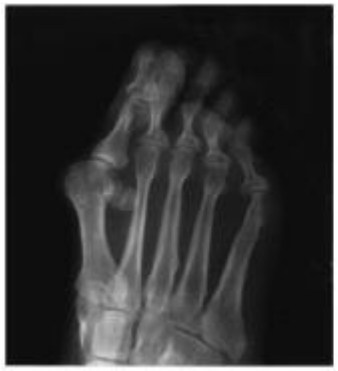
Νεφροί και Βιολογικές Θεραπείες

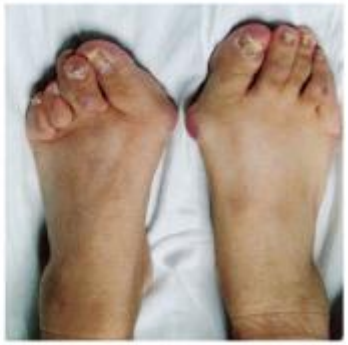
Δρ Ντιούδης Χρίστος

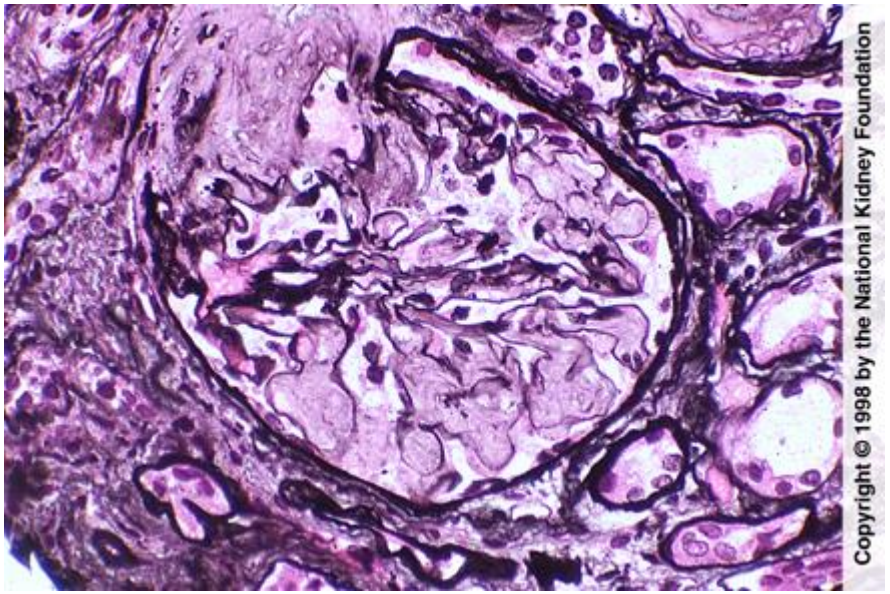
Νεφρολόγος ΜΤΝ ΔΡΑΜΑΣ

Σκοπός

Έχουν θέση οι Βιολογικοί Παράγοντες στη θεραπεία ασθενών με Ρευματικό Νόσημα και Νεφρική Δυσλειτουργία;;







Ρευματικά Νοσήματα και Νεφρική συνοσηρότητα

Ρευματικά Νοσήματα που σχετίζονται με νεφρικές σπειραματικές βλάβες

- Συστηματικός Ερυθυματώδης Λύκος
- Ρευματοειδής Αρθρίτιδα
- Μικτή νόσος του Συνδετικού Ιστού
- Ρευματικός Πυρετός
- Αγκυλωτική Σπονδυλίτιδα
- σ. Reiter’s
- Δερματομυοσίτιδα/πολυμυοσίτιδα
- Σκληρόδερμα
- Υποτροπιάζουσα πολυχονδρίτιδα
- Αγγειίτιδα

Νεφρική Νόσος στη Ρευματοειδή Αρθρίτιδα

- Μεμβρανώδης Σπειραματονεφρίτιδα
- Μεσαγγειοϋπερπλαστική Σπειραματονεφρίτιδα (±IgA εναποθέσεις)
- Διάχυτη υπερπλαστική Σπειραματονεφρίτιδα
- Ρευματική Αγγειίτιδα
- Αμυλοείδωση

Σημαντική νεφροτοξικότητα από φάρμακα που χορηγούνται στη θεραπεία της Ρευματοειδούς αρθρίτιδας

NSAIDS	**1. Οξεία διάμεση νεφρίτιδα με Νόσο των ελάχιστων αλλοιώσεων** **2. Οξεία σωληναριακή νέκρωση**
GOLD SALTS	1. Μεμβρανώδης ΣΝ 2. Νόσος των ελάχιστων αλλοιώσεων 3. Οξεία σωληναριακή νέκρωση
D-PENICILLAMINE	1. Μεμβρανώδης ΣΝ 2. Ταχέως Εξελισσόμενη ΣΝ 3. Νόσος των ελαχίστων αλλοιώσεων
CYCLOSPORINE	1. Χρόνια νεφρική αγγειοπάθεια 2. Χρόνια διάμεση νεφροπάθεια

Μικρού βαθμού νεφροτοξικότητα από φάρμακα που χορηγούνται στη θεραπεία της ρευματοειδούς αρθρίτιδας

METHOTREXATE	**1. Οξεία σωληναριακή νέκρωση**
AZATHIOPRINE	1. Οξεία διάμεση νεφρίτιδα
ANTIMALARIALS	1. Επιδείνωση νεφρικής λειτουργίας σε προϋπάρχουσα ΧΝΑ κυρίως σε ηλικιωμένους ασθενείς (J Rheumatol 1995;22:34-7) 2. Αυξημένος κίνδυνος αμφιβληστροειδοπάθειας
SULFASALAZINE	;
LEFLUNOMIDE	;

Πιθανές επιπλοκές από την αντιρευματική αγωγή σε ασθενείς με ΡΑ και ΧΝΑ / ΑΙΜΚ

Corticosteroids	**1. Επιδείνωση αζωθαιμίας** **2. Κατακράτηση Na+** **3. Αντίσταση στην ινσουλίνη** **4. Υπέρταση**
NSAIDS	1. Επιδείνωση νεφρικής λειτουργίας 2. Αυξημένος κίνδυνος αιμορραγίας πεπτικού
Methotrexate	1. Τοξική συσσώρευση
Azathioprine	1. Δυσκολία ρύθμισης κατάλληλης δόσης
Cyclosporine	1. Αυξημένος κίνδυνος νεφροτοξικής βλάβης, υπέρτασης, σπασμών, τρόμου
Hydroxychloroquine	1. Επιδείνωση νεφρικής λειτουργίας σε προϋπάρχουσα ΧΝΑ κυρίως σε ηλικιωμένους ασθενείς (J Rheumatol 1995;22:34-7) 2. Αυξημένος κίνδυνος αμφιβληστροειδοπάθειας, μυοπάθειας, νευροπάθειας, μυοκαρδιοπάθειας
Leflunomide	1. Μπορεί να χορηγηθεί χωρίς τροποποίηση της δόσης (Beaman et al 2002)
Sulphasalazine	1. Πιθανή απορρόφηση και τοξική συσσώρευση 2. Ασφαλής χορήγηση σε αιμοκάθαρση από Akiyama et al 2003 !!

Rheumatology 2008;47:350–354
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doi:10.1093/rheumatology/kem370

Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study

S. Karie[1], F. Gandjbakhch[2], N. Janus[1], V. Launay-Vacher[1], S. Rozenberg[2], C. U. Mai Ba[1], P. Bourgeois[2] and G. Deray[1]

Objectives. The prevalence of kidney disease (KD) indicators together with the profile of RA drugs prescribed in RA patients was investigated in the MATRIX study (MeThotreXate And Renal Insufficiency).
Methods. Renal function (RF) was assessed using Cockcroft–Gault (CG) and abbreviated Modification of Diet in Renal Disease (aMDRD) study formulae.
Results. Serum creatinine (SCr) was normal in 81.4% of the 129 patients included. According to the National Kidney Foundation (NKF) classification, the distribution by stage of KD was, using the aMDRD and CG formulae, as follows: stage 1: 11.3% and 11.4%; stage 2: 20.0% and 20.3%; stage 3: 15.0% and 24.1%; stage 4: 0% and 1.3%; stage 5: 0%. Proteinuria, haematuria and leucocyturia were observed in 16%, 17% and 20% of the patients, respectively. Using the aMDRD and CG formulae, 36% and 38% of the prescriptions made in patients with glomerular filtration rate (GFR) <60 ml/min required a dosage adjustment. Among the patients with GFR <60 ml/min, 83–90% received at least one drug that required a dosage adjustment and 67–70% received at least one drug that was potentially nephrotoxic, according to aMDRD or CG formulae, respectively. Five (50%) and 8 (47%) patients did not have appropriate MTX dosage adjustment according to their stage of KD with aMDRD or CG formulae, respectively.
Conclusion. Systematic estimation of RF with CG or aMDRD formulae and urine dipstick are necessary in RA patients. In patients with KD at high risk for drug toxicity, dosage should be adapted to RF.

