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Case Report

Syphilitic optic neuritis in a patient with congenital vascular anomaly: a case report

病例一宗：一名有先天性血管異常的梅毒性視神經炎患者

A Reich, A Wójcik-Maciejewicz, J Kalinowska

A 42-year-old man with unusual ocular involvement complicating secondary syphilis is demonstrated. The patient was admitted to the dermatological department because of erythematous plaques on the hands and soles. Prior to admission these lesions were misdiagnosed as erythema multiforme and treated with systemic corticosteroids. Besides the skin lesions the patient complained of headache and blurred vision in the right eye. Unilateral optic neuritis was diagnosed. The ocular problem was eventually diagnosed as a manifestation of secondary syphilis. Interestingly, a congenital anomaly of the right anterior cerebral artery was also found using computed angiotomography.

本文展示一名四十二歲男子在第二期梅毒感染期間的不尋常眼部病變。此病人因手部及腳掌的紅色斑塊入住皮膚科病房；在入院前，其皮損被誤診爲多形性紅斑，並曾給予口服類固醇治療。皮損以外，病人亦伴隨頭痛及右眼視力模糊的病徵，終被診斷爲單邊視神經炎，並歸納爲第二期梅毒病情的一部分。有趣地，電腦掃描血管造影同時發現其大腦前動脈有著先天性血管異常。

Keywords: Optic neuritis, prozone phenomenon, syphilis

關鍵詞：視神經炎，前區現象，梅毒

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Introduction

Over the last decade a significant increase in the prevalence of syphilis has been noted not only in developing countries, but also in the United States and Western Europe. Therefore, *Treponema pallidum* infection has still to be considered as a significant and real medical problem. Syphilis may involve nearly every organ resulting in a wide number of clinical presentations and for that reason it has received the name: "great imitator".[1] The disease can be easily misdiagnosed and inappropriately treated, particularly in patients

who demonstrate less common syphilis subtypes. A high index of suspicion is required to reach the correct diagnosis in such unusual cases. Here, we present a male patient with secondary syphilis manifesting as an atypical ocular involvement. We postulate that the development of optic neuritis was probably facilitated by a congenital anomaly of the brain vessel. We would also like to point out that the prozone phenomenon may lead to difficulties in making the diagnosis of syphilis.

Case report

A 42-year-old man was admitted to our department because of erythematous plaques distributed symmetrically on the hands and soles (Figure 1). Skin lesions first appeared about two months prior to admission and were misdiagnosed by a local dermatologist as drug-induced erythema multiforme, because the patient had taken non-steroidal anti-inflammatory drugs (ibuprofen and naproxen) for tendinitis of the left metatarsus a couple of weeks prior to the onset of the skin lesions. Topical and systemic corticosteroids (prednisone 30 mg/day) in combination with acyclovir (0.2 g 5x/day) and antihistamines (clemastine 1 mg 2x/day) were prescribed. As no improvement was observed, the patient was referred to our department for further investigation and treatment two months later.

On admission, the patient demonstrated symmetrical, well-demarcated, partially hyperkeratotic, confluent erythematous plaques with annular (collarette) scaling on the palms and soles (Figure 1). The skin lesions were slightly painful. The histology of the skin lesions revealed psoriasis-like reaction pattern with mixed inflammatory infiltrate in the dermis (Figure 2). Detailed physical examination also revealed blurred vision in the right eye with photophobia. Furthermore, the patient complained of chronic headache lasting for the past two months. On further questioning, the patient admitted that about seven months prior to the admission he had a casual heterosexual intercourse with an unknown woman.

Because of the eye symptoms the patient was examined by an ophthalmologist (J.K.) and was found to have oedema of the right optic nerve papilla. Elevation of the disc area in the right eye was also seen by ultrasonography (Figure 3c), and visual impairment with a visual acuity of 0.2 was found in the right eye during the evaluation of the visual field (Figure 3e). Fluorescein angiography of the right eye fundus demonstrated fuzzy borders of the right optic disc (Figure 3a). Except for the optic nerve pathology, ophthalmological and neurological examinations were unremarkable. The basic laboratory investigations (blood cell morphology, erythrocyte sedimentation rate, C-reactive protein level, urine examination, liver enzymes, renal function tests, serum glucose level, serum lipids, blood coagulation, chest X-ray examination, prostate specific antigen, CA 19-9 antigen, carcinoembryonic antigen) were either within the normal range or negative. The histology of the skin lesions revealed a psoriatic reaction pattern.

