modified 2-chamber view; right panel: 4-chamber view.

Figure 2. Endomyocardial biopsy from the left ventricle. Light microscopy (Masson's trichrome staining) shows marked cytoplasmic vacuolization of the myocytes with periodic acid-Schiff-positive granular deposits (insert).

Figure 3. Endomyocardial biopsy from the left ventricle. Transmission electron microscopy shows lamellar and curvilinear cytoplasmic inclusion bodies in the myocytes.

vacuolization of the myocytes, mild interstitial fibrosis, no evidence of inflammation or vasculitis (including immunohistology), no amyloid deposition, and no cell necrosis. Transmission electron microscopy (Figure 3) revealed accumulation of numerous lamellar and curvilinear inclusion bodies in the myocytes. Molecular pathology (nested polymerase chain reaction) disclosed no infections of the myocardium with enteroviruses, adenoviruses, parvovirus B19, human herpesvirus 6, Epstein-Barr virus, or *Borrelia burgdorferi*.

The diagnosis of Fabry disease was excluded by molecular genetic testing. The serum CQ level was 0.27 mg/l, which is in the therapeutic range. Ophthalmologic examination revealed signs of chronic CQ intoxication (bull's-eye maculopathy of the left eye).

CQ medication was discontinued. Followup 14 months later showed persistence of the complete AV block. The serum enzyme levels had decreased slightly. From a clinical point of view, there was no indication of congestive heart failure, but there was progression of retinopathy and visual loss.

As seen in our case, there are no clinical signs that indicate unambiguously that cardiotoxicity was induced by CQ. Further, there is no correlation between the different organ toxicities (cardiomyopathy, retinopathy, neuromyopathy), which would permit analogous diagnostic conclusions, and the determination of blood levels is not accurate for detecting CQ toxicity (serum level was in the therapeutic range), due to the complex pharmacokinetics and the large interindividual fluctuation range in the metabo-

Table 1. Details of chloroquine/hydroxychloroquine-induced cardiomyopathies (case reports including histologic studies of the myocardium).