Μέθοδος Cockcroft-Gault

$$\text{CCr (mL/min)} = \frac{(140 - \text{age}) \times \text{lean body weight [kg]}}{\text{Cr [mg/dL]} \times 72}$$

Εξίσωση MDRD

GFR, in mL/min per 1.73 m2 = 170 x (SCr[mg/dL])exp[-0.999] x
(Age)exp[-0.176] x (BUN [mg/dL])exp[-0.170] x
(Alb [g/dL])exp[+0.318] x (0.762 if female) x (1.18 if black)

Νεφρική Βλάβη

Kidney damage was suggested by the presence of proteinuria (≥1+), haematuria (≥1+) or uninfectious leucocyturia (≥1+ without nitrite).

http://www.kidney.org/professionals/KLS/gfr_calculator.cfm

http://nephron.com/mdrd/default.html

Στάδια της ΧΝΝ σύμφωνα με τις οδηγίες της KDOQI

Στάδια	Περιγραφή	GFR	Επίπτωση
1	Νεφρική βλάβη με φυσιολογικό ή αυξημένο GFR	≥ 90 ml/min/1.73 m^2	3.3%
2	Νεφρική βλάβη με ήπια μείωση του GFR	60-89	3%
3	Μέτρια μείωση του GFR	30-59	4.3%
4	Μεγάλη μείωση του GFR	15-29	0.2%
5	Νεφρική ανεπάρκεια τελικού σταδίου	<15	0.2%

Rheumatology 2008;47:350–354
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Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study

TABLE 2. Prevalence of KD in RA patients according to NKF classification in MATRIX study patients

Stage	GFR (ml/min/1.73 m^2)	Prevalence, *n* (%)	
		aMDRD formula *n* = 80[b] (%)	CG formula *n* = 79[c] (%)
Stage 1	≥90 + Kidney damage[a]	9 (11.3)	9 (11.4)
Stage 2	60–89 + Kidney damage[a]	16 (20.0)	16 (20.3)
Stage 3	30–59	12 (15.0)	19 (24.1)
Stage 4	15–29	0	1 (1.3)
Stage 5	<15	0	0
All stages		37 (46.3)	45 (57.0)

Conclusion

This prospective observational study showed that the prevalence of KD indicators in RA patients is common. Nearly half of the RA patients are presenting a KD according to NKF classification.

Rheumatology key messages

- SCr is not sufficient to estimate RF in RA patients.
- In patients with KD at high risk for drug toxicity, dosage should be adapted to RF.

Βιολογικές Θεραπείες: επιδράσεις στα νεφρά

Είναι νεφροτοξικοί οι βιολογικοί παράγοντες;;;

Anti-TNFα	**Infliximab** **Etanercept** **Adalimumab** **Cetrolizumab pegol** **Golimumab**
Anti-IL_6	Tocilizumab
Anti-IL_1Ra	Anakinra
Anti-B cells	Rituximab
Anti-T cell costimulation	Abatacept
Anti-IL 1	Canakinumab

Βιολογικοί παράγοντες: επίδραση στη νεφρική λειτουργία

Infliximab **Etanercept** **Adalimumab** **Cetrolizumab pegol** **Golimumab** **Tocilizumab** **Rituximab** **Abatacept** **Canakinumab**	**1. Δεν επηρεάζει τη νεφρική λειτουργία** **2. Δεν απαιτείται προσαρμογή δόσης σε ήπια νεφρική ανεπάρκεια** **3. Νεφρική αυτοανοσία (anti-TNF)**
Anakinra	1. Δεν απαιτείται προσαρμογή δόσης στην ήπια νεφρική ανεπάρκεια 2. Χορήγηση με προσοχή στη μέτρια νεφρική ανεπάρκεια (50ml/min>Clcr>30 ml/min)

Βιολογικές θεραπείες σε ασθενείς με Ρευματικό Νόσημα

Οι μεγάλες κλινικές μελέτες ΔΕΝ συμπεριέλαβαν ασθενείς με κάθαρση κρεατινίνης <50 ml/min

(Θεραπευτικός μηδενισμός;;)

Φαρμακοκινητική των Βιολογικών παραγόντων

ΔΕΝ υπάρχουν επίσημα φαρμακοκινητικά δεδομένα σε ασθενείς με μέτρια ή σοβαρή νεφρική ανεπάρκεια

JPP Journal of Pharmacy and Pharmacology

JPP 2005, 57: 1407–1413

The pharmacokinetics of etanercept in patients with end-stage renal disease on haemodialysis

Burl R. Don, Gregory Spin, Ivan Nestorov, Matt Hutmacher, Aubri Rose and George A. Kaysen

Conclusions

The pharmacokinetics of etanercept in patients with chronic renal failure on haemodialysis are similar to those in patients with normal renal function. It is, therefore, feasible to administer etanercept to HD patients without adjusting the dose.

American Journal of Hematology 71:219–222 (2002)

Treatment of a Patient With End-Stage Renal Disease With Rituximab: Pharmacokinetic Evaluation Suggests Rituximab Is Not Eliminated by Hemodialysis

Anand P. Jillella,* Paul M. Dainer, Andre M. Kallab, and Celalettin Ustun
Medical College of Georgia, Department of Medicine, Section of Hematology, Augusta, Georgia

The purpose of this study was to determine if therapeutic levels of Rituximab could be achieved in a patient with renal failure being dialyzed and if Rituximab is removed by hemodialysis. A 54-year-old man with low-grade lymphoma and renal failure on hemodialysis received 8 weekly treatments of Rituximab at 375 mg/M^2. Serum Rituximab levels were obtained before and after each treatment, before and after dialysis following each treatment, as well as in the dialysate fluid. The serum levels of Rituximab increased gradually with each treatment and were comparable to levels in patients with normal renal function. The postdialysis levels were higher than the predialysis levels as a consequence of hemo-concentration after dialysis. Rituximab was not detected in the dialysate fluid. The patient developed life-threatening hyperkalemia after the fourth treatment, which we believe occurred secondary to tumor lysis. Therapeutic levels of Rituximab may be maintained in patients undergoing dialysis. Rituximab is not eliminated by hemodialysis. Am. J. Hematol. 71:219–222, 2002.

Key words: Rituximab; follicular lymphoma; low-grade lymphoma; renal failure; tumor lysis; hemodialysis

Φαρμακοκινητική των Βιολογικών παραγόντων σε ασθενείς με φυσιολογική νεφρική λειτουργία

- Η βιοδιαθεσιμότητα είναι έως και 100%
- Η κατανομή είναι κυρίως αντιγονοειδική
- Η αποβολή επιτελείται κυρίως μέσω φαγοκυττάρωσης

- Εξαίρεση αποτελεί το Anakinra που αποβάλλεται όπως η κρεατινίνη και μειώνεται σε νεφρική ανεπάρκεια

Εκτός ενδείξεων (off label use) χορήγηση βιολογικών παραγόντων σε ασθενείς με Ρευματικό Νόσημα και νεφρική ανεπάρκεια (στάδια 1-4)

Παρουσίαση case reports

Anti-TNF treatment in secondary amyloidosis

V. Ortiz-Santamaria, M. Valls-Roc, M. Sanmartí, A. Olivé

Rheumatology 2003;42:1425–1426

Follow-up	Painful joints	Swollen joints	CRP (mg/l)	ESR (mm/1st h)	Creatinine (mg/dl)	Proteinuria (g/24 h)
Patient A						
Baseline	26	13	30	24	1.15	0.70
10 months	8	5	22.3	25	1.6	n.d.
22 months	4	2	0	7	1.23	0.34
28 months	3	0	10	8	1.31	0.55
Patient B						
Baseline	2	1	16.9	58	2.7	1.95
10 months	2	1	20.1	113	2.6	1.14
16 months	0	1	9	53	2.23	0.48
Patient C						
Baseline	3	7	38.7	110	2.45	1.18
10 months	0	3	0	51	2	0.36

CRP, C-reactive protein (normally <5 mg/l); ESR, erythrocyte sedimentation rate; n.d., not determined.