Bearing in mind the history of casual sexual intercourse, sexually transmitted disease was suspected but all tests (VDRL – Venereal Disease Laboratory Research test, HIV antibody screening, *Chlamydia trachomatis* direct fluorescent-antibody swab staining, *Neisseria gonorrhoeae* culture) were negative at that time. In the meantime, the patient underwent detailed imaging of the brain in order to explain the unilateral oedema of the right optic nerve disc. Magnetic resonance imaging of the brain revealed no abnormalities, but computed angiotomography of the intracranial vessels demonstrated a congenital vessel anomaly: the lack of the A1 segment of the right anterior cerebral artery (Figure 4). However, this anomaly could not explain the oedema of the right eye papilla and visual impairment as the other segments of the anterior cerebral artery

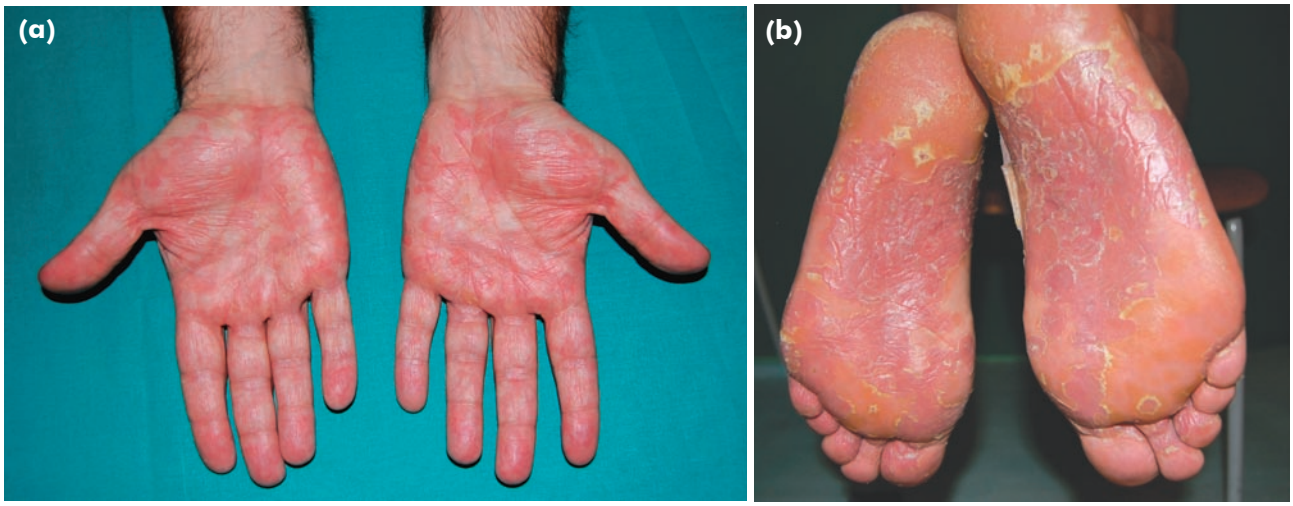

Figure 1a. (a) Well demarcated, confluent erythematous plaques with circular scaling on both palms. (b) Symmetric, partially hyperkeratotic, confluent erythematous plaques with scaling on both soles.