Study	Age/Sex	Diagnosis	Drug	Years	CD, g	R/NM	cAVB	Cardiac Diagnostics	Histology	EM	CLB	Symptoms	Followup
Hughes (1) ¹⁰	62 F	RA	CQ	2.5	330	M		NA	A			AHF	† (4 mo)
Motan (2) ¹¹	68 F	RA	CQ	14	1900		+	NA	A			NA	†
Godeau(1) ¹²	36 F	SLE	CQ	NA	700	R	+	NA	EMB	+	+	NA	† (1 yr)
Ratliff ¹³	58 F	DLE	HCQ	10	730	NMR	+	Hypertrophy, rCMP	EMB	+	+	CHF	↑ (7 mo post >) incl. histol.
	59 M	SLE	HCQ	2	290			NA	EMB	+	+	CHF	NA
McAllister ⁷	33 F	SLE	CQ	11	1100	NM		Hypertrophy	EMB	+	+	CHF	NA
	73 F	SLE	CQ	8	730			Hypertrophy	A	+	+	CHF	†
Verny (1) ¹⁴	56 F	SLE	CQ	16	1170	NM	+	Echo: normal	EMB	+	–	Syn	cAVB→ (1 yr post >)
Iglesias C ¹⁵	59 F	DLE	CQ	25	2280	M	+	Hypertrophy, rCMP	A	+	+	CHF	†
August ¹⁶	81 F	RA	CQ	25	NA	R		Hypertrophy	A	+	+	AHF	†
Veinot ¹⁷	60 F	RA	CQ	10	912	NM	+	Hypertrophy, systolic dysfunction	A	+	+	CHF	†
Baguet ¹⁸	58 F	SLE	HCQ	25	4380	NM		Hypertrophy, rCMP	EMB	+	+	CHF	↑ (8 mo post >)
			CQ	2	660								
Teixeira ¹⁹	58 F	RA	CQ	9	820		+	Echo: normal	EMB	+	+	Syn	NA
Roos ²⁰	53-73, FFM	1 SLE→ 2 RA→	CQ HCQ	NA (3)	NA (3)	M (1)		Dilated CMP (1)	A/A/EMB	+++	++–	CHF	†† NA
Charlier ²¹	42 F	RA	CQ	7	756		+	Echo: normal	A	+	+	Syn	†
Freihage ²²	50 F	RA	CQ	6	1100			Hypertrophy, rCMP	EMB + Expl.	+	+	CHF	TX (3 mo post >)
Nord (1) ⁸	31 F	SLE	HCQ	12	1750	NM		Dilated CMP	A + EMB	+	–	CHF	†
Naqvi ²³	61 F	SLE	CQ	23	~2300		+	Hypertrophy, rCMP, MRI: DE	EMB	+	–	CHF + Syn	↑ (7/16 mo post >)
Keating ²⁴	39 F	SLE	HCQ	4	580			Hypertrophy, systolic dysfunction	EMB	+	+	Syn	NA
Reffellmann ²⁵	67 F	RA	CQ	20	1825			Hypertrophy, diast. dysf., MRI:DE	EMB	+	–	CHF	NA
Costedoat ⁹	59 F	DLE	CQ	8	680	NMR	+	Hypertrophy, rCMP	Expl.	+	+	CHF	TX (4 mo post>)
			HCQ	4	580								
Cotroneo ²⁶	51 F	JRA + SLE	HCQ	31	~3400	R		Hypertrophy, rCMP	EMB	+	+	CHF	↑ (2 yrs post >) incl. histol.
Jimenez ²⁷	56 M	RA	CQ	6	550			Hypertrophy, rCMP	EMB	+	+	CHF	↑ (2 yrs post >)
Soong ²⁸	55 F	SLE	HCQ	10	1460			Systolic dysfunction	EMB	+	–	CHF + ARF	† (3 mo post >)
	65 F	SSc + SS	HCQ	25	3650			Diastolic dysfunction	EMB	+	+	CHF	↑ (3 mo post >)
Manohar ²⁹	64 F	SLE	HCQ	10	NA			Hypertrophy, syst. + diast. dysf.	EMB	+	+	CHF	↑ (9 mo post >)
Saussine (2) ³⁰	48 F	LE	CQ	3	225		+	Echo: normal	EMB			Syn	NA
Fragasso ³¹	74 M	Malaria	CQ	(10)	15			Systolic dysfunction	EMB			CHF	↑ (9 mo post >)
Lee ³²	52 F	RA	HCQ	13	1898			Hypertrophy, rCMP, MRI:DE	EMB	+	+	Syn	↑ echo (4 mo post >)
Pieroni ³³	64 F	MCTD	CQ	5	1095			Hypertrophy, rCMP	EMB	+	+	CHF	NA
Muthu-krishnan ³⁴	66 F	SLE	HCQ	10	1460		+	Hypertrophy, rCMP	EMB			CHF	† (2 mo post >)
Newton-Cheh ³⁵	47 M	SLE	HCQ	14	2190			Hypertrophy, rCMP	EMB	+	+	CHF	echo + CHF→ (1 yr post >)
Hartmann ³⁶	75 F	RA	HCQ	10	NA			Hypertrophy, syst. + diast. dysf.	EMB	+	+	AHF	↑ (6 mo post >)
Our patient	65 F	RA	CQ	35	3195	R	+	Hypertrophy, diast. dysf., MRI:DE	EMB	+	+	(CHF)	cAVB→ (14 mo post >)

(1): Case 1. (2) Case 2. ↑ Improvement. → Unchanged. † Death. >: withdrawal of CQ/HCQ; A: autopsy; AHF: acute heart failure; ARF: acute renal failure;

cAVB: complete AV block; CD: cumulative dose; CHF: congestive heart failure; CLB: curvilinear bodies; CMP: cardiomyopathy; CQ: chloroquine; DE: delayed enhancement; diast.: diastolic; DLE: discoid lupus erythematosus; dysf.: dysfunction; echo: echocardiography; EM: electron microscopy; EMB: endomyocardial biopsy; Expl.: explanted heart; HCQ: hydroxychloroquine; histol.: histology; MCTD: mixed connective tissue disease; MRI: magnetic resonance imaging; NA: not available; NM: neuromyopathy; R: retinopathy; (J)RA: (juvenile) rheumatoid arthritis; rCMP: restrictive cardiomyopathy; SSc: systemic sclerosis; (S)LE: (systemic) lupus erythematosus; SS: Sjögren's syndrome; Syn: syncope; syst.: systolic; TX: heart transplant.

lism of the substance⁴. Thus, the cardiac process may be asymptomatic for a long period.