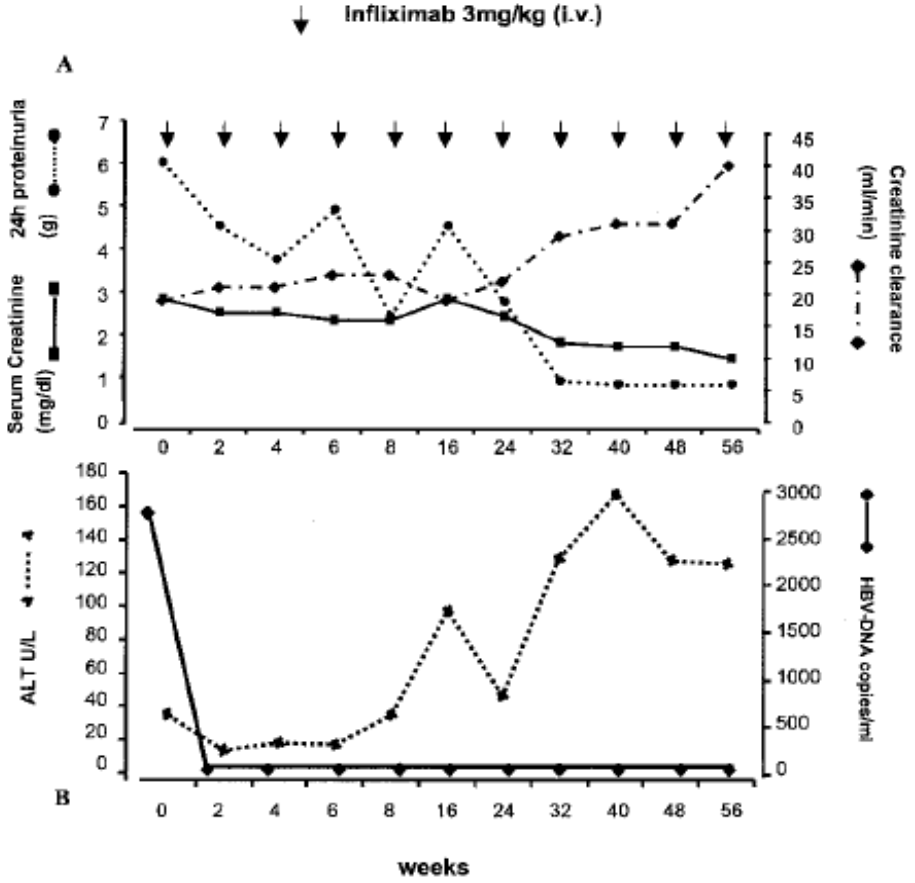
Βιολογική θεραπεία με 3mg/kg Infliximab
Αιτία δευτεροπαθούς αμυλοείδωσης η Ρευματοειδής Αρθρίτιδα

Συμπέρασμα: Όχι επιδείνωση νεφρικής λειτουργίας, όχι άλλες παρενέργειες

ARTHRITIS & RHEUMATISM
Vol. 52, No. 8, August 2005, pp 2519–2520
DOI 10.1002/art.21216

Improvement of Renal Function and Disappearance of Hepatitis B Virus DNA in a Patient With Rheumatoid Arthritis and Renal Amyloidosis Following Treatment With Infliximab

Maria Grazia Anelli, Diletta Domenica Torres, Carlo Manno, Crescenzio Scioscia, Florenzo Iannone, Michele Covelli, Francesco Paolo Schena, and Giovanni Lapadula



Conclusion

evidence of HBV reactivation. Our patient had a complete and prolonged disappearance of HBV DNA after 1 year of treatment with infliximab, and improved renal function with a reduction of daily proteinuria. However, continued laboratory and clinical monitoring is required.

Efficacy of etanercept in patients with AA amyloidosis secondary to rheumatoid arthritis

T. Nakamura[1], S. Higashi[1], K. Tomoda[2], M. Tsukano[2], S. Baba[3]

Patient/ Age/ Sex	Disease duration RA/Amyloidsis (years)	SAA1 gene polymorphism	Prior DMARDs	Associated Prednisolone (mg/day)	Organ involvement	Proteinuria (g/day) Initial*	Proteinuria (g/day) Last**	Serum creatinine (mg/dl) Initial*	Serum creatinine (mg/dl) Last**	Follow-up (weeks)
1/53/F	12/11	1.3/1.3	CYC, MTX BU, SASP	0	Kidney	2.6	0.6	4.3	4.5	68
2/57/F	25/2	1.1/1.3	CYC, MTX GST, CyA TCR, SASP	5	Kidney Digestive tract Thyroid	3.2	1.2	5.3	3.6	56
3/70/M	43/5	1.3/1.3	GST, BU MTX, AU	10	Kidney	1.9	1.7	2.3	2.2	20
4/60/F	37/9	1.2/1.3	MTX, IM CYC, BU LEF, SASP	2	Kidney Heart, thyroid Bladder Digestive tract	1.8	0.3	0.9	0.9	37
5/59/F	6/2	1.2/1.3	BU, D-p, AU TCR, CYC MTX	5	Kidney Thyroid Digestive tract	2.5	1.2	4.0	3.8	32
6/72/F	4/2	1.3/1.3	CYC, MTX BU, CyA	10	Kidney	1.2	0.3	0.5	0.4	37
7/54/F	15/4	1.3/1.3	BU, MTX SASP, TCR CYC	3	Kidney Thyroid Digestive tract	2.9	0.8	2.6	2.4	54

CYC: cyclophosphamide; MTX: methotrexate; BU: bucillamine; SASP: sulfasalazine; GST: sodium aurothiomalate; CyA: ciclosporin; TCR: tacrolimus; AU: auranofin; IM: azathioprine; LEF: leflunomide; D-p: D-penicillamine.
*,** The value of initial (before etanercept) - and last (the index time) - visit following treatment with etanercept between follow-up periods.

Clinical and Experimental Rheumatology 2007; **25**: 518-522.

Rheumatol Int
DOI 10.1007/s00296-009-1108-z

CASE REPORT

Etanercept treatment in rheumatoid arthritis patients with chronic kidney failure on predialysis

Soo-Kyung Cho · Yoon-Kyoung Sung · Songree Park · Sang-Cheol Bae

Conclusion

three cases suggest that etanercept might be a potential treatment option for RA patients with chronic kidney failure on predialysis. Larger trials are needed, however, to further support its use in this patient group.

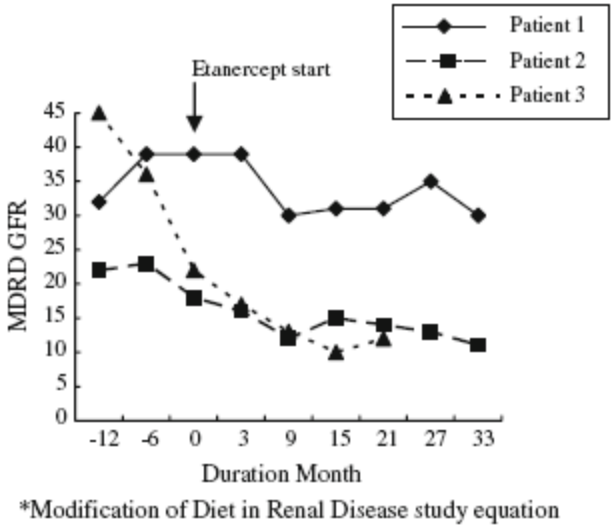


Fig. 2 Change in MDRD* GFR during etanercept treatment. *Modification of Diet in Renal Disease study equation

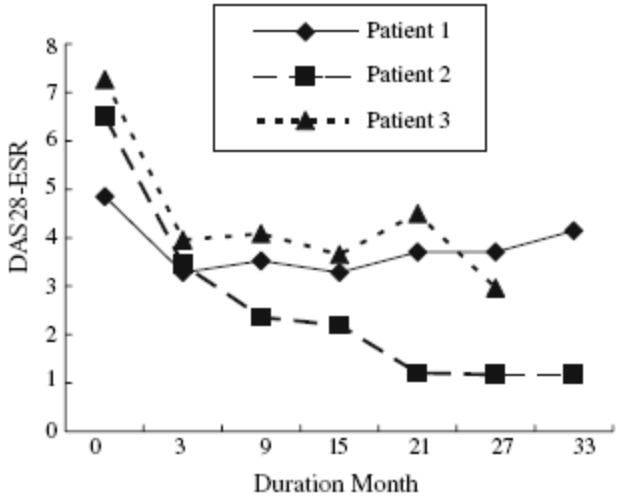


Fig. 1 The disease activity score (DAS) 28-ESR at baseline and during treatment

Anti-tumour necrosis factor α therapy in patients with impaired renal function

Axel J Hueber, Andac Tunc, Georg Schett, Bernhard Manger

Ann Rheum Dis 2007;**66**:981–982. doi: 10.1136/ard.2006.069211

Table 1 Characteristics of patients with renal insufficiency and anti-tumour necrosis factor α therapy