filled from the other side with the aid of the anterior communicating artery. As syphilis was still suspected (due to the morphology of the skin lesions), syphilis serology was repeated (both treponemal and non-treponemal) and all treponemal tests were highly positive (FTA – fluorescent treponemal antigen test: titre-1:8000, TPHA – *Treponema pallidum* haemagglutination test, FTA-ABS – fluorescent treponemal antibody-absorption test: titre 1:8000). The VDRL test was also positive, at a dilution titre of 1:64. The patient's wife was concomitantly proven to be negative for syphilis. Cerebrospinal fluid of the patient was collected and sent for laboratory examination. The patient was started on doxycycline 100 mg bid while waiting for the results. Cerebrospinal fluid analysis showed a slight elevation of the total protein content (69 mg/dl, reference: 15-45 mg/dl); while the other investigations were within the normal range (3 cells/μl, glucose 50.5 mg/dl, chloride anions 123 mmol/l, sodium 149 mmol/l, potassium 2.7 mmol/l). The serology of the cerebrospinal fluid revealed positive FTA (titre 1:10) and TPHA tests; however, the VDRL test was negative. Anterior optic neuritis complicating secondary syphilis was diagnosed and the treatment was changed, according to Polish guidelines, to intravenous crystalline penicillin G (6 million units every six hours for twelve days) followed by procaine penicillin (1,200,000 units i.m. for two weeks).[2] The treatment resulted in resolution of the skin lesions and complete recovery of the ophthalmologic symptoms. Four months after the completion of treatment, the titres of VDRL and FTA tests in serum decreased significantly to 1:8 and 1:1300, respectively. Moreover, subsequent ophthalmologic examination was

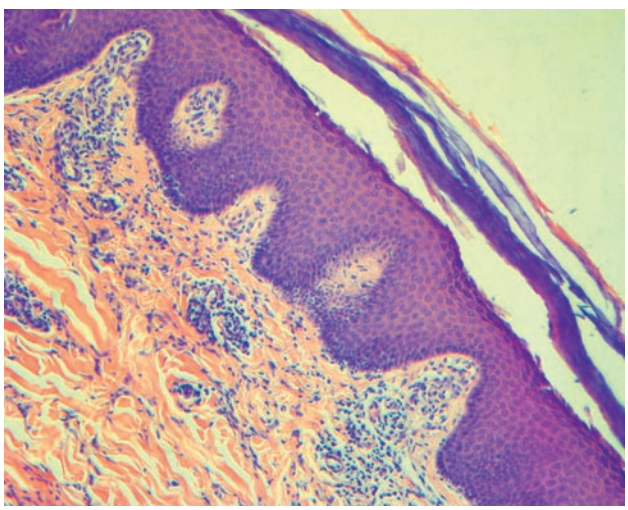

Figure 2. Histology of the skin lesions: psoriasis-like reaction pattern with papillomatosis, hypergranulosis and hyperkeratosis and mixed inflammatory infiltrate containing numerous plasma cells in the dermis (H&E, original magnification x 200)