Because of the small number of cases and the lack of systematic studies, it is impossible to calculate the incidence of CQ cardiotoxicity; however, a considerable number of undetected cases can be assumed. To date, reports have been published on 35 patients with biopsy-proven cardiomyopathy^{7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36} and on 30 patients with total AV block only^{9,30,37,38}. Moreover, 12 of those patients with cardiomyopathy exhibited complete AV block as well (Table 1). Most patients were treated with CQ, but in recent years there has been a clear trend toward HCQ. All except one of them (who had recurrent malaria) had connective tissue diseases (predominantly RA and SLE).

The cumulative dose of CQ/HCQ (15–5040 g) and the duration of treatment (2–31 years) vary greatly. Our patient had the longest duration of treatment (35 years) and one of the highest cumulative doses (3195 g).

To date, it has not been possible to establish predictive values for any of the measures, such as age, sex, duration of treatment, cumulative dose, or underlying illness, in order to estimate toxicity in individual cases.

Cardiac complications include conduction disturbances and cardiomyopathy. As in our patient, several cases have been described in the literature in which complete AV block precedes the cardiomyopathy and the medication continues to be administered because of improper evaluation of the pathogenesis^{9,15,23}. We could not determine other causes for the AV block, and there is no known accumulation of higher-grade AV conduction disorders in conjunction with RA³⁹. Recently, the case of a patient with sick sinus syndrome as a result of CQ therapy was also reported³².

The cardiomyopathy is predominantly of the restrictive type (with diastolic dysfunction), but mainly systolic impairment has also been reported (Table 1). The most common pathological result in cardiac imaging is myocardial hypertrophy. Congestive heart failure is the prevailing clinical symptom. However, some patients have very few, discrete symptoms, or none at all (as in our case, in which we found no indication of restrictive kinetics, either).

In view of the large number of variables in the clinical hypothesis, the histological examination plays an extremely important role. As a rule, the morphology of the tissue damage caused by CQ/HCQ is identical in all organs involved. Light microscopic study reveals a vacuolar myopathy. Ultrastructurally, lamellar and so-called “curvilinear” inclusion bodies can be demonstrated. The curvilinear bodies are comma-shaped structures which in human pathology occur only in cases of CQ damage and in neuronal ceroid lipofuscinosis, a group of hereditary neurodegenerative disorders in children^{7,8,40}.

While curvilinear bodies definitively document the pathogenesis of CQ toxicity, the presence of lamellar inclusion bodies is also described after the administration of amiodarone and in other storage diseases⁴¹ (Table 2). In

Table 2. Differential diagnoses of chloroquine/hydroxychloroquine cardiomyopathy.

Connective tissue diseases	Systemic lupus erythematosus Rheumatoid arthritis Dermatomyositis Polymyositis
Varia	Steroid myopathy Other causes for conduction disturbances Hypertensive heart disease Hypertrophic cardiomyopathy sui generis
Storage diseases	Fabry disease Niemann-Pick disease Amiodarone-induced cardiomyopathy Other lysosomal storage diseases
Inflammation	Amyloidosis Viral myocarditis Lupus myocarditis Vasculitis

particular, Fabry disease, which is also accompanied by myocardial hypertrophy, can make the differential diagnosis difficult^{20,28}.

The range of differential diagnoses in the case of vacuolar myopathy revealed under light microscopy is considerably larger and includes the connective tissue diseases and steroid myopathy^{2,3} (Table 2). Because rheumatic diseases often involve the cardiovascular system, and cortisone preparations are frequently prescribed, overlaps can occur and the symptoms of toxic damage are often ascribed to the underlying rheumatic disease and its complications.

To avoid the sampling error of blind biopsies (because of a patchy distribution of the pathological process in the myocardium) we took MR-guided biopsies from the left ventricle, following the delayed enhancement pattern in MRI⁴². Both the vacuolar myopathy (Figure 2) as well as the curvilinear bodies (Figure 3) were unequivocally documented in the myocardial specimen, so that the diagnosis of CQ cardiotoxicity was definitive. Further, the following diseases were excluded by means of differential diagnosis and testing: coronary artery disease, myocarditis and vasculitis (because of the underlying rheumatic disease), viral myocarditis, amyloidosis, steroid myopathy, and Fabry disease.