	Patient										
	1	2	3	4	5	6	7	8	9	10	11
Age (years)	30	64	65	65	67	71	72	63	76	50	34
Sex	M	M	F	F	F	F	F	F	M	M	F
Diagnosis	RA	RA	RA	RA	RA	RA	RA	RA	RA	PsA	JRA
Use of anti-TNFα therapy	ETC	ETC	ETC	ETC	ETC	ADM, INX, ETC	ADM, INX, ETC	INX	INX	INX	INX
Concomitant diseases:											
Hypertension	+	–	+	+	+	+	+	+	+	+	+
Diabetes	+	–	–	–	–	+	–	+	+	–	–
Non-steroidal anti-inflammatory drug nephropathy	–	–	–	–	–	–	+	+	–	–	–
Sarcoidosis	–	–	–	–	–	–	–	–	–	–	+
EULAR response	Good	Good	None	Good	None	Mod	None	None	None	Rem	Good
Creatinine (mg/dl)											
Month 0	1.34	4.32	1.13	1.5	1.99	1.5	1.09	1.34	1.57	1.12	ESRD
Month 3	1.41	4.33	1.19	1.54	1.81	1.6	1.23	1.34	1.21	1.13	
Month 6	1.38	4.85	1.07	1.59	1.96	1.9	1.12	1.46	1.05	1.04	
End of study interval (months)	1.71 (17)	5.46 (22)	1.26 (24)	2.2 (19)	2.47 (13)	2.1 (15)	1.13 (10)	1.45 (22)	2.14 (21)	1.2 (20)	
Maximum	1.71	5.46	1.26	2.2	2.47	2.1	1.31	1.68	2.14	1.24	

ADM, adalimumab; ETC, etanercept; ESRD, end stage renal disease; EULAR, European League Against Rheumatism; F, female; INX, infliximab; JRA, juvenile rheumatoid arthritis; M, male; Mod, moderate response; NSAID, non-steroidal anti-inflammatory drug; PsA, psoriatic arthritis; RA, rheumatoid arthritis; Rem, clinical remission; TNFα, tumour necrosis factor α.

Two patients were treated with all biological therapy (ETC, ADM and INX); the others were treated with only one biological therapy. The end of the study interval indicates the duration of our observation period with any of the biological treatments. Patients responding to this treatment continued to receive anti-TNFα therapy. Values in parentheses denote the period of the study time of the study interval for each patient in months.

Anti-tumour necrosis factor α therapy in patients with impaired renal function

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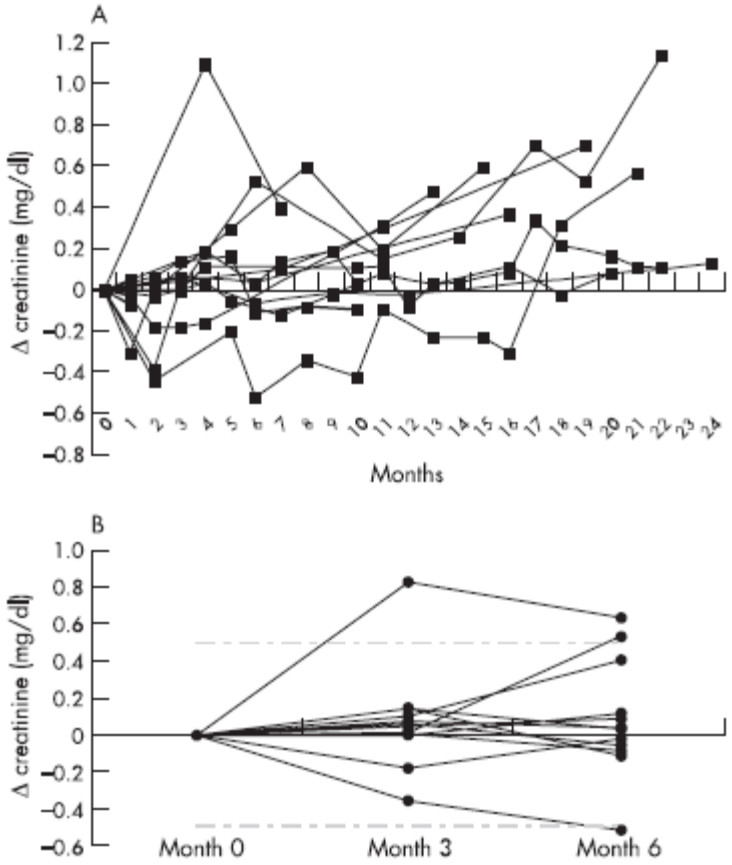


Figure 1 Course of creatinine in renal insufficiency with concomitant anti-tumour necrosis factor alpha (TNFα) therapy. (A) Time course of change (Δ) in serum creatinine concentrations in 10 patients during anti-TNFα therapy. (B) Creatinine changes (Δ) within the first 6 months of anti-TNFα therapy. Dashed-dotted line depicts change in creatinine of 0.5 mg/dl. No significant increases, as analysed by Friedman's test.

ΣΥΜΠΕΡΑΣΜΑ

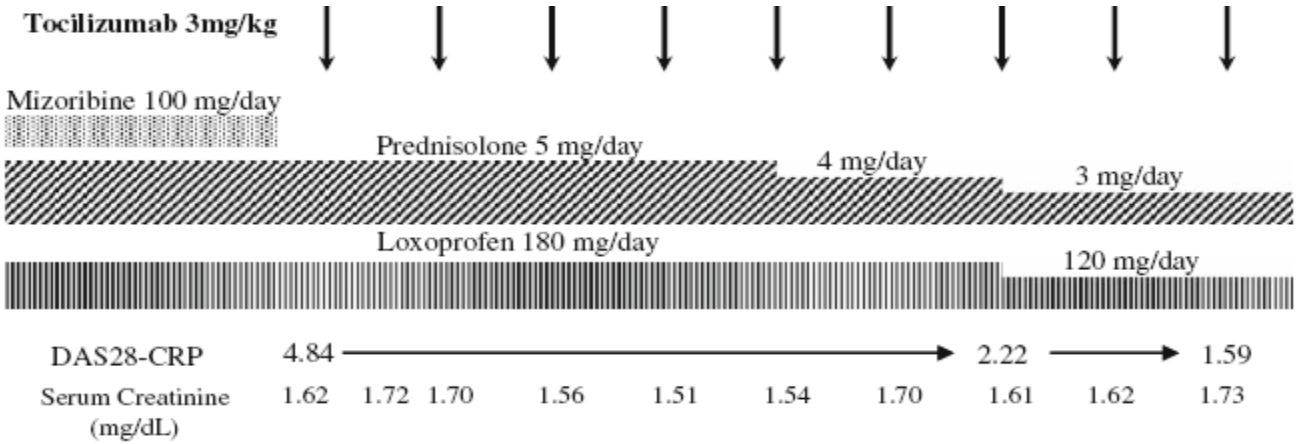
been excluded from these trials.[6–8] In conclusion, our data indicate that the use of TNFα inhibitors has no negative effect on renal function in patients with kidney disease.

