Acquired Sexual Paraphilia in Patients With Multiple Sclerosis

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Background: Sexual dysfunction in patients with multiple sclerosis is typically characterized by diminished libido, erectile and ejaculatory dysfunction in men, and poor lubrication and anorgasmia in women. In contrast, hypersexual behavior and paraphilias are distinctly uncommon in this population of patients, but have been associated with various focal brain lesions.

Patient and Methods: We describe a man with clinically definite multiple sclerosis who developed profound and abrupt disinhibition and paraphilic behavior during an exacerbation.

Results: Neuroimaging revealed a marked increase in the number of enhancing lesions in the right sides of the hypothalamus and mesencephalon and extending into the right sides of the red nucleus, substantia nigra, and internal capsule. The altered sexual behavior was characterized by an obsessive and insatiable desire to touch women’s breasts.

Conclusions: Acquired sexual paraphilic behavior is uncommon in patients with multiple sclerosis but may occur when inflammatory demyelination involves the hypothalamic and septal regions of the basal prosencephalon. Our experience with this man illustrates the great difficulty involved in treating such patients when the paraphilic behavior becomes persistent.

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MULTIPLE sclerosis (MS), a central nervous system demyelinating disease, can be accompanied by a broad diversity of neurological deficits and is the most common disabling neurological disorder of young people. The most common disability involves a progressive loss of ambulation due to lower extremity weakness and spasticity, often based on myelopathy. A host of cognitive and psychiatric manifestations have been well documented in patients with MS. Dementia,1-3 depression,4,6 bipolar affective disease,7 and fatigue-related cognitive dysfunction8 have all been associated with the disorder. Although it has been reported that hypersexuality and paraphilic behavior can occur with various focal brain lesions in humans,9 these behavioral phenomena have been only rarely described in patients with MS.10,11 We describe a patient with MS who developed hypersexuality, disinhibition, and a sexual paraphilia following a short-term exacerbation of inflammatory demyelination involving the preseptal region of the basal prosencephalon. These behaviors were therapeutically recalcitrant and eventually led to his incarceration.

REPORT OF A CASE

A 36-year-old right-handed man was first diagnosed as having MS in 1993. At birth, the patient had an occipital extra-axial hematoma. In addition, he had an auditory perceptual problem in elementary school and was tutored from the age of 7 to 10 years. He graduated from high school with fair grades and dropped out of college after 1½ semesters. The patient described occasional marijuana use but denied alcohol abuse. Before the emergence of the reported aberrant sexual behavior, he had no significant psychological history.

The patient was well until June 1993, when he developed an intermittent tremor of the right hand followed by right-sided paresis. One month later, he experienced an episode of oblique binocular diplopia. A magnetic resonance imaging scan of the brain demonstrated multifocal, high-signal, T2-weighted white matter abnormalities throughout the brain. These occurred in the periventricular, hypothalamic, and brainstem regions (Figure 1).
Axial proton density–weighted images showed symmetric high-signal changes throughout the hypothalamus and septal region bilaterally (Figure 1). Coronal T2-weighted imaging revealed a large hyperintensity in the hypothalamic region adjacent to the third ventricle. T1-weighted images with gadolinium showed evidence of scattered areas of punctate enhancement in the subinsular zones, the internal capsule, the region of the hypothalamus, and the deep white matter.

High-signal intensity changes observed in the mesencephalon were adjacent to a low-signal appearance of the red nuclei, substantia nigra, and superior colliculi, taking on the appearance of the “face of the giant panda” sign (Figure 2). To our knowledge, this sign has not previously been reported in patients with MS, but has been associated with Wilson disease. The patient’s serum ceruloplasmin level was tested and was within normal limits. Somatosensory evoked potentials revealed abnormal conduction velocities from the median nerve to the somatosensory cortex. Visual evoked potentials demonstrated diminished amplitudes and prolongation of P100 latencies bilaterally, indicative of an occult optic neuropathy. Brainstem auditory evoked potentials and electroencephalographic recordings were within normal limits. An analysis of the cerebrospinal fluid showed an elevated protein of 78 and 2 oligoclonal bands. A diagnosis of MS was made at that time. The patient was treated with intravenous methylprednisolone, which was followed by substantial improvement. He started disease-modifying therapy with interferon beta-1b, $8 \times 10^6$ U subcutaneously every other day, but had to discontinue this medication after several months due to his loss of medical insurance.