Based on strict histological (ultrastructural) criteria, the diagnosis of CQ/HCQ-induced cardiomyopathy has been confirmed pathologically in only 24 patients to date (Table 1).

The prognosis for patients with this cardiomyopathy appears to be mixed: heart transplants had to be performed in 2 patients with refractory heart failure^{9,22}. Thirteen patients died (most of them soon after the diagnosis was established). The course of the illness was not clear for 8 patients, and an improvement was described in only 10 cases (Table 1).

It must be noted that cardiotoxicity is difficult to diagnose under longterm treatment with CQ/HCQ and is presumably often overlooked in everyday clinical practice. Early detection is of utmost importance, as no therapy is available, the reversibility of organ damage is questionable, and severe courses of illness have been described. In case of longterm treatment and high cumulative doses, we propose at least annual followup examinations (including electrocardiography). If myocardial damage is suspected, further diagnostic measures including ultrastructural examination of myocardial tissue are required.

ACKNOWLEDGMENT

The authors thank Dr. M. Farr (Department of Cardiology, Heart and Diabetes Center NRW, Ruhr University of Bochum, Bad Oeynhausen, Germany) for conducting the molecular genetic testing for Fabry disease.

ERNST TÖNNESMANN, MD; INGO STROEHMANN, MD, Department of Internal Medicine, Kaiser-Karl-Klinik, Bonn; REINHARD KANDOLF, MD, PhD; HARTWIG WOLBURG, PhD, Institute for Pathology and Neuropathology, University of Tübingen; KATHARINA STRACH, MD, Department of Radiology, University of Bonn; FRANK MUSSHOFF, PhD, Institute of Forensic Medicine, University of Bonn; KLAUS TIEMANN, MD; THORSTEN LEWALTER, MD, Department of Cardiology, University of Bonn, Germany. Dr. Stroehmann is deceased. Address correspondence to Dr. E. Tönnemann, Kaiser-Karl-Klinik, Graurheindorfer Str. 137, D-53117 Bonn, Germany.
E-mail: e.toennesmann@t-online.de

REFERENCES

- Costedoat-Chalumeau N, Leroux G, Amoura Z, Piette JC. Hydroxychloroquine dans le traitement du lupus: le renouveau. *Rev Méd Interne* 2008;29:735-7.
- Gérard JM, Stoupe N, Collier A, Flament-Durand J. Morphologic study of a neuromyopathy caused by prolonged chloroquine treatment. *Eur Neurol* 1973;9:363-79.
- Rewcastle NB, Humphrey JG. Vacuolar myopathy: clinical, histochemical, and microscopic study. *Arch Neurol* 1965;12:570-82.
- Tett SE. Clinical pharmacokinetics of slow-acting antirheumatic