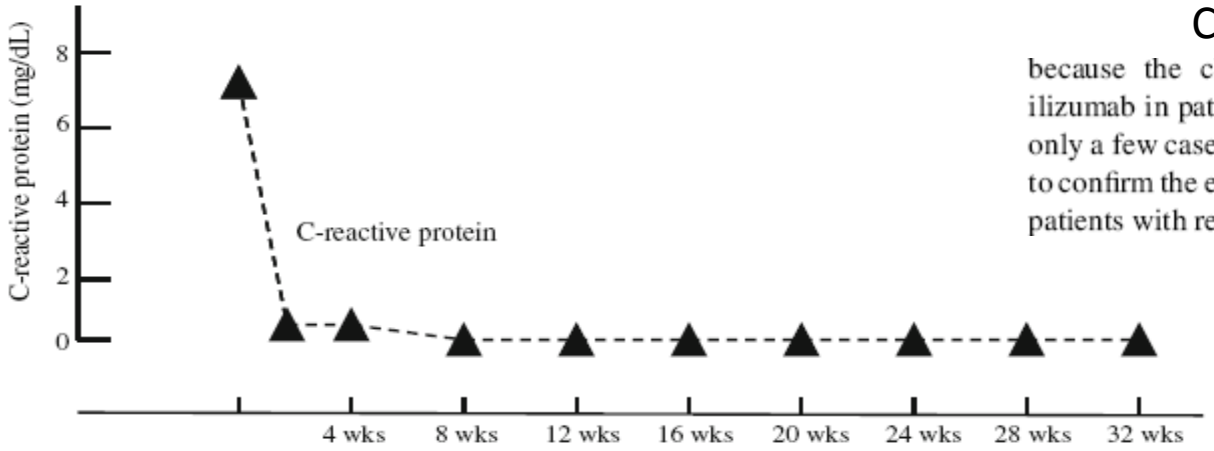
Mod Rheumatol
DOI 10.1007/s10165-009-0263-0

LETTER

A case of active rheumatoid arthritis with renal dysfunction treated effectively with tocilizumab monotherapy

Takashi Kato · Ichiro Koni · Ryo Inoue · Susumu Kitajima · Mitsuhiro Kawano · Masakazu Yamagishi





Conclusion

because the clinical usefulness of etanercept and tocilizumab in patients with renal dysfunction is suggested by only a few case reports, further investigations are necessary to confirm the exact safety of treatment with the biologics in patients with renal dysfunction.

Eur J Haematol 2003: 71: 128–129

Case Report

Treatment of a patient with chronic renal failure with rituximab for a follicular lymphoma: safe and successful option of rituximab therapy

Abstract: A 47-yr-old woman presented a chronic renal failure for 5 yr, with a creatinine clearance of 12 mL/min. In June 2002, she had a right axillary lymph node (of 4 cm diameter). A biopsy revealed a follicular lymphoma (histology: follicular small cleaved-cell). She had Ann Arbor stage III disease, with a high tumor burden according to the GELF criteria. She received rituximab as single first-line treatment (375 mg/m^2 by intravenous infusion for a total of four dosages: days 1, 8, 15 and 22). Rituximab therapy was extremely well tolerated, and we obtained a partial response, 4 wk after completing the treatment. In January 2003, she received one maintenance course of rituximab. Six weeks after maintenance therapy, a complete response was achieved.

In conclusion, rituximab represents an unproblematic, safe, and successful treatment option in the case of end-stage renal failure.

Εκτός ενδείξεων (off label use) χορήγηση βιολογικών παραγόντων σε ασθενείς με Ρευματικό Νόσημα και νεφρική ανεπάρκεια τελικού σταδίου (Αιμοκάθαρση)

Παρουσίαση case reports

Case Report

Infliximab Treatment in a Patient with Rheumatoid Arthritis on Hemodialysis

RANJU SINGH, RAQUEL CUCHACOVICH, WENQUN HUANG, and LUIS R. ESPINOZA

ABSTRACT. We describe a 60-year-old woman with active rheumatoid arthritis (RA) and endstage renal disease secondary to hypertensive nephrosclerosis undergoing hemodialysis. She had tried multiple antirheumatic medications; however, their usefulness was limited due to toxic side effects or lack of efficacy. She was then treated with chimeric antitumor necrosis factor monoclonal antibody (infliximab), which resulted in immediate improvement in clinical and laboratory measures. After about 2 years of therapy, no side effects have been observed. This report expands the spectrum of infliximab to include RA patients with renal insufficiency. (J Rheumatol 2002;29:636–7)

Conclusion

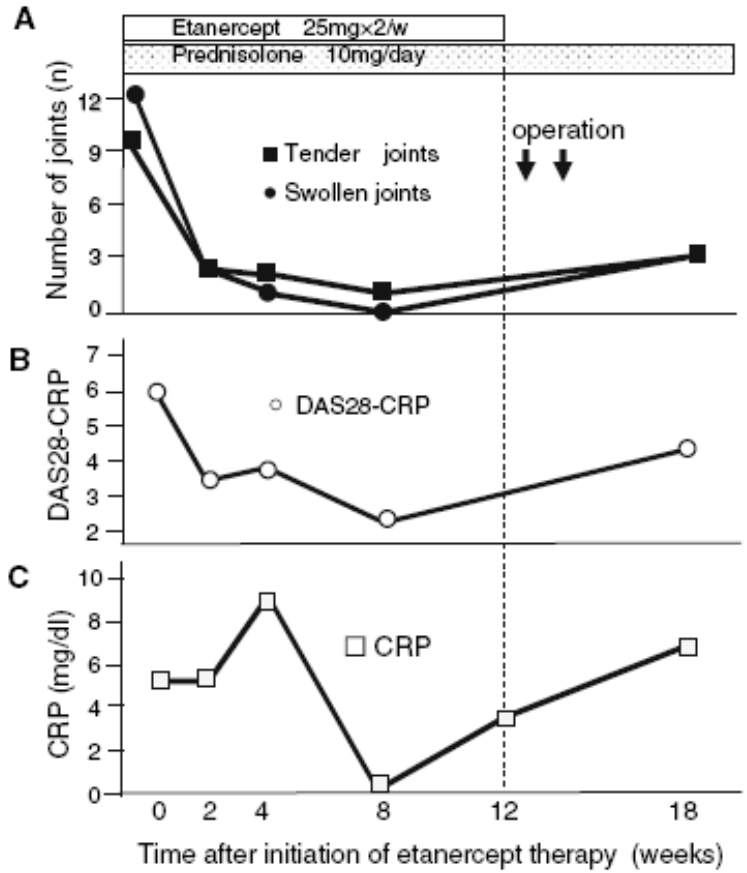
This case study suggests that infliximab treatment might be safe, well tolerated, and effective therapy for RA patients with ESRD undergoing hemodialysis. In addition, this case illustrates the longterm efficacy of infliximab despite the lack of concomitant administration of MTX. Larger trials are needed to support its use in these patients.

Mod Rheumatol (2008) 18:293–295
DOI 10.1007/s10165-008-0041-4

CASE REPORT

Use of etanercept in a patient with rheumatoid arthritis on hemodialysis

Yuko Sugioka · Kentaro Inui · Tatsuya Koike



Conclusion

We report a case in which etanercept therapy was used successfully for a patient with RA on HD. Administration of etanercept may thus be useful for RA patients on HD in short term as an alternative treatment.

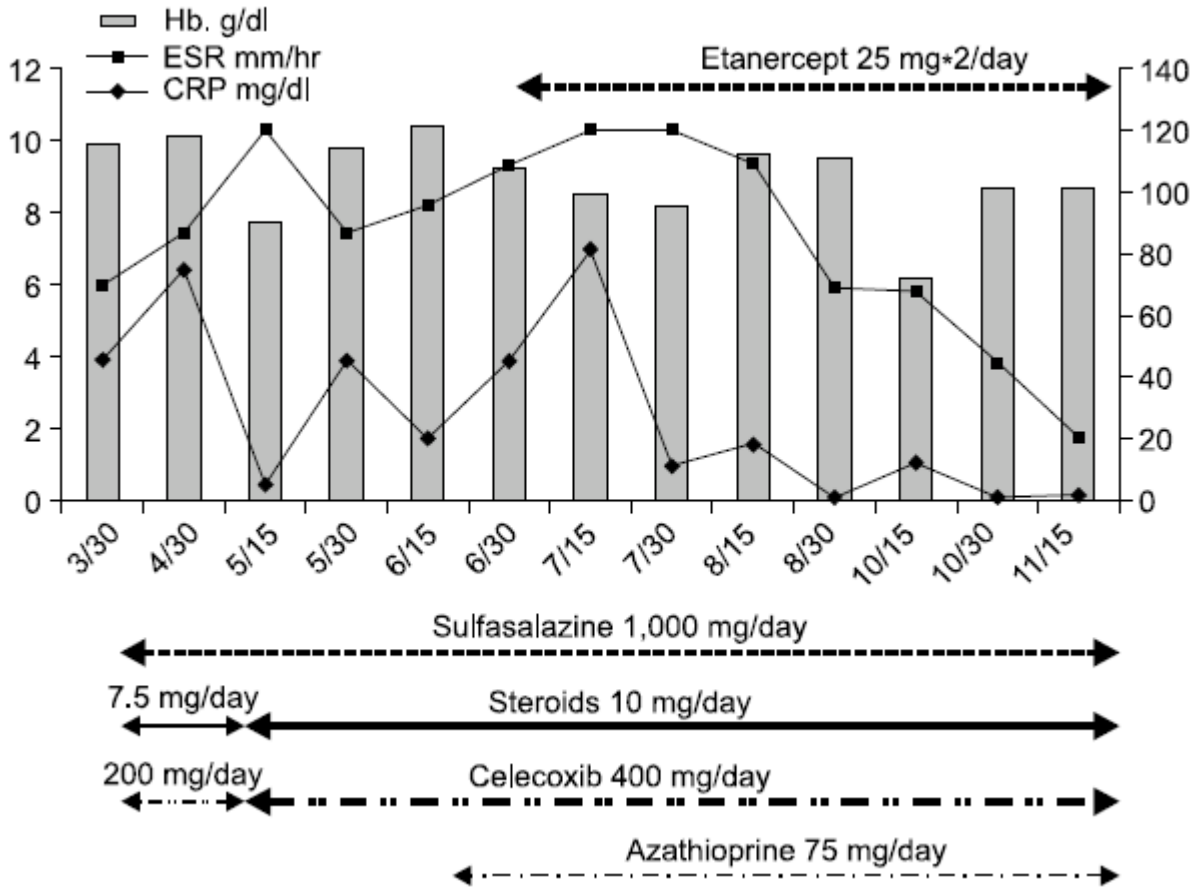
A Case of Treatment with Etanercept in Rheumatoid Arthritis Patient on Hemodialysis

