CASE REPORT

Chameleons everywhere

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SUMMARY

We report the case of an HIV-infected man returning from Thailand with secondary syphilis with general symptoms, hepatitis and a pulmonary mass lesion. A cerebrospinal fluid examination showed no signs of neurosyphilis. Two months after successful treatment with benzathine penicillin he presented with a mass lesion in the brain suspected to be a glioma or glioblastoma, which turned out to be a syphilitic gumma. Syphilis remains a great imitator in clinical medicine. Syphilitic brain gummata can develop within a few months.

BACKGROUND

Our case shows that syphilis continues to be a great imitator, a 'chameleon' in clinical medicine, and should be included in the differential diagnosis of cerebral and pulmonary mass lesions and hepatitis in patients with risk of attracting sexually transmitted diseases. We were surprised, in this case, by the very short time taken to develop syphilitic brain gummata.

CASE PRESENTATION

A 40-year-old man presented to the emergency department with persistent fatigue, excessive sweating and pain in the right thorax 7 weeks after a trip to Thailand. Truncal exanthema appeared after taking ibuprofen. No fever, muscle or joint pain, or other skin lesions or gastrointestinal symptoms were apparent. The patient was diagnosed with an HIV-1 infection 7 years ago. Without antiretroviral therapy the CD4 count values were between 412 and 570 cells/µL and HI-viraemia between 3600 and 25 000 copies/mL. Apart from anal condylomata acuminata, no other illnesses were noted.

INVESTIGATIONS

The patient was subfebrile with truncal macular skin exanthema. Laboratory testing revealed normochromic anaemia (haemoglobin 126 g/L), differentiation of leucocytes were without pathological findings. Platelets, serum glucose and renal retention values were within normal range. C reactive protein was slightly elevated (25 mg/L), transaminase levels were 2–4 fold and alkaline phosphatase level was 5-fold above upper normal limit. D dimers were severely elevated at >1000 µg/L. CT scan ruled out a pulmonary embolism. However, there was an unclear consolidation around the lingula (figure 1). An ultrasound of the abdomen revealed no pathologies. Blood and citrate blood cultures were negative. Serology tests for hepatitis A/B, Epstein-Barr virus, cytomegalovirus and Varicella-Zoster virus indicated past infection; hepatitis C virus RNA was negative. Antibodies against *Brucella* and *Coxiella burnetii* could not be found. The syphilis serology was positive with *Treponema pallidum* haemagglutination assay (TPHA) of 1:40 960 and venereal disease research laboratory (VDRL) 1:32, it had been negative 1 year earlier. Owing to slight paraesthesia of the right hand and the HIV infection, a lumbar puncture was performed, which revealed no evidence of neurosyphilis. The TPHA cerebrospinal fluid/serum index was negative. During treatment with benzathine penicillin 1×2.4 Mio U per week by intramuscular injection for 3 weeks, the subjective symptoms declined, the liver values returned to normal, VDRL declined and the aetiologically unclear opacity in the lingula was reduced in size (figure 2). Partner treatment for syphilis was performed.

Two months later, the patient reported increasing headaches. MRI of the brain revealed a mass lesion (figure 3), and because of suspected glioma/

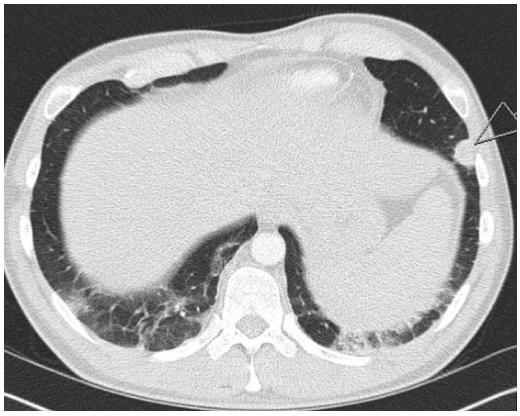

Figure 1 Thorax CT scan 31 May: wedge-shaped mass lesion in the lingual.