- drugs. *Clin Pharmacokinet* 1993;25:392-407.
5. Marmor MF, Carr RE, Easterbrook M, Farjo AA, Mieler WF. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (a report by the American Academy of Ophthalmology). *Ophthalmology* 2002;109:1377-82.
6. Stein M, Bell MJ, Ang LC. Hydroxychloroquine neuromyotoxicity. *J Rheumatol* 2000;27:2927-31.
7. McAllister HA Jr, Ferrans VJ, Hall RJ, Strickman NE, Bossart ML. Chloroquine-induced cardiomyopathy. *Arch Pathol Lab Med* 1987;111:953-6.
8. Nord JE, Shah PK, Rinaldi RZ, Weisman MH. Hydroxychloroquine cardiotoxicity in systemic lupus erythematosus: A report of 2 cases and review of the literature. *Semin Arthritis Rheum* 2004;33:336-51.
9. Costedoat-Chalumeau N, Hulot JS, Amoura Z, Delcourt A, Maisonneuve T, Dorent R, et al. Cardiomyopathy related to antimalarial therapy with illustrative case report. *Cardiology* 2007;107:73-80.
10. Hughes JT, Esiri M, Oxbury JM, Whitty CW. Chloroquine myopathy. *Q J Med* 1971;40:85-93.
11. Motan J, Topinka I, Dura J, Kvapilova H. Chlorochinova kardiodystrofie [Chloroquine cardiomyopathy]. *Vnitř Lek* 1978;24:1122-8.
12. Godeau P, Guillemin L, Fechner J, Blety O, Herremans G. Les troubles de conduction au cours du lupus érythémateux: fréquence et incidence dans une population de 112 patients. *Ann Méd Interne* 1981;132:234-40.
13. Ratliff NB, Estes ML, Myles JL, Shirey EK, McMahon JT. Diagnosis of chloroquine cardiomyopathy by endomyocardial biopsy. *N Engl J Med* 1987;316:191-3.
14. Verny C, de Gennes C, Sébastien P, Huong Du LT, Chapelon C, Piette JC, et al. Troubles de la conduction cardiaque au cours d'un traitement prolongé par chloroquine — Deux nouvelles observations. *Press Méd* 1992;21:800-4.
15. Iglesias Cubero G, Rodriguez Reguero JJ, Rojo Ortega JM. Restrictive cardiomyopathy caused by chloroquine. *Br Heart J* 1993;69:451-2.
16. August C, Holzhausen HJ, Schmoltd A, Pompecki R, Schröder S. Histological and ultrastructural findings in chloroquine-induced cardiomyopathy. *J Mol Med* 1995;73:73-7.
17. Veinot JP, Mai KT, Zarychanski R. Chloroquine related cardiac toxicity. *J Rheumatol* 1998;25:1221-5.
18. Baguet JP, Tremel F, Fabre M. Chloroquine cardiomyopathy with conduction disorders. *Heart* 1999;81:221-3.
19. Teixeira RA, Martinelli Filho M, Benvenuti LA, Costa R, Pedrosa AA, Nishioka SA. Cardiac damage from chronic use of chloroquine: A case report and review of the literature. *Arq Bras Cardiol* 2002;79:85-8.
20. Roos JM, Aubry MC, Edwards WD. Chloroquine cardiotoxicity: Clinicopathologic features in three patients and comparison with three patients with Fabry disease. *Cardiovasc Pathol* 2002;11:277-83.
21. Charlier P, Cochand-Priollet B, Polivka M, Goldgran-Tolédano D, Leenhardt A. Cardiomyopathie à la chloroquine révélée par un bloc auriculo-ventriculaire complet [Chloroquine cardiomyopathy revealed by complete AV block. A case report]. *Arch Mal Coeur Vaiss* 2002;95:833-7.
22. Freihage JH, Patel NC, Jacobs WR, Picken M, Fresco R, Malinowska K, et al. Heart transplantation in a patient with chloroquine-induced cardiomyopathy. *J Heart Lung Transplant* 2004;23:252-5.
23. Naqvi TZ, Luthringer D, Marchevsky A, Saouf R, Gul K, Buchbinder NA. Chloroquine-induced cardiomyopathy — echocardiographic features. *J Am Soc Echocardiogr* 2005;18:384-8.
24. Keating RJ, Bhatia S, Amin S, Williams A, Sinak LJ, Edwards WD. Hydroxychloroquine-induced cardiotoxicity in a 39-year-old woman with systemic lupus erythematosus and systolic dysfunction. *J Am Soc Echocardiogr* 2005;18:981. e1-5.
25. Reffellmann T, Naami A, Spuentrup E, Kühl HP. Contrast-enhanced magnetic resonance imaging of a patient with chloroquine-induced cardiomyopathy confirmed by endomyocardial biopsy. *Circulation* 2006;114:357-8.
26. Cotroneo J, Sleik KM, Rene Rodriguez E, Klein AL. Hydroxychloroquine-induced restrictive cardiomyopathy. *Eur J Echocardiogr* 2007;8:247-51.
