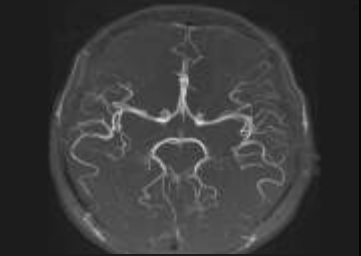


VII CURSO DE ACTUALIZACIÓN EN ENFERMEDADES AUTOINMUNES de la AADEA
Marbella, Málaga. 7 y 8 de Noviembre 2014.

Caso clínico

VASCULITIS DEL SISTEMA NERVIOSO CENTRAL RECIDIVANTE ASOCIADA A ENFERMEDAD DE BEHÇET

*C. Leyva Prado, E. Ortiz López, R. Delgado Villa, A. Hidalgo, C. Borrachero I. Martín Suárez,
Unidad de Enfermedades Autoinmunes Complejo Hospitalario de Huelva-Juan Ramón Jiménez.*





ANTECEDENTES PERSONALES:

- Mujer de 57 años que consulta en urgencias en el año de 1998 por disminución de conciencia y hemiparesia izquierda.
- Alergia a Moxifloxacino y fentanilo transdérmico.
- Ex fumadora de tabaco (1 paq/diario).
- No HTA. No DM. No DLP.
- Obesidad clase II.
- Criterios de bronquitis crónica con uso de inhaladores desde hace 20 años.
- Vida basal: independiente para todas las actividades básicas de la vida diaria.



AÑO 1998...

- Exploración física:

Nivel bajo de conciencia asociado a hemiparesia izquierda.

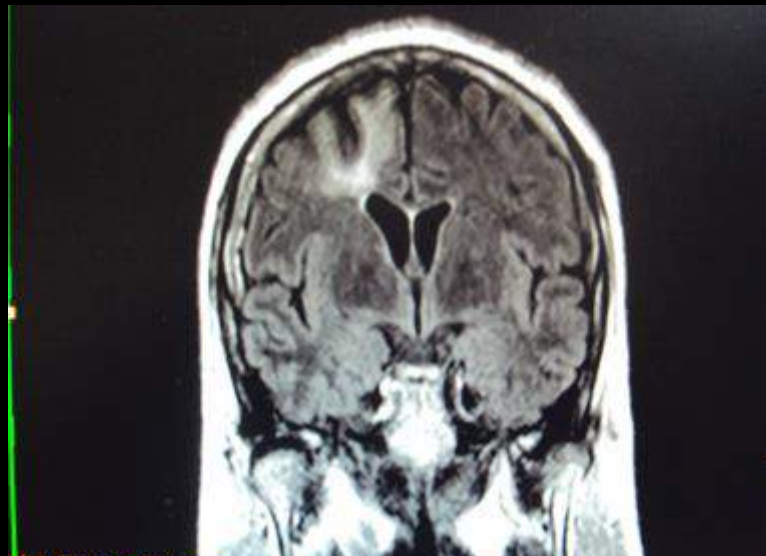
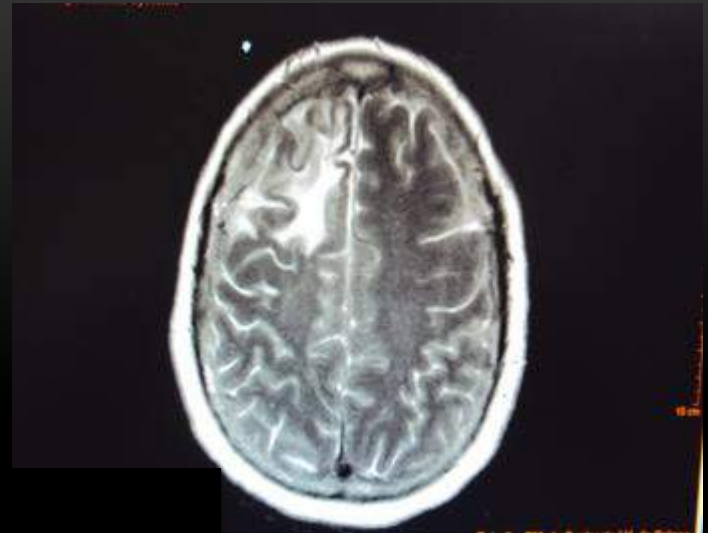


- TAC cráneo con contraste:

Lesión de aspecto tumoral frontal derecha con edema perilesional.