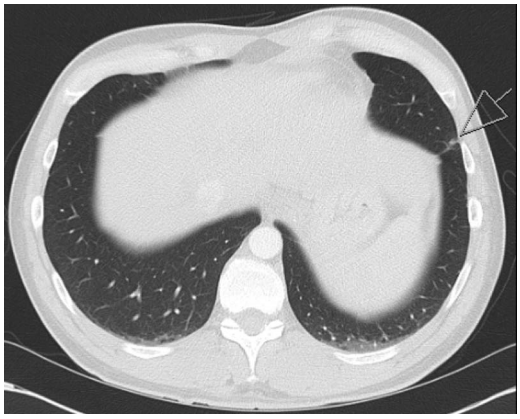

Figure 2 Thorax CT scan 29 September: regredient mass lesion in the lingula.

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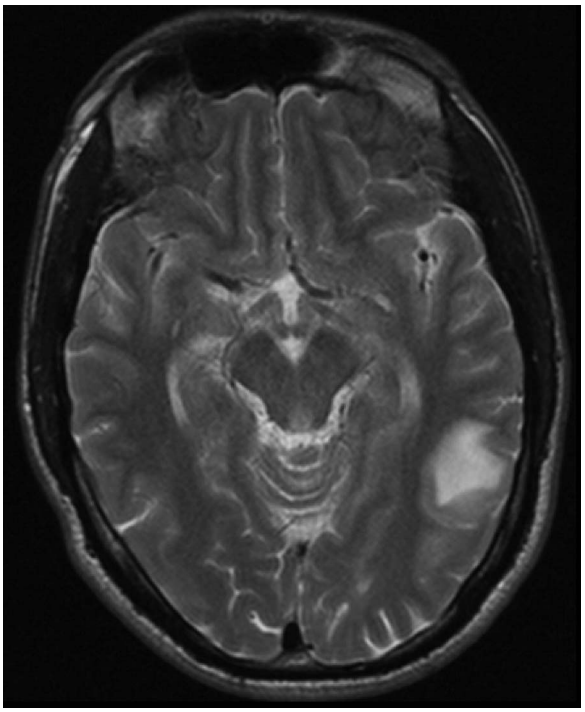

Figure 3 Brain MRI 1 October: mass lesion measuring 28×20×22 mm in the left parietal lobe.

glioblastoma the lesion was removed by osteoclastic craniotomy. The histology provided no evidence of neoplasia, but indicated an abscessed process without caseation with epithelioid cell macrophages and plasma cells without evidence of a pathogen despite processing with special dyes and immunohistochemistry. *T. pallidum* was established using eubacterial PCR. There was also an increase in the TPHA and VDRL. Table 1 shows the TPHA/VDRL progress with therapy details. There were no psychiatric or neurological symptoms such as insomnia, mood disorders, memory impairment, disorientation, psychosis, hearing loss or paralysis of the cranial nerves evident before, during or after treatment except a slight paraesthesia in the right hand after playing play-station for some hours.

TREATMENT

Intravenous treatment with penicillin G 6×4 Mio U/day for 14 days was administered. The symptoms regressed completely, TPHA and VDRL titres decreased and the pulmonary and cerebral lesions could no longer be detected.

