Tabes dorsalis progressing to general paresis after 20 years despite routine penicillin therapy

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SUMMARY A man with a history of treatment for early syphilis presented with tabes dorsalis. Despite receiving a course of penicillin accepted as adequate by the World Health Organisation the illness progressed to tabo-paresis after 20 years. Reinfection cannot be excluded.

Introduction

Authorities on the treatment of symptomatic neurosyphilis, although agreeing that penicillin is the drug of choice, vary considerably in their recommendation of both the total amount of penicillin to be administered and the duration of the treatment. Based on Hahn's work, the World Health Organisation maintains that 10-15 days' treatment with daily procaine penicillin is acceptable. This regimen is recommended by the United States Public Health Service,\textsuperscript{3,4} by Morton and Harris,\textsuperscript{5} and in standard textbooks on medicine.\textsuperscript{6-10}

Glatt\textsuperscript{11} recently questioned whether the amount of penicillin necessary to cure established neurosyphilis is yet known. King and Nicol,\textsuperscript{12} Catterall,\textsuperscript{13} and Brain\textsuperscript{14,15} all recommended three weeks' treatment and Merritt,\textsuperscript{16} 3-4 weeks.

Case report

FIRST ILLNESS

In 1957 a 52-year-old man was referred to the National Hospital for Nervous Diseases, Queen Square, London, at the suggestion of an optician whom he had attended for routine examination. He had no specific symptoms. He gave a past history of treatment for syphilis at St Mary's Hospital, London, in 1938 (records are no longer available).

Clinical findings

Findings on examination included a tabetic facies, bilateral optic atrophy, and Argyll-Robertson pupils. Higher mental functions were not impaired. There was generalised hypotonia, and the characteristic distribution of facial, sternal, and ulnar border hypalgesia was noted. Deep pain sensation of the Achilles tendon was lost. Vibration sense was absent in both legs and joint-position sense was lost in the toes. Only the knee jerks were diminished; the Romberg test gave a negative result and the gait was normal. Signs of aortic regurgitation were noted—blood pressure of 150/60 mmHg, collapsing pulse, and a clearly audible to-and-fro aortic murmur.

Laboratory findings

The results of investigations before and after treatment are shown in Table I. Penicillin 12 megaunits intramuscularly was given over a period of 10 days with no side effects. No further details were available, but procaine penicillin 1 megaunit daily was the accepted regimen at this hospital at that time.

Annual attendance at the outpatient department as well as postgraduate demonstrations and examinations are recorded until 1973. Apart from some deterioration of visual acuity no new symptoms developed and no further laboratory tests were performed.

SECOND ILLNESS

On 21 December 1977 this man, now aged 72 years, was admitted to the acute psychiatric ward at St Mary Abbots Hospital, London. He complained of unsteadiness but denied any other symptoms. The caretaker of his lodgings stated that over several weeks he had changed completely from being a quiet tenant to being totally distracted. At nights he became restless and agitated and complained that people were entering his room. He had taken to going out into the street at night in his pyjamas and shouting out.

Psychiatric history

On admission the patient complained of hearing voices at night which frightened him. He was
disorientated and could not recall how he had arrived in the hospital bed. Long-term memory and proverb interpretation were impaired and he was unable to cope with simple arithmetical tasks.

This acute hallucinosis with disturbed behaviour was considered by the psychiatrist to be a very unusual presentation of tabo-paresis, which was suggested only when the various physical signs were noted. At this time his doctors were completely unaware of any past history; the patient only vaguely remembered being treated for syphilis in his youth.

Clinical findings
The physical findings were as before, with the addition of generalised muscle tremor, slurred speech, and a broad-based abnormal gait. His pupils were now unequal; the left was smaller than the right and there was a left-sided ptosis. Gross eighth nerve deafness was later detected by audiometry.

Progression and treatment
In the few days after admission the patient's condition deteriorated rapidly. He became unmanageable at night, was unable to dress or feed himself, and was doubly incontinent. A left-sided hemiparesis developed together with a pyrexia due to a urinary tract infection.

The laboratory findings at this time are shown in table II, together with those 15 months after a 10-day course of procaine penicillin. Within a week of starting treatment a remarkable clinical improvement occurred and the hemiparesis mysteriously disappeared. Unfortunately, the personality disorder did not completely resolve and two years later he remains a suspicious paranoid individual, although at times he can be a flamboyant, entertaining, and eccentric old gentleman.

Discussion
Cases of tabes progressing to general paralysis of the insane (GPI) were described in the pre-penicillin era, usually after insufficient treatment.\textsuperscript{17,18} Cases of classical neurosyphilis after insufficient penicillin treatment for early syphilis have also been described recently.\textsuperscript{19}

Cases of relapsing neurosyphilis after penicillin treatment have also been reported. Dattner\textsuperscript{20} described instances of failure of the CSF to return to normal but maintained that once the findings in the CSF had become normal for a year relapses were almost unknown. The concept of Dattner and Thomas\textsuperscript{21} in assessing the CSF is often quoted; this maintains that if the cell count becomes and remains within normal limits after treatment the disease is no longer active in the central nervous system. King and Nicol\textsuperscript{2} commented that this should not be taken as "an absolute rule." Dowzenko and Krysztowiak\textsuperscript{22} have reported two very unusual cases of relapsing neurosyphilis.

Wilner and Brody\textsuperscript{23} reported that more than 50% of patients with GPI developed further neurological signs after penicillin treatment. This, however, is usually interpreted as scar-tissue injury rather than reactivation of the disease.

There have been reports that penicillin has failed to reach the CSF in spirochaetid concentrations during recommended treatment schedules with procaine penicillin in neurosyphilis\textsuperscript{24,25} and that spirochaetid forms\textsuperscript{26,27} and \textit{Treponema pallidum} have persisted in the CSF after penicillin therapy.\textsuperscript{28}

Despite these reports, present opinion remains confident that penicillin is still successful in preventing the development of further gross manifestations of neurosyphilis. This was what Martin affirmed in 1972.\textsuperscript{29}
**Table II: Laboratory results during second illness**

<table>
<thead>
<tr>
<th>Date</th>
<th>Blood test results</th>
<th>CSF findings/test results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TPHA (titre)</td>
<td>VDRL (titre)</td>
</tr>
<tr>
<td>22.12.77</td>
<td>+ (1/5120)</td>
<td>+ (1/32)</td>
</tr>
<tr>
<td>6.4.79</td>
<td>+ (1/5120)</td>
<td>+ (1/16)</td>
</tr>
<tr>
<td>15 months</td>
<td>after treatment</td>
<td></td>
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</tbody>
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* Lymphocytes
† Normal value <0.05 IU/l.
‡ Because of Christmas holiday CSF was probably not examined on the day of collection.
§ Not accurately reported owing to contamination.

TPHA = *T. pallidum* haemagglutination assay; VDRL = Venereal Disease Research Laboratory (test); RPCFT = Reiter protein complement-fixation test; FTA-ABS = fluorescent treponemal antibody absorbed (test).
In conclusion, two authorities whose criteria for the assessment of cure in cases of neurosyphilis were first suggested 20 years ago stated: "The arrest of the disease can only be regarded as having been achieved when the CSF is normal and the VDRL is negative."14 15 "In the absence of clinical progression and with tests of CSF which become and remain normal it is nevertheless a wise precaution to perform further tests of the CSF after a further two years."12

In the light of this case I think it reasonable to advise that if the CSF does not return to normal, lumbar puncture should be performed every two years and be repeated indefinitely; attendance at follow-up should be ensured.

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References