By September 1994, he began to experience severe fatigue and the reemergence of diplopia. He was employed in the television industry as a production engineer until he went on disability in October 1994. At that time, he noted a persistence of oblique binocular diplopia, upper extremity tremors, episodic dysarthria, and moderate ataxia with some stumbling. He also complained of urinary urgency, but had no bowel or sexual dysfunction. He was treated again with methylprednisolone, 1 g/d intravenously, for 5 days. During the next month, the interferon beta-1b therapy was restarted, and no further exacerbations were noted until May 1995. At that time, his family observed a steady progression in behavioral de-
cline, characterized by poor judgment, impulsivity, and inappropriate sexual contact with strangers.

The patient voluntarily admitted himself, at the request of his family, to an inpatient psychiatric facility for 2 weeks in July 1995. Family members reported that the patient began to have drastic changes in behavior that included approaching and asking “sexually explicit” questions of strangers and masturbating 10 to 12 times per day. The most troubling behavior was his inappropriate actions toward women, characterized by reaching out and touching their breasts. He described this as an irresistible urge and said that he felt “quenched” or relieved after the act, despite recognizing how inappropriate these actions were. He felt helpless to control these actions. The patient’s sister described him as “like a predator” in seeking out women to touch their breasts. He also began to smoke cigarettes and was rarely seen without a cigarette in his mouth.

The patient presented to our MS clinic on August 2, 1995, after discharge from the psychiatric facility. He denied visual loss, vertigo, tinnitus, hearing loss, facial pain, alteration in facial or body sensation, and Lhermitte and Uhthoff phenomena. However, he did have dysarthric speech. There had been no problems with arthralgia, myalgia, galactorrhea, dry eyes or dry mouth, oral or genital ulceration, and alopecia. There was no history of hallucinations or significant psychiatric problems.

The cerebrospinal fluid demonstrated no oligoclonal bands, normal VDRL test results, negative acid-fast bacilli test results, and negative bacterial, fungal, and viral cultures. The test result for a cryptococcal antigen was negative. The patient did not have human T-tropic virus 1 or Lyme disease. In the cerebrospinal fluid, the white blood cell count was 0.07/µL; protein level, 6.4 g/dL; glucose level, 57 mg/dL (3.2 mmol/L); synthesis rate, 5.1 (upper limit of normal, 3.3); and IgG index, 0.63 (upper limit of normal, 0.58). Thyroid function test results were normal. The testosterone level was low at 163 ng/dL (5.7 nmol/L) (normal range, 300-2000 ng/dL [10.4-41.6 mmol/L]). A follow-up magnetic resonance imaging scan demonstrated severe lesions in the region of the hypothalamus and the septal region, as previously observed.

The patient participated in neuropsychological testing on 3 separate occasions in 1995. The first examination, on January 11, 1995, revealed the presence of mild cognitive impairments within the context of average intellectual functioning, as measured by the Wechsler Adult Intelligence Scale–Revised. His performance on typical measures of frontal lobe functioning, such as the Wisconsin Card Sorting Test, the Booklet Category Test, and the Stroop color test, was intact. He also demonstrated intact performances on structured tests of verbal memory (Wechsler Memory Scale Revised–Logical Memory), attention and concentration, and basic language skills. In contrast, on less structured measures of memory, such as the list-learning task of the California Verbal Learning Test, his performance was impaired due to perseverative errors, intrusions, and false-positive errors. His memory for visual material was mildly reduced on the Rey Osterrieth Complex Figure and the Visual Reproduction subtests of the Wechsler Memory Scale–Revised. He also demonstrated some errors on measures of motor programming. The evaluator concluded that the patient’s findings were most consistent with a diffuse pattern of subcortical brain dysfunction.

A brief reevaluation several months later, on August 8, 1995, essentially replicated the previous findings, with average intellectual functioning and intact performances on traditional measures of frontal lobe functioning (Wisconsin Card Sorting Test and the Booklet Category Test); however, mild difficulties were noted on measures of oral fluency and confrontation naming. This evaluator concluded that the findings were consistent with a diffuse demyelinating disease, such as MS. However, involvement of frontal and subcortical systems was also suggested by the examples of behavioral disinhibition from the clinical history and behavioral observations during the examination, despite the patient’s intact performances on more traditional tests of frontal dysfunction.

Additional testing, completed on November 17, 1995, repeated measures of motor programming and the Stroop color test and added measures of olfaction. Consistent with previous testing, the patient’s performance on the Stroop color test was within normal limits, and he made some perseverative and sequencing errors on tests of bimanual programming. In addition, on a confrontation test of olfactory functioning, he was only able to spontaneously identify 1 of 5 odors; he identified 3 of 5 when provided with a multiple choice format. It was concluded, based on the present and previous findings and on the patient’s behavioral history, that involvement of frontal and subcortical systems was likely and that perhaps there was greater involvement of orbitofrontal systems.

