Current Psychiatry

CASES THAT TEST YOUR SKILLS

Mr. S' worsening depression and paranoia baffle clinicians. A detailed look at his medical history suggests an illness that is often overlooked in psychiatric diagnosis.

Beware the men with toupees

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HISTORY Treatment-refractory depression

Mr. S, age 78, has a history of depression that has not responded to selective serotonin reuptake inhibitors and electroconvulsive therapy (ECT).

According to his niece, Mr. S had become withdrawn, suspicious, and forgetful. Several times over the past year, police found him wandering the streets and brought him to the community hospital's emergency room.

During one emergency room visit, he complained of decreased appetite, poor sleep, and depressed mood. He was subsequently admitted to the psychiatric unit, where he was treated with ECT and discharged on citalopram, 20 mg/d. His symptoms did not improve and he became ataxic and incontinent of urine.

Mr. S' family placed him in a nursing home, where he became increasingly paranoid. The attending physician prescribed risperidone, 3 mg/d, with no effect. He was then transferred to our psychiatric facility.

At admission, Mr. S told us that a group of men disguised in toupees and mustaches were out to kill him. He said these men had recently killed his niece—with whom he had just spoken on the phone and had seen at the hospital. He suspected that these men were after his money, hired a woman to impersonate his niece and spy on him, and planned to bury his body and his niece's in a remote place.

On evaluation, Mr. S was suspicious, guarded, and uncooperative, and often ended conversations abruptly. He denied auditory and visual hallucinations, was not suicidal or homicidal, and denied abusing drugs or alcohol. He said constant fear of his imminent murder left him feeling depressed.

Physical and neurologic exams were unremarkable except for mild ataxia. Mr. S' Folstein Mini-Mental State Examination score was 19/30, indicating moderate cognitive impairment.

Mr. S' history and behavior suggest depression with psychotic features. Do we have enough information for a diagnosis?

Dr. Greenberg's and Tampi's observations

Mr. S is displaying mood symptoms consistent with his prior diagnosis of depression, but with new-onset psychosis as well.

Because of Mr. S' neurobiologic symptoms, it is improper to diagnose depression with psychotic features without first performing a full medical and neurologic workup. The differential diagnosis needs to include medical and neurologic diagnoses, including:

- delirium secondary to urinary tract infection
- Alzheimer's and/or vascular dementia
- normal-pressure hydrocephalus
- substance abuse.

A complete dementia and delirium workup and detailed medical history are imperative.

FURTHER HISTORY Risky behavior

Further history reveals that Mr. S had been having sexual intercourse with prostitutes since his early teens and that this habit continued into his 70s. He had been diagnosed with syphilis in his teens and again in his 50s. Both times he refused to complete the recommended penicillin regimen because he was embarrassed by the diagnosis and had falsely believed that a single penicillin injection would cure him.

Lab tests showed a white blood cell count of 3.5 and a weakly reactive serum venereal disease research laboratory (VDRL) reading.

Box 1

Syphilis: Forgotten but not gone

Reporting of syphilis cases in the United States began in 1941.[1] At about that time, Yale University and the Mayo Clinic began conducting clinical trials of penicillin in syphilis treatment.[2]

Thanks to the advent of penicillin, syphilis incidence has declined dramatically since 1943, when 575,593 cases were reported.[3] Only 5,979 cases were reported to the U.S. Centers for Disease Control and Prevention in 2000.[4] A slight increase in cases, mainly among homosexual men, was reported in 2001.[1,4]

The AIDS epidemic and the emergence of crack/cocaine use[5,6] were believed to have triggered a brief increase in cases that peaked in 1990. This was likely caused by the high-risk sexual behavior observed in individuals with sexually transmitted diseases and the practice of exchanging sex for drugs.[6]

Could Mr. S' syphilis—inadequately treated in his youth—be causing his depression and paranoia decades later? If so, how would you confirm this finding?

Dr. Greenberg's and Tampi's observations

Mr. S has a longstanding history of syphilis secondary to high-risk sexual activity. This, combined with the lab findings and his worsening depression and paranoia, points to possible neurosyphilis.

Syphilis, caused by the spirochete *Treponema pallidum*, can traverse mucous membranes and abraded skin. Transmission is most common

Box 2

Syphilis: Prevalence and risk factors

Prevalence

- **6,103** cases reported in 2001
- **More prevalent** among men than women (2.1:1), probably because of elevated prevalence among homosexual men
- **African-Americans** accounted for 62% of cases in 2001. Prevalence in African–Americans that year was 16 times greater than in whites

Risk factors

- **Presence of HIV** infection or other sexually transmitted disease
- **Unprotected sex**
- **Residence in urban areas**
- **Substance abuse**
- **Homosexuality**

Source: References 5 and 6

during sexual activity but also occurs through blood transfusions and nonsexual lesion contact and from mother to fetus.

Because syphilis and its psychiatric effects are relatively uncommon *(Box 1)*, many psychiatrists do not consider neurosyphilis in high-risk patients who present with depression, dementia, or psychosis *(Box 2)*.