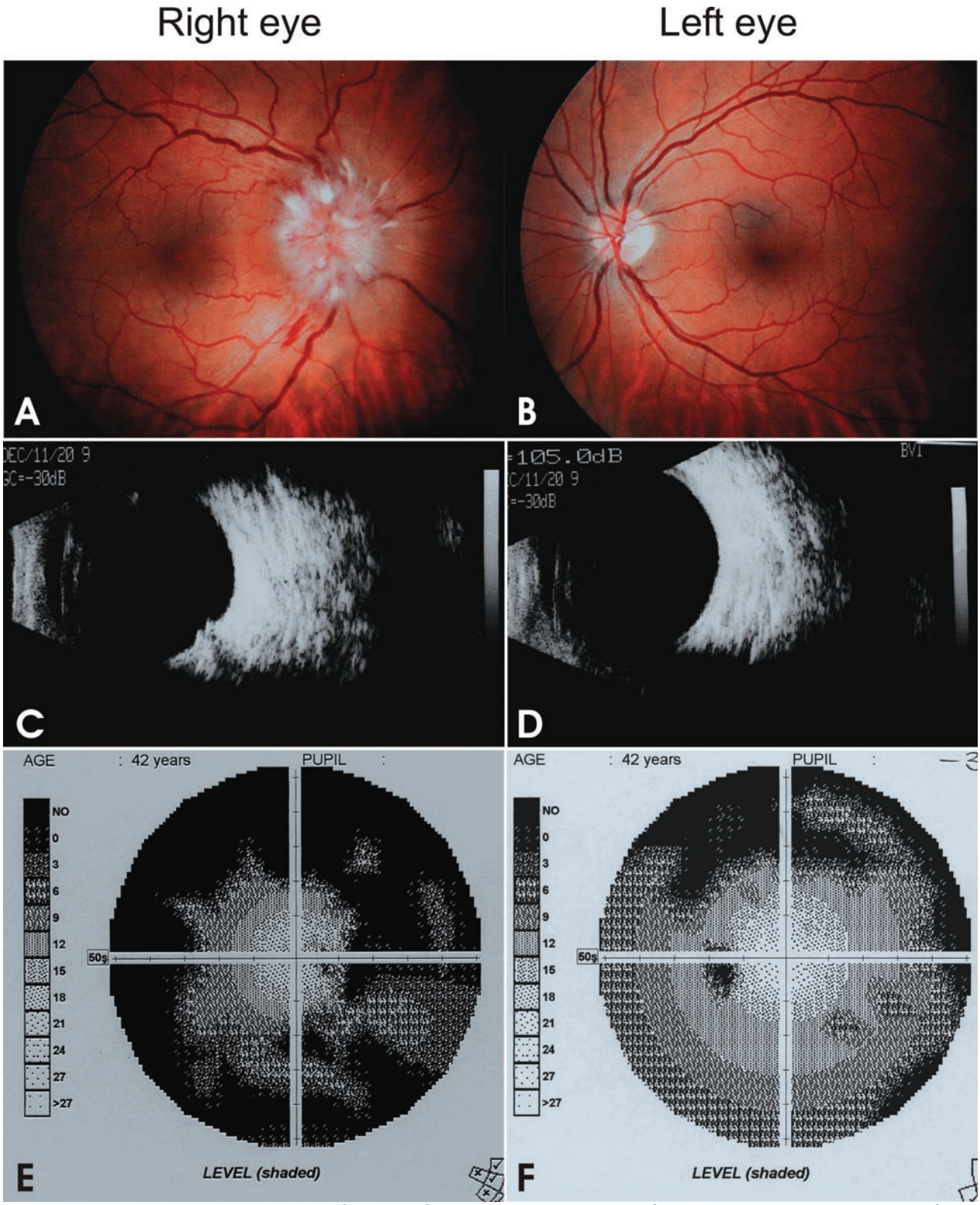

Figure 3. Fluorescein angiography of the eye fundus (A, B): elevation of the right optic nerve disc with fuzzy borders and hyperfluorescent vessels and areas of hypofluorescence resulting from microscopic haemorrhages (A), normal fundus of left eye (B). Sonography of eyes (C, D): elevation of the right optic nerve papilla (C), normal sonography view of the left eye (D). Assessment of visual field (E, F): marked impairment of the visual field in the right eye (E), normal result of the visual field in the left eye (F) (darker areas correspond to poorer vision).