Dae Hyun Baek, Eun Ju Song, Myoung Ha Lee, Sang Ryul Lee, Su-Ah Sung, Young-Hwan Hwang, Jin-Wuk Hur

Department of Internal Medicine, Eulji University College of Medicine, Seoul, Korea

Disease-modifying antirheumatic drugs (DMARDs) have been used for rheumatoid arthritis (RA) with the aim of controlling synovitis and reducing radiologic progression. Although methotrexate (MTX) is one of the most effective DMARDs, it may cause severe adverse effects. Especially, hematologic toxicity including leukopenia, thrombocytopenia, and fatal pancytopenia is reported in patients with impaired renal function, since renal excretion constitutes the major route of MTX elimination. Tumor necrosis factor-α (TNFα) inhibitors are well-established biologic agents for the treatment of RA and their clinical efficacy and safety are already demonstrated. But there were few reports on the efficacy and safety in dialysis patients. We described a case of hemodialysis patient with refractory RA that was successfully treated with etanercept, and discussed with literature review.

대 한 류 마 티 스 학 회 지
Vol. 15, No. 4, December, 2008


Hb. g/dl
ESR mm/hr
CRP mg/dl
Etanercept 25 mg*2/day
12
10
8
6
4
2
0
140
120
100
80
60
40
20
0
3/30
4/30
5/15
5/30
6/15
6/30
7/15
7/30
8/15
8/30
10/15
10/30
11/15
Sulfasalazine 1,000 mg/day
7.5 mg/day
Steroids 10 mg/day
200 mg/day
Celecoxib 400 mg/day
Azathioprine 75 mg/day

Nephrol Dial Transplant (2009) 24: 676–678
doi: 10.1093/ndt/gfn646
Advance Access publication 25 November 2008

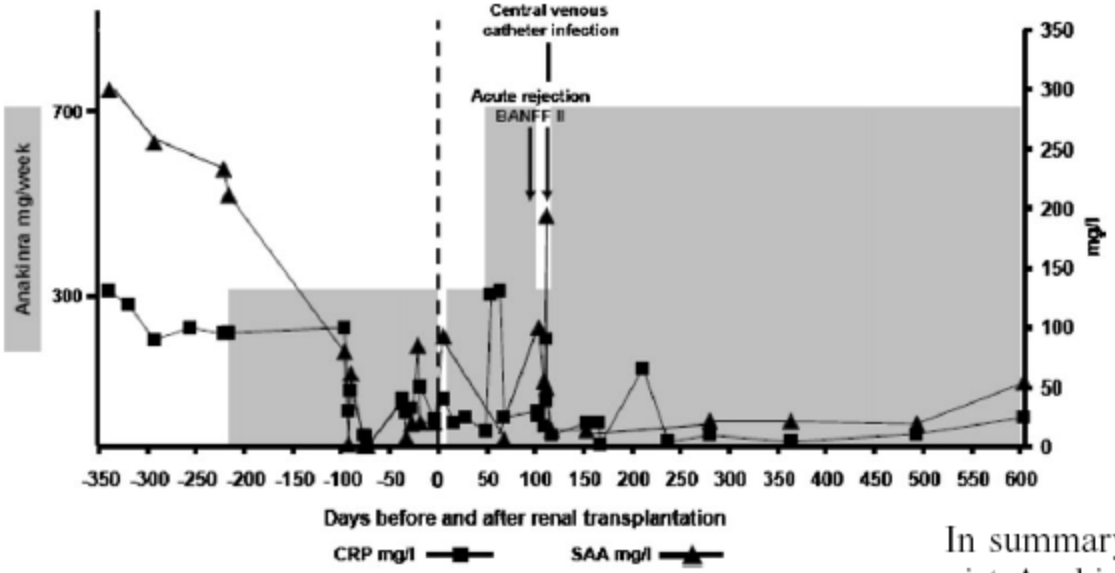
NDT
Nephrology Dialysis Transplantation

Exceptional Case

Successful treatment of familial Mediterranean fever with Anakinra and outcome after renal transplantation

Christian Moser[1], Gudrun Pohl[2], Isabella Haslinger[3], Sylvia Knapp[3], Dorota Rowczenio[4], Tonia Russel[4], Helen J. Lachmann[4], Ursula Lang[1] and Josef Kovarik[1]

Successful treatment of FMF with Anakinra and outcome after renal transplantation



In summary, we perceived evidence that the IL-1 antagonist Anakinra might be a safe and effective substance for the treatment of colchicines-resistant patients with FMF on haemodialysis, as well as after successful kidney transplantation. We therefore conclude that prospective studies on a larger number of patients are necessary to prove this hypothesis.

Joint Bone Spine 76 (2009) 424–426

Case report

Anakinra is a possible alternative in the treatment and prevention of acute attacks of pseudogout in end-stage renal failure

Nadia Announ, Gaby Palmer, Pierre-André Guerne, Cem Gabay*

Division of Rheumatology, Department of Internal Medicine, University Hospitals of Geneva and University of Geneva School of Medicine, Geneva, Switzerland

Accepted 7 January 2009
Available online 16 March 2009

Abstract

We describe the case of a 71-year-old man with recurrent pseudogout attacks affecting multiple joints. He had end-stage renal failure that contra-indicated the use of non-steroidal anti-inflammatory drugs and was resistant to therapy with glucocorticoids. Based on the recent findings that interleukin (IL)-1β is involved in crystal-induced inflammation, the patient received anakinra, a specific IL-1 inhibitor, in order to treat an acute attack of pseudogout. In addition, anakinra was administered as preventive therapy 3 days per week after each hemodialysis session. Under this treatment, he did not present any severe episode of arthritis after a follow-up of 8 months. This observation suggests that anakinra is efficacious and safe for the prevention of crystal-induced arthritis in patients with severe renal failure.