HOW SYPHILIS BECOMES NEUROSYPHILIS

Primary syphilis incubates for 10 to 90 days following infection. After this period, an infectious chancre appears along with regional adenopathy. If untreated, the chancre will disappear but the infection will progress.

Secondary syphilis is characterized by skin manifestations and occasionally affects the joints, eyes, bones, kidneys, liver, and CNS. Common effects include condylomata—highly infectious warty lesions—and a diffuse maculopapular rash on the palms and soles. These lesions disappear if left untreated, but most patients then either enter syphilis' latent stage or experience a potentially fatal relapse of secondary syphilis.[5]

Latent syphilis usually remains latent or resolves, but about one-third of patients with latent syphilis slowly progress to tertiary syphilis. Neurosyphilis, one of the main forms of tertiary syphilis, can surface 5 to 35 years after an untreated primary infection.[7]

There are four categories of neurosyphilis:

- **General paresis** results in dementia, changes in personality, transient hemiparesis, depression, and psychosis.
- **Tabes dorsalis** degenerates the posterior columns and dorsal root ganglia of the spinal cord. This results in ataxia, parasthesias, decreased proprioception and vibratory sense, Argyll Robertson pupil (an optical disorder in which the pupil does not react normally to light), neurogenic bladder, and sharp shooting pains throughout the body.
- **Meningovascular neurosyphilis** can result in cranial nerve abnormalities, symptoms of meningitis, and cerebral infarctions.
- **Asymptomatic** but with CSF positive for syphilis.

Neurosyphilis is fatal if untreated, and treatment usually does not eliminate symptoms but prevents further progression. Approximately 8% of patients with untreated primary syphilis develop neurosyphilis.[5,7]

Standard nontreponemal tests, such as the VDRL or rapid plasmin reagin, can be used to screen for syphilis. Because these tests often produce false positives, confirm positive results with a syphilis-specific test, such as the fluorescent treponemal antibody absorption (FTA-ABS) test, microhemagglutination assay for antibodies to *T pallidum*, and the *T pallidum* hemagglutination assay.

If neurosyphilis is suspected, CSF testing is strongly recommended. Diagnostic findings include elevated white blood cell and protein

counts and a positive VDRL. If the CSF is negative, refer the patient for treatment anyway because false negatives are common. Patients with consistent neurologic symptoms, positive VDRL and/or FTA-ABS, and negative CSF are diagnosed with neurosyphilis and warrant treatment.[7]

How would you manage Mr. S' psychiatric symptoms concomitant with medical treatment of late-stage syphilis?

Dr. Greenberg's and Tampi's observations

Although no specific guidelines exist for treating psychosis secondary to neurosyphilis, atypical antipsychotics remain the first-line treatment. Atypicals do not interact significantly with penicillin and can be given safely with syphilis treatment. Atypicals also are better tolerated than typical antipsychotics and produce fewer extrapyramidal symptoms, which are common among older patients and those with neurologic diseases.

Screening for syphilis. Every patient with a history of high-risk sexual behavior who presents with new-onset dementia or psychosis should be screened for syphilis. Sexual history can be difficult to obtain from some patients and family members, so communication between providers becomes crucial. Obtain lab test results from other care team members to monitor compliance, and coordinate patient education with other doctors on safe sexual practices.

TREATMENT Taking his medicine

Mr. S refused further testing and emergency conservatorship was sought. Citalopram was discontinued and risperidone was gradually increased to 6 mg at bedtime. He remained paranoid and delusional.

A brain MRI showed chronic ischemic small-vessel disease. HIV testing was negative, and serum FTA-ABS was reactive. CSF showed elevated protein and white blood cell count with a nonreactive VDRL and a reactive FTA-ABS. A diagnosis of neurosyphilis was made, and treatment was initiated with aqueous crystalline penicillin G, 4 million units every 4 hours for 2 weeks.

Mr. S was discharged back to the nursing home where his penicillin injections were continued. His paranoia diminished slightly but he remained ataxic, incontinent, and confused. He was discharged from the nursing home but needed confirmative HIV screening and repeated CSF testing to determine if syphilis treatment was effective.

Six months after treatment, Mr. S' niece reports that his paranoia has decreased. He has not needed additional psychiatric hospitalizations.

References

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Bottom Line

Neurosyphilis can cause disabling neurobiologic effects, but psychiatrists often do not consider this infectious disease. Watch for risk factors in patients who present with dementia, personality changes, depression, or psychosis. Refer all at-risk patients for syphilis testing.

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Related resources

- Merck Manual. www.merck.com. Search: "syphilis"
- U.S. Centers for Disease Control and Prevention—Syphilis elimination: History in the making. www.cdc.gov. Click on "Health Topics A-Z," then click on "S" and find "syphilis."
- National Institute of Allergy and Infectious Disease. www.niaid.nih.gov. Search: "syphilis"

DRUG BRAND NAMES

Citalopram • Celexa

Risperidone • Risperdal

DISCLOSURE

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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