- Ingreso en el servicio de Neurocirugía donde se inicia tratamiento antiedematoso (Dexametasona) con posterior toma de biópsia.

Scane: Philips Medical Systems





QUÉ HA SUCEDIDO CON LA DEXAMETASONA?

- Tras el tratamiento a base de dexametasona la paciente queda asintomática.
- Alta por Neurocirugía: Con resultado de biopsia, tratamiento en pauta descendente de corticoides hasta suspender y referida a la consulta de Medicina Interna.
- **URGENCIAS:**

AFTAS OROGENITALES, PANICULITIS CUTÁNEA, PSEUDOPANICULITIS, ARTRALGIAS Y REPARICIÓN DE LA CLÍNICA NEUROLÓGICA.

Biopsia???



“Vasculitis pequeño vaso”

- Ante el cuadro clínico sugestivo de enfermedad de Behçet se inicia tratamiento con glucocorticoides orales y azatioprina.



Neuro-Behçet's disease: epidemiology, clinical characteristics, and management

Adnan Al-Araji, Desmond P Kidd

2009

Lancet Neurol 2009; 8: 192–204

Neurology Department,
University Hospital of North
Staffordshire, Stoke-on-Trent,
UK (A Al-Araji FRCP); and
Department of Clinical
Neurosciences, Royal Free
Hospital, London, UK
(D P Kidd FRCP)

J Neurol (2014) 261:1662–1676
DOI 10.1007/s00415-013-7209-3

REVIEW

Diagnosis and management of Neuro-Behçet's disease: international consensus recommendations

Seema Kalra • Alan Silman • Gulsen Akman-Demir • Saeed Bohlega • Afshin Borhani-Haghighi •
Cris S. Constantinescu • Habib Houman • Alfred Mahr • Carlos Salvarani •
Petros P. Sfikakis • Aksel Siva • Adnan Al-Araji

2014

The New England Journal of Medicine

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FEBRUARY 1, 1990

Number 5

A CONTROLLED TRIAL OF AZATHIOPRINE IN BEHÇET'S SYNDROME

HASAN YAZICI, M.D., HALIT PAZARLI, M.D., COLIN G. BARNES, M.D., YALÇIN TÜZÜN, M.D.,
YILMAZ ÖZYAZGAN, M.D., ALAN SILMAN, M.D., SERVER SERDAROĞLU, M.D.,
VELIEDDIN OĞUZ, M.D., SEBAHATTIN YURDAKUL, M.D., GEORGE E. LOVATT, M.D.,
BERRIN YAZICI, SHENAZ SOMANI, AND ASUMAN MÜFTÜOĞLU, M.D.

Brit. J. Ophthalmol. (1973) **57**, 706

Long-lasting remission of Behçet's disease after chlorambucil therapy

Mala respuesta: Neutropenia severa

MOHAMED IBRAHIM ABDALLA AND NOUR EL-DIN BAHGAT

*From the Department of Ophthalmology, and the Department of Medicine, Ain Shams University,
Cairo, Egypt*

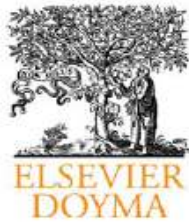
Low dose cyclosporin A versus pulsed cyclophosphamide in Behçet's syndrome: a single masked trial

Yilmaz Özyazgan, Sebahattin Yurdakul, Hasan Yazici, Binnur Tüzün, Aydın İşçimen, Yalçın Tüzün, Turgay Aktunç, Halit Pazarli, Vedat Hamuryudan, Asuman Müftüoğlu

Se inician pulsos mensuales de **ciclofosfamida 750 mgs** con buena respuesta durante 2-3 años aproximadamente de forma inicial pero con una recidiva neurológica y cutánea al espaciar los pulsos.

