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

A J H GILES

From the Department of Venereology, Pilgrim Hospital, Boston, Lincolnshire

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's¹ work, the World Health Organisation² maintains that 10-15 days' treatment with daily procaine penicillin is acceptable. This regimen is recommended by the United States Public Health Service,^{3,4} by Morton and Harris,⁵ and in standard textbooks on medicine.⁶⁻¹⁰

Glatt¹¹ recently questioned whether the amount of penicillin necessary to cure established neurosyphilis is yet known. King and Nicol,¹² Catterall,¹³ and Brain^{14,15} all recommended three weeks' treatment and Merritt,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

hypoalgesia 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

Address for reprints: Dr A J H Giles, Department of Venereology, Pilgrim Hospital, Sibsey Road, Boston, Lincs PE21 9QS

Received for publication 13 May 1980

TABLE 1 Laboratory results during first illness

	<i>Blood test results</i>			<i>CSF findings/test results</i>						
<i>Date</i>	<i>Kahn</i>	<i>Wassermann (units)</i>	<i>ESR (mm/hr)</i>	<i>Cells* (× 10⁶/l)</i>	<i>Protein (g/l)</i>	<i>Wassermann (units)</i>	<i>Pandy</i>	<i>Nonne-Apelt</i>	<i>Lange</i>	
17.11.57 At diagnosis	+	+	(28)	51	62	1.4	+	(15)	+	5555432111
21.7.58 8 months after treatment	+	−†		4	0.7	+	(4)	±	−	0011210000
23.5.59 18 months after treatment				6	0.7	−	+	±		0001211000

*Lymphocytes

†Not quite negative

+ Positive; ± weakly positive; - negative

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.^{17 18} Cases of classical neurosyphilis after insufficient penicillin treatment for early syphilis have also been described recently.¹⁹

Cases of relapsing neurosyphilis after penicillin treatment have also been reported. Dattner²⁰ 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 Thomas²¹ 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 Nicol¹² commented that this should not be taken as "an absolute rule." Dowzenko and Krysztofiak²² have reported two very unusual cases of relapsing neurosyphilis.

Wilner and Brody²³ 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 spirochaetocidal concentrations during recommended treatment schedules with procaine penicillin in neurosyphilis^{24 25} and that spirochaetal forms^{26 27} and *Treponema pallidum* have persisted in the CSF after penicillin therapy.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 1972.²⁹

TABLE II Laboratory results during second illness

Date	Blood test results				CSF findings/test results								
	TPHA (titre)	VDRL (titre)	FTA-ABS	RPCFT	FTA IgG	IgM	ESR (mm/hr)	Cells* ($\times 10^6/l$)	Protein (g/l)	TPHA (titre)	VDRL (titre)	FTA-ABS (titre)	IgG† (IU/l)
22.12.77 At diagnosis	+	(1/5120) + (1/32)	+	+	+	-	41	0±	2.0	+	§	+	2.83
6.4.79 15 months after treatment	+	(1/5120) + (1/16)	+	+				4	0.7	+	(1/10 000) (1/2)	+	0.31 (>1/40)

*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.
¶PHA = *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.

I should like to thank Dr R Ross-Russell and Dr M de Mowbray, for their permission to report this case, and Mrs Mary Robinson for her work on the preparation of the manuscript.

References

- Hahn RD. Some remarks on the management of neurosyphilis. *J Chronic Dis* 1961;13:1-5.
- Idspø O, Guthe T, Willcox RR. Penicillin in the treatment of syphilis. *Bull WHO* 1972;47, suppl 12:38-40.
- Center for Disease Control. *VD Fact Sheet* 1973. Washington DC: United States Department of Health, Education and Welfare 74:8195. 1974:25.
- Sparling PF. Diagnosis and treatment of syphilis. *N Engl J Med* 1971;284:650.
- Morton RS, Harris JRW. *Recent Advances in Sexually Transmitted Diseases*. Edinburgh: Churchill Livingstone 1975:166.
- Matthews WB, Miller H. *Diseases of the Nervous System*. 2nd ed. Oxford: Blackwell Scientific Publications 1975:196.
- Holmes KK. Syphilis. In: Thorn GW, Adams RD, Braunwald E, Isselbacher KJ, Petersdorff RG, eds. *Harrison's Principles of Internal Medicine*. 8th ed. New York: McGraw-Hill Book Co, 1977:926.
- Williams D. Infections of the meninges and the nervous system. In: Bodley Scott R, ed. *Price's Textbook of the Practice of Medicine*. 11th ed. London: Oxford University Press, 1973:1208.
- Matthews WB. Infections of the nervous system. In: Bodley Scott R, ed. *Price's Textbook of the Practice of Medicine*. 12th ed. Oxford: Oxford University Press, 1978:1331.
- Garrod LP, Lambert H, O'Grady F. *Antibiotic and Chemotherapy*. 4th ed. Edinburgh: Churchill Livingstone, 1973.
- Glatt MM. Neurosyphilis yesterday and today. *Lancet* 1979;i:383.
- King A, Nicol CS. *Venereal Diseases*. 3rd ed. London: Baillière Tindall, 1975:147, 154, 155.
- Catterall RD. *A Short Textbook of Venereology*. 2nd ed. London: English Universities Press Ltd, 1974:159.
- Brain WR, Walton JN. *Brain's Diseases of the Nervous System*. 7th ed. London: Oxford University Press, 1969:414.
- Walton JN. *Brain's Diseases of the Nervous System*. 8th ed. Oxford: Oxford University Press, 1977:464.
- Merritt HH. *A Textbook of Neurology*. 5th ed. Philadelphia: Lea & Febiger, 1973:135.
- Stokes JH, Beerman H, Ingraham NR. *Modern Clinical Syphilology*. 3rd ed. Philadelphia & London: Saunders WB, 1945.
- Kampmeier RH. *Essentials of Syphilology*. Oxford: Blackwell Scientific Publications, 1944:352.
- Luxon L, Lees AJ, Greenwood RJ. Neurosyphilis today. *Lancet* 1978;i:90-3.
- Dattner B. Penicillin failures in neurosyphilis. *Am J Syph Gonorr Vener Dis* 1949;33:571-5.
- Dattner B, Thomas E. *The Management of Neurosyphilis*. New York: Grune & Stratton. London: Heinemann, 1944.
- Dowzenko A, Krysztofiak B. Relapses in the CSF and acquired resistance to penicillin in cases of neurosyphilis. *J Neurol Sci* 1965;2:197-202.
- Wilner E, Brody JA. Prognosis of general paresis after treatment. *Lancet* 1968;ii:1370-1.
- Mohr JA, Griffiths W, Jackson R, et al. Neurosyphilis and penicillin levels in CSF. *JAMA* 1976;236:2208-9.
- Yoder FW. Penicillin treatment of neurosyphilis. *JAMA* 1975;232:270-1.
- Collart P, Borel L-J, Durel P. Study of the effect of penicillin in late syphilis: persistence of *Treponema pallidum* following treatment: I Late syphilis-experimental. *Ann Inst Pasteur* 1962;102:596-615.
- Collart P, Borel L-J, Durel P. Significance of spiral organisms found after treatment in late human and experimental syphilis. *Br J Vener Dis* 1964;40:80-9.
- Edmund C, Tramont MC. Persistence of *Treponema pallidum* following penicillin G therapy. *JAMA* 1976;236:2206-7.
- Martin JP. Conquest of general paralysis. *Br Med J* 1972;i:159-60.