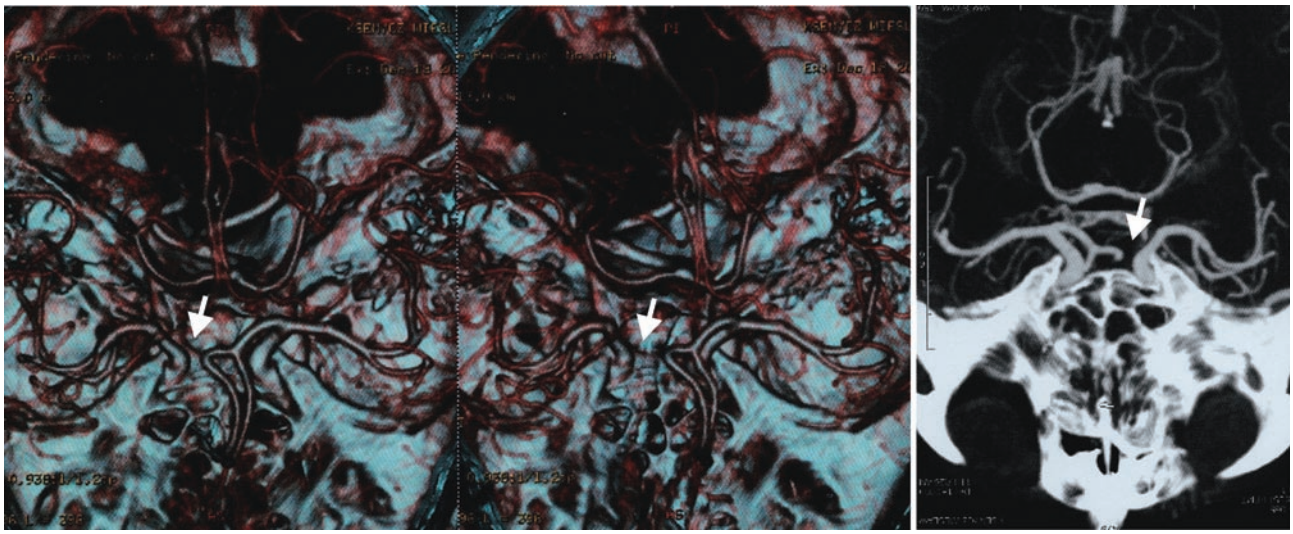

Figure 4. Angiotomography of cerebral vessels: the lack of the A1 segment of the right anterior cerebral artery (arrow).

unremarkable apart from slight paleness of the right optic disc.

Discussion

Ocular involvement in syphilis may be silent or may mimic nearly every ophthalmological condition, presenting as either uveitis, choroiditis, interstitial keratitis, retinal vasculitis, chorioretinitis, anterior optic neuritis, retrobulbar optic neuritis, dacryadenitis or scleritis.[3-5] According to Aldave et al, uveitis is the most common ocular finding in syphilis.[6] On the other hand, an isolated optic neuritis is considered to be a very rare manifestation of *T. pallidum* infection.[5,7] In the pre-antibiotic era about 3% of patients with secondary syphilis had eye problems.[3] Importantly, an increasing number of cases of ophthalmic syphilis has been reported recently.[8,9] Ocular symptoms of syphilis are of great importance as they may be the first and only manifestation of the disease.[5,7] Unlike longstanding tertiary syphilis, the neurological findings of secondary syphilis usually respond completely to penicillin,[4] as in our patient. However, if misdiagnosed and inappropriately treated, ocular lesions in syphilis may become irreversible, resulting in permanent visual impairment.[5]

Importantly, many patients who were recently diagnosed with ocular syphilis were also co-infected with HIV.[5,10] It could be suggested that the immunodeficiency related to HIV might predispose to more severe disease, including ocular involvement. Our patient was negative for HIV, but we suspected that systemic corticosteroids initiated prior to the admission might have facilitated ocular damage. A similar suggestion was mentioned by Solebo and Westcott.[11] Of note is that we also found an ipsilateral congenital brain vessel anomaly. To the best of our knowledge, this is the first description of such a cerebral artery anomaly in ocular syphilis. In our opinion, it is possible that this anomaly might somehow have contributed to the involvement of the right eye. It would be interesting to analyse whether other subtle brain abnormalities might be relevant to neurosyphilis. Recent data have also indicated that certain strains of syphilis are more likely to cause neurosyphilis.[12,13] It is currently not clear if they are also important for ocular syphilis.

We would also like to underline another important aspect of syphilis diagnostics, namely the prozone phenomenon, which may sometimes significantly delay the diagnosis of syphilis. We suspect that the initial VDRL examination could be a false negative result because his serum was not sufficiently diluted. The prozone phenomenon in syphilis testing refers to a false negative response resulting from overwhelming antibody titres which interfere with the proper formation of the antigen-antibody lattice network necessary to visualise a positive flocculation test. The prozone phenomenon is most commonly observed in secondary syphilis, when high levels of antibodies are present in the blood. As VDRL or similar tests are sometimes used for syphilis screening, it is of great importance for clinicians to remember about this aspect of syphilis diagnostic as it can lead to the misdiagnosis of *T. pallidum* infection. We would also like to point out that the VDRL test is not suitable for screening, both for blood and cerebrospinal fluid. This is not only due to the prozone phenomenon, but also because it is estimated that the VDRL test is negative in up to 50% of patients with neurosyphilis.[7]

In conclusion, we would like to emphasise the necessity of syphilis screening in every patient with ocular damage of unknown aetiology. In line with Bandettini di Poggio et al,[7] we support the view that the presence of ocular involvement in syphilis patients is suggestive of involvement of the CNS and should be considered synonymous with neurosyphilis.[7]

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