Reumatología Clínica

www.reumatologiaclinica.org



Caso clínico

Neurobehçet

Germán Latorre
Rocío García C

Hospital Clínico San Carl

El tratamiento de las manifestaciones neurológicas de la EB es controvertido dada la heterogeneidad clínica y fisiopatológica, la dificultad para predecir el curso clínico y la ausencia de ensayos controlados. Se suelen utilizar dosis altas de metilprednisolona intravenosa en los brotes y añadir un tratamiento de fondo con inmunosupresores para evitar las recaídas⁸. No hay prueba alguna sobre el inmunosupresor que pueda ser más útil en casos de neurobehçet, y su uso se basa en observaciones empíricas. Los fármacos más utilizados son azatioprina, methotrexate o pulsos mensuales de ciclofosfamida; se desaconseja el uso de ciclosporina por haberse descrito un empeoramiento de las manifestaciones neurológicas^{9,10}. La decisión de utilizar uno u otro fármaco se

basa en criterios operacionales y en recomendaciones de grupos de trabajo y de mesas de expertos, más que en pruebas científicas sólidas. Sobre otros fármacos utilizados para las manifestaciones oculares o sistémicas de la EB, como micofenolato mofetilo, infliximab o etanercept, no se tiene por el momento información disponible sobre su potencial utilidad en el neurobehçet^{11,12}. En

2009



AÑO 2000...

- En este año nuestra paciente presenta **crisis parciales secundariamente generalizadas** coincidiendo con manifestaciones continuas de **aftas orales y paniculitis**.
- Hasta el año 2003 presenta múltiples brotes de **vasculitis cerebral** y déficit neurológico incapacitante por las que recibió en varias ocasiones pulsos de esteroides y con ello se modifica el tratamiento inmunosupresor:
 - **TALIDOMIDA**
 - **METOTREXATO**
 - **MICOFENOLATO DE MOFETILO**
- Con una buena respuesta con la cual se controla la clínica neurológica y cutáneomucosa.

Review Article

New Evidence-Based Treatment Approach in Behçet's Disease

Erkan Alpsoy

Department of Dermatology and Venerology, Akdeniz University School of Medicine, 07059 Antalya, Turkey

2012

2.2.7. Thalidomide. The drug selectively inhibits TNF- α synthesis. In a randomised, double blind, placebo-controlled study with 63 patients, a remission of OUs, GUs, and PPLs was detected in 22% of the patients over 8 weeks. During the 6-month treatment 30% of the patients remained free of lesions. Thalidomide therapy, however, was associated with exacerbation of EN [45]. In addition, the effects of the drug are temporary, and discontinuation of the treatment results in recurrence of the OUs and GUs. The effectiveness of the thalidomide is lost about 20 days after discontinuation of the drug. Neurological side effects and teratogenic risk of thalidomide limit the clinical application.

Thalidomide: A review of approved and investigational uses

[S.James Matthews](#), PharmD, [Christopher McCoy](#), PharmD

Accepted: January 25, 2003;





Ophthalmology

Volume 110, Issue 5, May 2003, Pages 1061–1065



Regular article

Mycophenolate mofetil as an immunomodulatory agent in the treatment of chronic ocular inflammatory disorders ☆

Stefanos Baltatzis, MD¹, Fehma Tufail, MD¹, Ellen N Yu, MD¹, Cindy M Vredeveld, BA¹, C.Stephen Foster, MD, FACS¹  

2.2.8. Azathioprine. Azathioprine, an important disease-modifying compound, shows an anti-inflammatory effect by suppressing both cellular and humoral immune responses. In a randomised, double-blind, placebo-controlled study [46] of 73 patients, azathioprine has been found to be an effective choice in OUs and GUs besides ocular inflammation and arthritis. Azathioprine was significantly better than placebo in preventing the development of new eye disease. Therefore, the authors concluded that the drug can be used prophylactically to prevent the eye involvement in young, male patients presenting with severe mucocutaneous lesions.

Myelotoxicity, gastrointestinal corrosion, opportunistic infections, and main side effects.

2.2.9. Cyclophosphamide. Cyclophosphamide is the fast-acting alkylating agent. It has been found as a beneficial therapeutic agent for eye disease and systemic vasculitis (neurologic involvement and arterial aneurysms). In a double-blind crossover study [47], it has been shown that the combination of cyclophosphamide and corticosteroid therapy is superior to corticosteroid therapy alone in eye involvement. Myelosuppression, pulmonary fibrosis, renal toxicity, hemorrhagic cystitis, infertility, malignancy, and alopecia are the major adverse effects of cyclophosphamide. Due to the severe toxicity, cyclophosphamide should be selected in cases with clinically significant disease who are refractory to other agents.



AÑO 2011...