27. Hernández Jiménez V, Saavedra Falero J, Navas R. Miocardiopatía restrictiva reversible secundaria a cloroquina (Cartas al editor) [Myocardopathy secondary to chloroquine — letter]. *Med Clin (Barc)* 2007;129:157.
28. Soong TR, Barouch LA, Champion HC, Wigley FM, Halushka MK. New clinical and ultrastructural findings in hydroxychloroquine-induced cardiomyopathy — A report of 2 cases. *Hum Pathol* 2007;38:1858-63.
29. Manohar VA, Moder KG, Edwards WD, Klarich KW. Restrictive cardiomyopathy secondary to hydroxychloroquine therapy. *J Rheumatol* 2009;36:440-1.
30. Saussine A, Lioriot M-A, Picard C, Lecerf V, Landry J, Scheer I, et al. Cardiotoxicité après un traitement au long cours par chloroquine chez deux patientes lupiques. *Ann Dermatol Vénéréol* 2009;136:530-5.
31. Fragasso G, Sanvito F, Baratto F, Martinenghi S, Doglioni C, Margonato A. Cardiotoxicity after low-dose chloroquine antimalarial therapy. *Heart Vessels* 2009;24:385-7.
32. Lee JH, Chung WB, Kang JH, Kim HW, Kim JJ, Kim JH, et al. A case of chloroquine-induced cardiomyopathy that presented as sick sinus syndrome. *Korean Circ J* 2010;40:604-8.
33. Pieroni M, Smaldone C, Camporeale A, Ierardi C, Dell'Antonio G, Bellocchi F, et al. Chloroquine-induced transition from dilated to restrictive cardiomyopathy (Images in cardiology). *J Am Coll Cardiol* 2011;57:515.
34. Muthukrishnan P, Roukoz H, Grafton G, Jessurun J, Colvin-Adams M. Hydroxychloroquine-induced cardiomyopathy: A case report. *Circ Heart Fail* 2011;4:e7-8.
35. Newton-Cheh C, Lin AE, Baggish AL, Wang H. A 47-year-old man with systemic lupus erythematosus and heart failure (Case 11-2011). *N Engl J Med* 2011;364:1450-60.
36. Hartmann M, Meek IL, van Houwelingen GK, Lambregts HPCM, Toes GJ, van der Wal AC, et al. Acute left ventricular failure in a patient with hydroxychloroquine-induced cardiomyopathy. *Neth Heart J* 2011;19:482-5.
37. El aichaoui S, Amine B, Saoud B, Guedira N, Allali F, Hajjaj-Hassouni N. Bloc auriculoventriculaire complet au cours d'un traitement par chloroquine [Complete auriculoventricular block during chloroquine treatment]. *Rev Méd Interne* 2007;28:134-6.
38. Puymirat E, Douard H, Roudaut R. Bloc auriculo-ventriculaire complet après prise de chloroquine au long cours [Complete auriculoventricular block after long-term chloroquine treatment]. *Rev Méd Interne* 2008;29:741-3.
39. Jurik AG, Moller P. Atrioventricular conduction time in rheumatoid arthritis. *Rheumatol Int* 1985;5:205-7.
40. Boldrini R, Biselli R, Santorelli FM, Bosmann C. Neuronal ceroid lipofuscinosis: An ultrastructural, genetic, and clinical study report. *Ultrastruct Pathol* 2001;25:51-8.
41. Tegnér R, Tomé FMS, Godeau P, Lhermitte F, Fardeau M. Morphological study of peripheral nerve changes induced by chloroquine treatment. *Acta Neuropathol* 1988;75:253-60.
42. Mahrholdt H, Goedecke C, Wagner A, Meinhardt G, Athanasiadis A, Vogelsberg H, et al. Cardiovascular magnetic resonance assessment of human myocarditis: A comparison to histology and molecular pathology. *Circulation* 2004;109:1250-8.

J Rheumatol 2012;39;5; doi:10.3899/jrheum.110959

Correction

Cardiomyopathy Caused by Longterm Treatment with Chloroquine: A Rare Disease or a Rare Diagnosis?

E. Tönnemann, I. Stroehmann, R. Kandolf, H. Wolburg, K. Strach, F. Musshoff, K. Tiemann, T. Lewalter.

Cardiomyopathy caused by longterm treatment with chloroquine: A rare disease or a rare diagnosis? *J Rheumatol* 2012;39:1099-1104. In Table 1 of the online version of this report, for the authors Roos, Friehage, and Nord, listed in Column 1, the entries intended for Column 10 under "Histology" are misaligned. The entries should read: "A/A/EMB" for Roos, "EMB" for Friehage, and "A" for Nord. The author listing in Column 1 "Jimenez" should read "Hernandez-Jimenez". A corrected pdf of this report is available from the online table of contents. To view/download the corrected version visit jrheum.org and follow the prompts to Volume 39, No. 5.

doi:10.3899/jrheum.110959.C1