DISCUSSION

To the best of our knowledge, this is one of the first reported episodes of secondary syphilis with skin exanthema affecting the lungs and liver. Secondary syphilis affecting the liver is present in about 25% of patients. Involvement of the lungs is recorded very rarely. In recent years, only nine cases have been recorded in the literature between 1965 and 2006.[1] Pulmonary lesions can appear as bilateral infiltrates, solitary or multiple subpleural nodules, pleural effusion or lymphadenopathy.[1] For the diagnosis, Coleman *et al*[2] propose the following clinical criteria: (1) historical and physical findings typical of secondary syphilis; (2) serological test results positive for syphilis; (3) pulmonary abnormalities seen radiographically with or without associated symptoms or signs; (4) exclusion of other forms of pulmonary disease, when possible, according to findings of serological tests, sputum smears and cultures, and cytological examination of sputum; and (5) response to antisyphilis therapy of signs found by radiological examination. In our case all points except the exclusion of other forms of pulmonary disease were positive. Owing to the HIV infection, a more aggressive diagnostic method could have been performed by examination of the sputum, bronchoalveolar lavage and lung biopsy to rule out other infection due to *Mycobacterium* spp, *Nocardia*, *Aspergillus* and *Pneumocystis jirovecii*, and to exclude tumour and systemic diseases. It appears that pulmonary syphilis is often associated with other extracutaneous localisations and hepatic involvement, as was seen in our patient. A good clinical and radiological response to penicillin therapy relies on its narrow spectrum and is an important diagnostic tool.[2]

Cerebral syphilitic gummata are rare manifestations of tertiary syphilis. Cases of cerebral gummata are declining considerably due to improved diagnostics leading to earlier treatment compared with the 19th and 20th centuries. Fargen *et al*[3] describe in their review how, in a series of 4000 test cases with syphilis in the 19th century, the incidence was so high that patients with symptoms of an intracranial tumour were first treated for syphilis and a brain tumour was only assumed after there was no response to this treatment.[4] The proportion of syphilitic gummata among operated brain tumours in the last published series by Oblu *et al*[5] in 1970 was only 0.1%. Syphilitic gummata are granulomatous lesions that can form in any organ. Central nervous gummata are predominantly located in the convex portion of the human brain.[3] Usually, a cerebral gumma occurs on average 15 years after the primary infection. The time frame of less than half a year in the case of our patient was exceptionally short. It is suggested in the review of Lynn and Lightman[6] that HIV accelerates and changes the clinical course of neurosyphilis and that co-infection with HIV increases the incidence of neurological complications of syphilis. Aggressive neurosyphilis can occur with either high or low CD4+ lymphocyte counts, because intact cell-mediated immune response is probably critical for the control of *T. pallidum* infection. Subtle functional T cell deficits are seen even in early HIV infection. This may be one of the reasons for the atypical presentation in our patient.

As in our case, TPHA and VDRL titres in the serum are usually positive at the time of diagnosis of cerebral syphilitic gummata, but often negative in the cerebrospinal fluid.

It is not possible, even today, to diagnose a cerebral syphilitic gumma non-invasively; empiric “ex juvantibus” treatment against syphilis in the face of a cerebral tumour is not indicated

Table 1 The course of TPHA/VDRL

	08-05-2007	02-06-2008	17-09-2008	10-10-2008	19-12-2008	14-07-2009
TPHA	1:<80	1:20 480	1:640	1:40 960	1:5120	1:320
VDRL		1:64	1:2	1:32	1:4	1:<2
Treatment		Tardocillin by intramuscular injection		Penicillin by intravenous injection		

TPHA, *Treponema pallidum* haemagglutination assay; VDRL, venereal disease research laboratory.

nowadays given the rarity of this clinical manifestation. Our case shows that syphilis continues to be the great imitator, the 'chameleon' in clinical medicine, and should be included in the differential diagnosis of cerebral and pulmonary mass lesions and hepatitis in patients with risk of attracting sexually transmitted diseases.

Learning points

- Syphilis continues to be the great imitator, the 'chameleon' in clinical medicine.
- Syphilis should be included in the differential diagnosis of hepatitis, cerebral and pulmonary mass lesions, and in patients with risk of attracting sexually transmitted diseases.
- *Treponema pallidum* haemagglutination assay and venereal disease research laboratory titres in the serum are usually positive at the time of diagnosis of cerebral syphilitic gummata, but often negative in the cerebrospinal fluid.
- Syphilitic brain gummata can develop within a few months.

Contributors Authors KS and HF have both substantially contributed to the conception of the work and the acquisition and interpretation of data. KS has drafted the work and HF has revised it critically. KS and HF approved the final version to be published.

Competing interests None.

Patient consent Obtained.

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