- Ingresa en Medicina Interna con diagnóstico de asma bronquial y dolor abdominal con estudios endoscópicos compatibles con **vasculitis intestinal**.
- Durante este ingreso se manifiesta clínica de **diplopía transitoria** sin cambios en relación a RM previa pero acompañada de artralgias, aftas y paniculitis por lo que se incluye en un contexto de **reactivación del Behçet** a pesar de tratamiento inmunosupresor.
- **TERAPIA BIOLÓGICA anti-TNF (Infliximab)**.
- Con buena tolerancia y respuesta, desapareciendo la clínica digestiva, cutánea y neurológica.

Review

QJM

TNF- α antagonists beyond approved indications: stories of success and prospects for the future

infliximab.²⁸ However, most patients experience

uveitic flares during the 3-year follow-up period

that were successfully treated with additional infliximab

infusions.²⁸ In the second trial, 12 patients

with BD and chronic, refractory posterior uveitis

received nine infusions of infliximab. The possibility that etanercept may be less effective

of 12 months and were followed for 12 months; immunosuppressive

the treatment of ocular inflammation has been implied by other studies as well. There are two

being treated with corticosteroids. double-blind placebo-controlled trials testing the ef-

ficacy of etanercept in ocular sarcoidosis and

was seen during the infliximab JIA-associated uveitis. Etanercept was not proven su-

perior to placebo for the treatment of chronic ocular

remission. Remission was sustained for 12 months. In sarcoidosis.⁶⁶ Infliximab on the other hand, has

remained in remission for 12 months. In sarcoidosis.⁶⁶ Infliximab on the other hand, has

Review Article

New Evidence-Based Treatment Approach in Behçet's Disease

Erkan Alpsoy

Department of Dermatology and Venerology, Akdeniz University School of Medicine, 07059 Antalya, Turkey

TABLE 3: Summary of evidence-based algorithmic treatment for articular Behçet's disease.

1st line	Colchicine, Colchicine + Benzathine penicillin, or anti-inflammatory analgesics
2nd line	Azathioprine, Corticosteroids
3rd line	Methotrexate, Salazopyrine, IFN- α , Anti-TNF- α

TABLE 4: Summary of evidence-based algorithmic treatment for ocular Behçet's disease.

1st line	*Topical: corticosteroids + mydriatics \pm cycloplegic agents Systemic: Corticosteroids, Cyclosporine-A, Azathioprine
2nd line	IFN- α , Anti-TNF- α
3rd line	Methotrexate, Mycophenolate mofetil, Cyclophosphamide, Rituximab

* Topical treatment as a sole agent should be restricted to those who has mild uveitis (anterior uveitis).

TABLE 6: Summary of evidence-based algorithmic therapy for Neuro-Behçet's disease.

1st line	Corticosteroids
2nd line	Azathioprine, cyclophosphamide, Anti-TNF- α , IFN- α
3rd line	Methotrexate, Anticoagulation

TABLE 7: Summary of evidence-based algorithmic therapy for gastrointestinal Behçet's disease.

1st line	Sulfasalazine, corticosteroids
2nd line	Azathioprine
3rd line	Anti-TNF- α

or cycloplegic agents can often control the disease [19]. Systemic corticosteroids should be the next step. It is wise to remember that systemic corticosteroids are also used in acute inflammatory ocular attacks of posterior uveitis, panuveitis, and retinal vasculitis [18]. Systemic corticosteroids should

Recommendation



EULAR recommendations for the management of Behçet disease

G Hatemi,¹ A Silman,² D Bang,³ B Bodaghi,⁴ A M Chamberlain,⁵ A Gul,⁶ M H Houman,⁷ I Kötter,⁸ I Olivieri,⁹ C Salvarani,¹⁰ P P Sfikakis,¹¹ A Siva,¹² M R Stanford,¹³ N Stübiger,¹⁴ S Yurdakul,¹ H Yazici¹

7. Neurological involvement

There are no controlled data to guide the management of CNS involvement in BD. For parenchymal involvement agents to be tried may include corticosteroids, IFN α , azathioprine, cyclophosphamide, methotrexate and TNF α antagonists. For dural sinus thrombosis corticosteroids

8. Ciclosporine A neurotoxicity

Ciclosporine A should not be used in patients with BD with central nervous system involvement unless necessary for intraocular inflammation.