Keywords: Chondrocalcinosis; IL-1; Pseudogout; End-stage renal failure

ΣΥΜΠΕΡΑΣΜΑΤΑ (Ι)

Υπάρχουν λίγες αναφορές στη βιβλιογραφία για τη χορήγηση βιολογικής θεραπείας σε ασθενείς με Ρευματοειδή Αρθρίτιδα και ΧΝΑ ή Αιμοκάθαρση Σύμφωνα με αυτές:

- Οι Βιολογικοί παράγοντες αποτελούν αποτελεσματική και ασφαλή θεραπευτική επιλογή στη Ρευματοειδή Αρθρίτιδα με ΧΝΑ
- Οι Βιολογικοί παράγοντες δεν επιδεινώνουν τη ΧΝΑ
- Οι Βιολογικοί παράγοντες χορηγούνται σε ασθενείς με Ρευματοειδή Αρθρίτιδα υπό Αιμοκάθαρση με επιτυχία

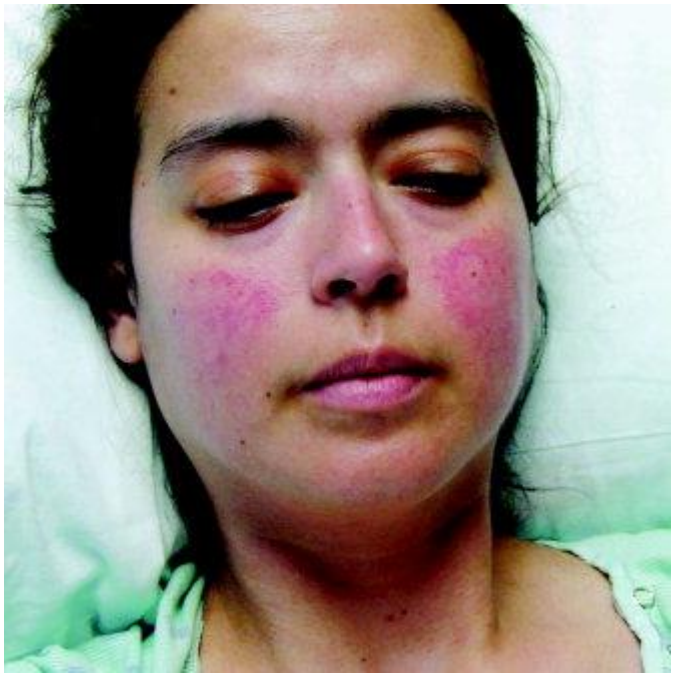
- Autoimmun Rev. 2010 Jan;9(3):188-93. Epub 2009 Oct 23.
- **Autoimmune diseases induced by biological agents: a double-edged sword?**
- Ramos-Casals M, Roberto-Perez-Alvarez, Diaz-Lagares C, Cuadrado MJ, Khamashta MA; BIOGEAS Study Group.
- Collaborators (32) Ramos-Casals M, Ayala MM, Brito-Zerón P, Callejas JL, Caminal-Montero L, Camps MT, Colodro A, de Ramón E, Díaz-Lagares C, Egurbide MV, Galiana D, García Hernández FJ, Gil A, Gómez de la Torre R, Hidalgo C, Jiménez-Alonso J, Martínez-Berriotxoa A, Medrano F, Micó ML, Muñoz S, Ocaña C, Oristrell J, Ortego N, Pallarés L, Pérez de Lis M, Perez-Alvarez R, Ruiz-Irastorza G, Salvador G, Sánchez-Roman J, Selva-O'Callaghan A, Soto MJ, Tolosa C.
- Laboratory of Autoimmune Diseases Josep Font, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Autoimmune Diseases, Hospital Clínic, Barcelona, Spain. mramos@clinic.ub.es
- **Abstract**
- Biological agents are increasingly used for a rapidly-expanding number of rheumatic and systemic autoimmune diseases, with a growing number of reports of the paradoxical induction of autoimmune processes, overwhelmingly associated with anti-TNF agents. In this review, we analyze the clinical characteristics and outcomes of autoimmune diseases developing after biological therapies through a baseline Medline search as one of the objectives of the BIOGEAS project, created by the Spanish Society of Internal Medicine. The latest update of our registry (15 July 2009) included more than 800 cases of autoimmune diseases secondary to biological therapies, including a wide variety of both systemic (lupus, vasculitis, sarcoidosis and antiphospholipid syndrome) and organ-specific (interstitial lung disease, uveitis, optic neuritis, peripheral neuropathies, multiple sclerosis and autoimmune hepatitis) autoimmune processes. The majority of cases appeared between one month and one year after initiation of the biological agent and complete resolution was observed in nearly 75% of cases after cessation of therapy. The induced autoimmune diseases with the poorest outcomes were interstitial lung disease, inflammatory ocular disease and central nervous system demyelinating diseases.

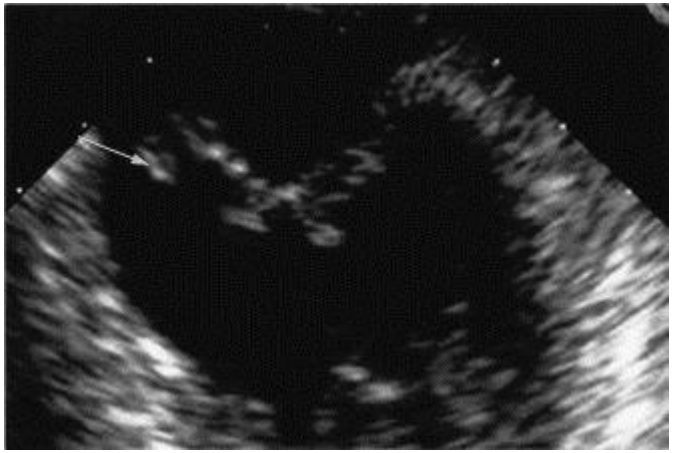
Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 55, No. 1, February 15, 2006, pp 163–166
DOI 10.1002/art.21702

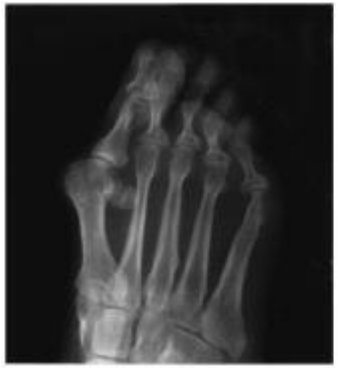
CASE REPORT

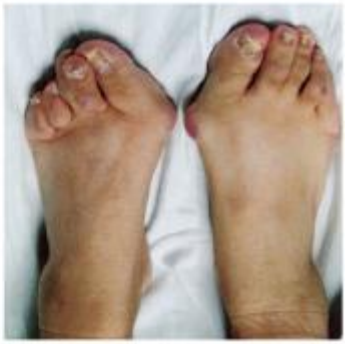
Infliximab-Related Lupus and Associated Valvulitis: A Case Report and Review of the Literature

TINA CHADHA AND JESUS EDWARD HERNANDEZ

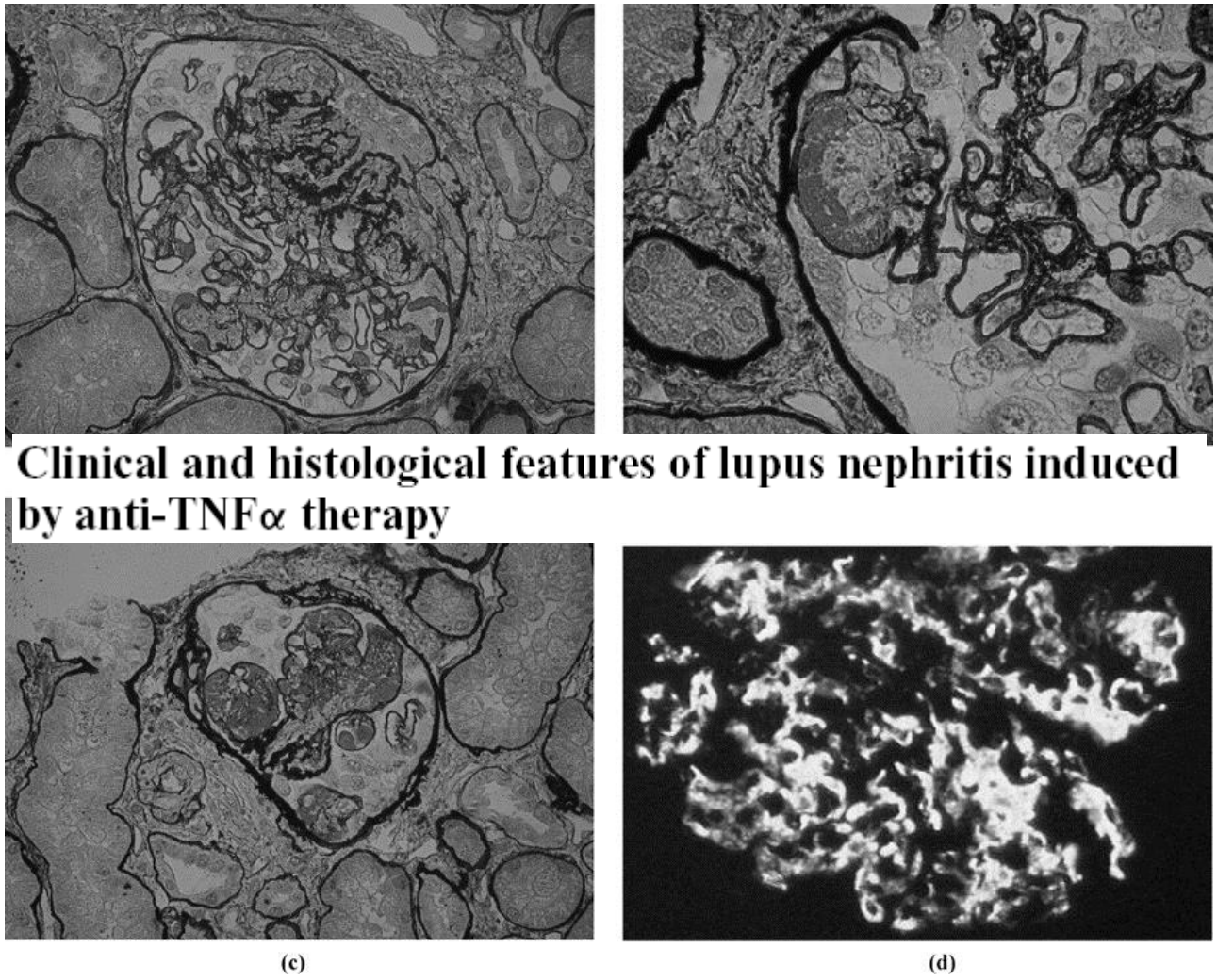








Segmental solidification of glomerular tuft due to endocapillary hypercellularity and increase of collagenous matrix



