Jarisch-Herxheimer reaction in a patient with neurosyphilis

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Abstract
An increase in Jarisch-Herxheimer reaction may be expected, related to an increase in the incidence of neurosyphilis due to a rise in primary and secondary syphilis in connection with HIV infections. In late syphilis treated with penicillin, neurosyphilis constitutes the chief hazard. Jarisch-Herxheimer reaction has been reported to occur in up to 75% of patients with dementia paralytica (general paralysis of the insane). The clinical spectrum of Jarisch-Herxheimer reaction varies. Minor reaction includes febrile temperatures, headache, myalgia, and malaise. Some patients with Jarisch-Herxheimer reaction have convulsions, an altered state of consciousness, focal neurological signs, and psychiatric manifestations. Fatalities due to Jarisch-Herxheimer reaction in patients with late syphilis have also been described.

Case history
A 40 year old white man, an unskilled worker, was admitted with progressive personality changes. There was a history of primary syphilitic infection 17 years previously. Specific serological tests for syphilis in blood and CSF were highly positive and CSF sedimentation showed signs of an inflammatory process. Ten hours after the start of penicillin treatment a severe symptomatic Jarisch-Herxheimer reaction with alteration of level of consciousness, pupillary changes, and focal neurological signs developed. Jarisch-Herxheimer reaction may occur in various settings, particularly in the treatment of syphilis. Investigation of CSF before the treatment may predict a potential risk. Corticosteroid treatment has been suggested for prevention.

Sero logical results

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+ = Reactive; – = non-reactive; VDRL = venereal disease research laboratory slide test; TPHA = Treponema pallidum haemagglutination assay; FTA-ABS = fluorescent treponemal antibody-absorption; IgM-SPHA = IgM-Solid-phase haemabsorption.
after two weeks. Repeated CT was normal. A meningo-vascular syphilis therefore seemed unlikely.

The response to treatment was confirmed by specific tests for syphilis six months and one year later (table).

**Discussion**

Historically the discovery of syphilis was quickly followed by the recognition of an acute reaction precipitated by specific treatment.4 The overt clinical features of the reaction were described in 1895 by Jarisch6 and in 1902 by Herxheimer and Krause.10

Similar reactions have been reported after treatment of other spirochetal infections (louse-borne relapsing fever, Vincent’s angina, rat bite fever, leptospirosis, yaws),11 other bacterial infections (brucellosis, tularemia, glanders, and anthrax),11 and of African trypanosomiasis.12 Singular reports describe Jarisch-Herxheimer reaction in treatment of *Pneumocystis carinii* pneumonia,13 meningococcal meningitis,14 and falci- parium malaria.15

In neurosyphilis Jarisch-Herxheimer reaction may take one or both of two forms: either a transient rise in temperature, chill, headache, malaise, myalgia during the first 24 hours after treatment with the drug (asympto- matic type) or an exacerbation of mental symptoms or other neurological signs during the first days (symptomatic type).

In the symptomatic type the variety of manifestations is related to the type of neu- rosyphilis. Patients with asymptomatic neurosyphilis rarely have Jarisch-Herxheimer reaction. Patients with dementia paralytica may react with convulsions, exacerbations of the existing psychoses, or focal neurological signs. The symptoms of patients with tabes dorsalis (locomotor ataxia) consisting of lightning pains, urinary retention, and constipation may be temporarily intensified during treatment or may appear for the first time. Jarisch-Herxheimer reaction may also be lethal, particularly in patients with gum- mas of the brain or coexisting mesoartitic aneurysm.3

No recent data are available concerning the incidence of Jarisch-Herxheimer reaction in neurosyphilis. In older reports16-17 asymptomatic reactions occur in 13% to 54%, symptomatic reactions in 1-7% to 11% of patients.

Pathogenesis of Jarisch-Herxheimer reaction remains poorly understood. Numerous mechanisms, such as release of treponemal breakdown products,9 hypersensitisation phe- nomena,10 allergic origin,19 endotoxaemia,20 and opioid withdrawal reaction21 have been proposed, but the exact cause remains obscure.

Histologically, Jarisch-Herxheimer reaction is manifest by acute inflammatory changes within syphilitic lesions. Capillaries and veins become congested, followed by swelling of the endothelial cells. Polymorphonuclear neutrophils and mononuclear leucocytes migrate through the vessel wall into the sur- rounding oedematous connective tissue.22 A peripheral leucocytosis and lymphopenia usually accompanies these histological alter- ations.4

Jarisch-Herxheimer reaction cannot be predicted on reliable indices. The frequency of reactions increases proportionally with white cell count and total protein in CSF. Hoekenga et al17 found the highest incidence of Jarisch-Herxheimer reaction in patients with dementia paralytica and in whom both cell count and protein content in CSF were raised. Incidence is not related to race or sex, duration of infection with syphilis, serological titre, or dose of penicillin. Luetic manifesta- tions such as gummas of the brain and of the larynx,2 aortic aneurysm due to syphilitic aortitis,3 luetic optic neuritis,23 and involve- ment of the auditory nerve24 have been described as having a potential risk for a dra- matic course of Jarisch-Herxheimer reaction.

The value of steroids in prevention of Jarisch-Herxheimer reaction remains unproved. Corticosteroids have been reported to exert some positive effect,25-26 and the use of corticosteroids (30–50 mg prednisone) before antibiotic treatment is recommended.2728 Although corticosteroids are able to reduce fever, they are not thought to prevent symp- tomatic Jarisch-Herxheimer reaction.29 It has been argued that the benefits they provide may be outweighed by the risks involved.26 In luetic organ manifestations like gumma and mesoartitic luetica, the use of corticosteroids seems justified.

Other attempts to prevent Jarisch- Herxheimer reaction by treatment with antihistamines, bismuth, and initial use of corticosteroids to treat patients with syphilis has not been reported.

Treatment of Jarisch-Herxheimer reaction depends on symptoms. The occurrence of Jarisch-Herxheimer reaction is not an indication for discontinuing treatment. It is useful to monitor cardiovascular function and control temperature every two hours during the first 48 hours from the start of any treatment for neurosyphilis.

Although Jarisch-Herxheimer reaction in neurosyphilis is rare and usually the asympto- matic type occurs, a symptomatic form may take a dramatic course, as in our patient, with deterioration of existing symptoms and the occurrence of additional neurological symp- toms.

Jarisch-Herxheimer reaction in a patient with neurosyphilis.