9. Mucocutaneous involvement

The decision to treat skin and mucosa involvement will depend on the perceived severity by the doctor and the patient. Mucocutaneous involvement should be treated according to the dominant or codominant lesions present.

9. Mucocutaneous involvement

Patients with resistant skin and mucosa findings can be treated with azathioprine, thalidomide, IFN α and in most resistant cases with TNF α antagonists. Azathioprine was also effective in preventing mucocutaneous lesions.⁵ One RCT⁹⁰ and three open studies⁹¹⁻⁹³ showed that thalidomide was effective for

5. Gastrointestinal involvement

There is no evidence-based treatment that can be recommended for the management of gastrointestinal involvement in BD. Agents such as sulfasalazine, corticosteroids, azathioprine, TNF α antagonists or thalidomide should be tried first before surgery, except in emergencies.

6. Joint involvement

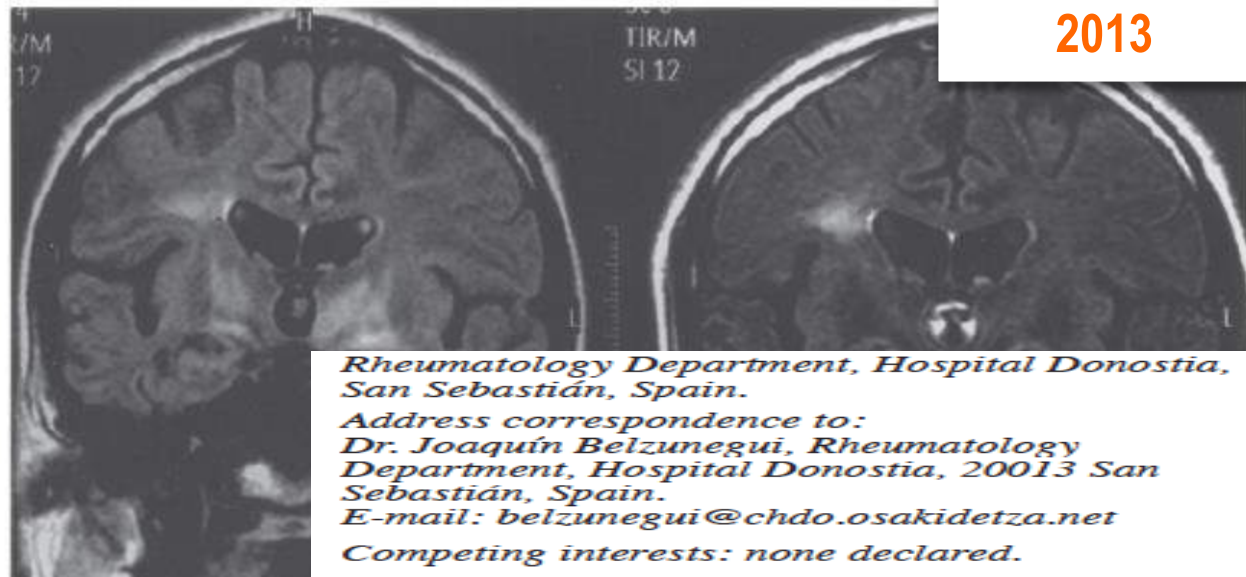
IFN α ,^{39 73} azathioprine⁵ and TNF α blockers⁷⁴ may be tried in rare cases with resistant, longer lasting and disabling attacks.



Efficacy of infliximab and adalimumab in the treatment of a patient with severe neuro-Behçet's disease

Sirs,

The use of anti-TNF drugs is increasing as part of the strategy for the treatment of systemic vasculitis (1). We present the case of a young man with neuro-Behçet's disease resistant to steroids, cyclophosphamide and azathioprine, who was successfully treated, first with infliximab and, one year later following new complications, with adalimumab.



ACTUALIDAD

En la actualidad no ha presentado nuevos brotes de Beçhet; mantiene actualmente esta estrategia de tratamiento (**infliximab, talidomida y esteroides**).

La paciente presenta escasas secuelas neurológicas y ausencia de otro daño orgánico crónico.

El neurobehçet puede comportarse como una enfermedad agresiva, recidivante y requerir diferentes estrategias inmunosupresoras a lo largo de la evolución, intentando minimizar efectos secundarios y daño orgánico.

ACTUALIDAD