Piccolo, T. et al. NDT Plus 2008 1:221-224; doi:10.1093/ndtplus/sfn060

NDT PLUS
Nephrology Dialysis Transplantation

Nephrol Dial Transplant (2005) 20: 2824–2826
doi:10.1093/ndt/gfi180
Advance Access publication 4 October 2005

Nephrology
Dialysis
Transplantation

Case Report

Infliximab and nephrotic syndrome

George Chin[1], Grant Luxton[1] and Jennet M. Harvey[2]

Infliximab and nephrotic syndrome

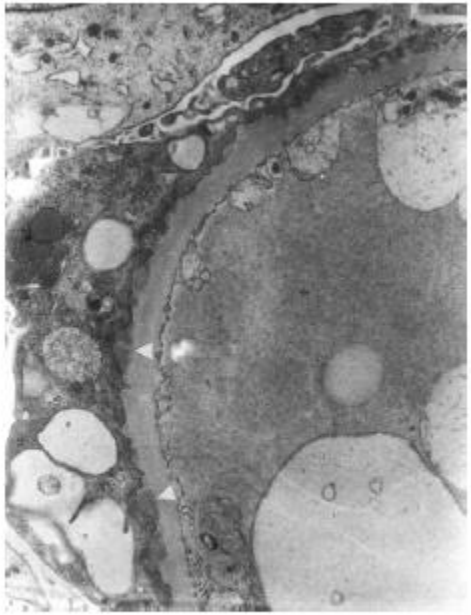


Fig. 1. Multiple small electron dense deposits are seen in the lamina rara externa beneath effaced podocytic processes. Arrowheads indicate two subepithelial deposits (×9000).

ΣΥΜΠΕΡΑΣΜΑ

Clinicians need to consider infliximab as a potential cause of renal injury in patients to whom it is given. This report describes a probable case of infliximab induced-membranous nephropathy which we believe to be the first case described in the literature.

Development of glomerulonephritis during anti-TNF-α therapy for rheumatoid arthritis

M. B. Stokes *et al.* | Nephrol Dial Transplant (2005) 20: 1400–1406

Table 1. Clinical characteristics of five RA patients with glomerulonephritis following anti-TNFα therapy

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age/sex	30/F	52/F	55/M	64/F	53/F
RA, duration (years)	JRA, 23	RA, 22	RA, 10	RA, 30	RA/SS, 30
Anti-TNFα therapy (mos)	Etanercept (30)	Adalimumab (3)	Etanercept (4)	Infliximab (10)	Etanercept (6)
Other current therapy	CS; MTX	CS; NSAID; MTX; MMF		CS; NSAID	Cytoxan Methotrexate
Previous therapy	Leflunamide Azathioprine	Infliximab Penicillamine Gold	Methotrexate	Etanercept Gold Penicillamine Methotrexate	Gold
Other systemic signs	None	None	Alopecia; rash; mononeuritis; Pulmonary infiltrates	None	Sensory neuropathy
SCr mg/dl (baseline)	4 (0.7)	3.7 (1.1)	3.0 ('normal')	1.0 (0.7)	0.7 (0.7)
UVp g/24 h (baseline)	7 (NA)	3.8 (Neg)	1 (Neg)	1.8 (Neg)	7.9 (Neg)
ANA titre (baseline)	1:640 (1:640)	1:640 (Negative)	1:320 (NA)	Neg (NA)	1:160 (1:160)
Anti-dsDNA (baseline)	1:180 (Neg)	1:25 (Neg)	Neg (NA)	Neg (NA)	Neg (NA)
C3, C4	Decreased	Decreased	Normal	Normal	Normal
Other serologies	IgG ACL+	Atypical ANCA +	P-ANCA +	ANCA neg	ANCA neg SSA/SSB +
Stop anti-TNFα?	Yes	Yes	No	Yes	Yes
Other Rx post-biopsy	CS; MMF	Solumedrol	Cytoxan	Cytoxan; CS	CS; CsA
Follow-up interval (mos)	16	4	9 (died)	8	3
SCr mg/dl	1.6	1.1	2.2	1.3	0.6
UVp g/24 h	1.0	1.7	NA	8.5	1.06
Biopsy findings	Lupus nephritis, (Class IV)	Lupus nephritis, (Class III)	Pauci-immune nec. + cresc. GN	Pauci-immune nec. + cresc. GN; AA amyloid	Membranous GN + renal vasculitis

Conclusions. Rheumatoid arthritis patients receiving anti-TNFα agents may develop glomerulonephritis via the induction of rheumatoid arthritis-related nephropathy or de novo autoimmune disorders.

Treatment of Complicated Sarcoidosis with Infliximab Anti–Tumor Necrosis Factor-α Therapy

Arthur M.F. Yee, MD, PhD, and Mark B. Pochapin, MD

Background: **Tumor necrosis factor-α (TNF-α) may have an important role in the clinical exacerbation of sarcoidosis.**

Objective: **To treat sarcoidosis with infliximab, a chimeric human–murine anti–human TNF-α monoclonal antibody.**

Design: **Case report.**

Setting: **U.S. academic medical center.**

Patient: **A 72-year-old woman with sarcoidosis presenting with severe protein-losing enteropathy, hypoalbuminemia, and proximal myopathy who had not responded adequately to corticosteroid therapy and whose clinical course was further complicated by acute tubular necrosis and renal failure requiring long-term hemodialysis.**

Intervention: **Intravenous infusion of infliximab, 5 mg/kg of ideal body weight; infusion was repeated at 2 and 6 weeks.**

Measurements: **Clinical response of enteropathic and myopathic symptoms and serum albumin level.**

Results: **Enteropathic and myopathic symptoms resolved after infliximab therapy, and the serum albumin level also improved. However, the clinical course was complicated by the development of a hypercoagulable state associated with circulating anticardiolipin antibodies, which prompted discontinuation of infliximab therapy.**

Conclusions: **Infliximab therapy was successful in a patient with sarcoidosis. Tumor necrosis factor-α may be an important mediator of clinical disease in sarcoidosis and could be an attractive target for therapeutic intervention. However, infliximab may cause adverse effects associated with cytokine cascade manipulation.**

Ann Intern Med. 2001;135:27-31. www.annals.org

For author affiliations, current addresses, and contributions, see end of text.

Φυματίωση στη ΧΝΑ/Αιμοκάθαρση

- Επίπτωση από 6.9 έως 52.5 φορές μεγαλύτερη από τον γενικό πληθυσμό
- Κλινική εικόνα ασαφής
- Συχνά εξωπνευμονική εντόπιση (ΤΒ λεμφαδενίτιδα, περιτονίτιδα)
- Η Mantoux σπανίως θετική
- Υψηλή θνητότητα έως 40%

ΣΥΜΠΕΡΑΣΜΑΤΑ (ΙΙ)

- Η χορήγηση Βιολογικής θεραπείας στη ΡΑ με νεφρική δυσλειτουργία θα πρέπει να λαμβάνει υπόψη:
  - την επαγώγιμη από τους αντι-TNF νεφρική αυτοανοσία
  - την μεγάλη επίπτωση των λοιμώξεων και κυρίως της φυματίωσης στους νεφροπαθείς
- Υπάρχει ανάγκη μεγάλων κλινικών μελετών που θα συμπεριλάβουν και ασθενείς με μέτρια και βαριά νεφρική ανεπάρκεια