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Ocular syphilis — indicator of previously unknown HIV-infection

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Summary *Objectives:* To detect the prevalence of HIV-co-infection in patients with ocular syphilis and to compare ocular syphilis in HIV-positive and -negative patients.
Methods: 24 consecutive patients treated for ocular syphilis at our hospital between 1998 and 2006 were evaluated retrospectively. Patients' characteristics, laboratory results (including syphilis serology, HIV status, CSF examination), major ophthalmologic finding, treatment and course were assessed. Data of HIV-positive and -negative patients were compared.
Results: Of the 24 patients with ocular syphilis, 11 were co-infected with HIV. Notably, the HIV-infection had previously been unknown in 7 of the 11 HIV-positive patients. 6 of these were in an early disease stage (CDC category A). Clinical and laboratory findings did not differ between HIV-positive and -negative patients except for the C-reactive protein (CRP), which was significantly higher in HIV-infected patients.
Conclusions: Ocular syphilis led to new diagnosis of HIV-infection in an unexpectedly high number of patients, which emphasises that patients with ocular syphilis must be screened for HIV-co-infection. According to our study the expected benefit is high because most of the patients newly diagnosed with HIV had high $CD4^+$ cell counts. These patients can be monitored and treated before the development of AIDS.

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Introduction

Syphilis has been recognized as a reemerging disease. Following the all time low incidence in Western Europe and the USA at the turn of the century, a resurgence of syphilis infections has been noticed in these regions, most often in urban areas and among persons at risk for co-infection with HIV.[1] In Germany, the overall incidence of syphilis (3.8/100,000 in 2006 with the highest local incidence of 16.8/100,000 in Berlin) is comparable to that reported for the USA (3.3/100,000 in 2006).[2,3] Due to this reemergence, ocular syphilis, previously a rare manifestation of the infection, is increasingly observed.[4–6] Ocular manifestations of syphilis are heterogeneous and difficult to diagnose solely by clinical presentation. They may be the presenting symptom of a previously undetected syphilis infection and can involve any structure of the eye from cornea to optic nerve.[7] Prompt diagnosis can prevent permanent disability because early treatment often leads to complete recovery.

Patients and methods

From 1998 to 2006, 24 patients (41 affected eyes) with ocular syphilis were treated at our institution. This is the only university hospital in Berlin and acts as a referral centre. It has 3200 beds, and 127,400 inpatients and 500,000 outpatients were treated here in 2006. Serologic testing for syphilis is part of the workup for unclear ocular symptoms and was conducted at the time of presentation. It led to the diagnosis, which was based on the following criteria:

(1) inflammatory disease of the eye, the optic nerve or orbital tissue;
(2) serological evidence for syphilis: reactive *Treponema pallidum* particle agglutination (TPPA) or hemagglutination (TPHA) test combined with either a venereal disease research laboratory (VDRL) test $>$1:4 or detection of FTA-Abs-IgM;
(3) improvement following adequate antimicrobial therapy.

One HIV-positive patient had a negative VDRL and IgM test but a typical history (primary syphilis with chancre followed by rash) and clinical findings at admission (persisting rash). Furthermore, he showed a reactive CSF VDRL that responded to penicillin therapy and became negative. Other diseases with possible ocular manifestations such as CMV-infection, tuberculosis, or sarcoidosis were ruled out by clinical examination and appropriate laboratory tests. Only patients whose HIV status had been tested were included. The study was conducted as a retrospective patients' chart review. Patients' characteristics, laboratory results including syphilis serology, HIV status, CSF examination and data on treatment were collected. A CSF WBC count $>20/mm^3$, a reactive CSF VDRL test result or an intrathecal *T. pallidum* index (ITPA) >3 was used to define neurosyphilis. ITPA was calculated as (TPHA-CSF IgG:total CSF IgG ratio) divided by (TPHA-serum IgG:total serum IgG ratio). Either one of these criteria was regarded as sufficient for the diagnosis of neurosyphilis.[8] All data were analysed with the Mann–Whitney test or Fisher's exact test using the PRISM and SPSS statistical package. Based on the primary site of inflammation ocular syphilis was classified as previously suggested: ''anterior uveitis'' involving iris and ciliary body; ''posterior uveitis'' involving choroid, retina and retinal pigment epithelium and including vasculitis (example in Figs. 1 and 2) and macular edema; and ''optic/perioptic neuritis'' including the papilla.[9] When all parts of the uveal tract were affected the manifestation was classified as ''panuveitis''.

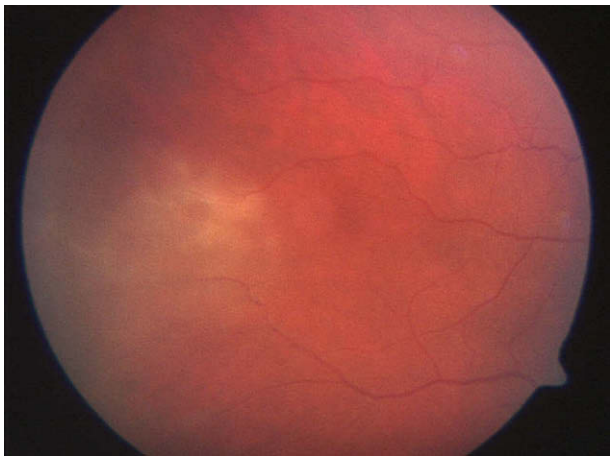

Figure 1 Fundoscopy of the right eye of a patient with vasculitis as manifestation of ocular syphilis.

Results

The incidence of ocular syphilis at our hospital between 1998 and 2006 ranged from 0/year (1999) to 6/year (2004 and 2006) with a mean of 2.7 patients/year. The presenting complaints consisted of ocular symptoms in 23 cases and of somnolence and pysychotic symptoms in 1 case. Ocular symptoms were similar throughout: blurred vision, visual

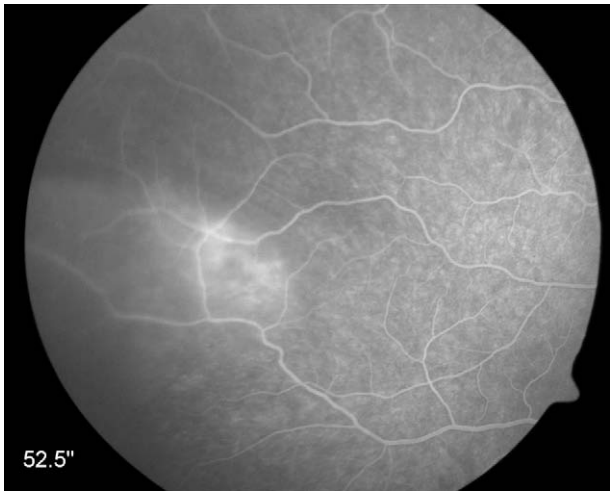

Figure 2 Fluorescein angiography of the same eye showing peripheral leakage.