Pertinent neurological examination findings included evidence of bilateral upper extremity cerebellar outflow tremors. There were slow alternating movements and finger sequences, with some irregularity in the right hand vs the left. Rhythm tapping was slow, again more prominent in the right hand compared with the left. Heel-to-shin testing demonstrated mild bilateral ataxia. There was no evidence of dysdiadochokinesia. Reflexes were 2+ and symmetric. Sensory examination results were intact to pinprick, temperature, vibratory sense, and proprioception.

During the following year, the patient had periods of excellent behavioral control, punctuated by episodes of impulsivity, sexual disinhibition, and inappropriate social contact. Therapy with a combination of fluvoxamine maleate and medroxyprogesterone acetate, 400 mg/wk, was started to treat the aberrant sexual urges and fatigue. The patient, and his caregivers, noted improvement in his behavioral control and his obsessive-compulsive tendencies to touch women’s breasts.

After approximately 9 months, the patient developed refractory orthostatic hypotension. A medical work-up failed to reveal any underlying causes. All medications, except interferon beta-1b, were discontinued and the orthostasis resolved.

Before his exacerbative episode in May 1995, this man had no history of sexually abnormal behavior. He held a steady job, was involved in a steady relationship,
and did not smoke cigarettes. However, during the 10 months following this exacerbation, he manifested a sexual paraphilia, incessant masturbation, chain-smoking, impulsivity, and extremely poor judgment. He accosted several women in group homes that he was placed in and female nurses at the hospital. He disabled the alarm in the group home so that he was able to go out unnoticed, and was subsequently located 40 hours later. During this time, he propositioned a 12-year-old girl in a movie theater, and then he sexually assaulted a second minor and another woman. Charges were brought against him, and he was eventually incarcerated.

**COMMENT**

Although paraphilias are uncommon, hypersexuality and paraplebic behavior are associated with several focal brain lesions, especially those that involve loss of integrity of the frontal lobes and diencephalic structures. \(^{11}\) Idiopathic paraphilias almost always begin in childhood, adolescence, or early adulthood, but rarely occur with new onset after the age of 30 years. Acquired paraphilias, in contrast, seem to be associated with focal brain injury, particularly in the frontal lobe, hypothalamic area, and septal nuclei. \(^{13}\)

Temporal lobe structures have an important role in sexual behavior. In patients with the Kluver-Bucy syndrome, a disorder caused by bilateral temporal lobe dysfunction, sexual overtures, masturbation, and attempted sexual contact are characteristic. \(^{14}\) Paraphilias have been associated with several other neurological diseases, such as epilepsy, postencephalitic parkinsonism, hypoxic brain injury, and hypothalamic tumors. \(^{9}\) Huws et al \(^{10}\) described a young man with MS who developed hypersexuality and fetishism, which eventually led to his imprisonment. A magnetic resonance imaging scan showed periventricular and frontal damage. In another report, hypersexuality and paraphilia were reported in a woman with MS, whose aberrant behavior included exhibitionism, incest, scopophilia, and zoophilia. She eventually was arrested on multiple accounts of sexual misconduct. She ultimately died while in jail, and an autopsy demonstrated severe demyelination in the frontal, thalamic, and mesencephalic regions. \(^{13}\)

Previous literature has suggested that the septal region of humans is important in mediating the human sexual response. Two patients who underwent ventriculoperitoneal shunt revision for normal-pressure hydrocephalus demonstrated abnormal sexual behavior after the shunts were placed. Both patients made sexually explicit comments toward women, tried to fondle the female nurses, and masturbated in public. A computed tomographic scan later showed that, in one case, the tip of the catheter was lodged in the septum in the medial aspect of the floor of the lateral ventricles at the junction of the frontal horns. In the second case, a computed tomographic scan revealed that the catheter tip had been inserted into the midline anterior hypothalamic-septal structures. \(^{15}\) Neither of these men displayed atypical sexual behavior before shunt revision. Miller et al \(^{16}\) also report of a malpositioned shunt inserted into the septal region that resulted in intense sexual disinhibition. To our knowledge, there has not been a documented case in the literature that describes aberrant sexual behavior attributed to ventriculoperitoneal shunts without septal injury.

Septal lesions and sexual stimulation have been described in several animal species. Animal studies provide most of the knowledge that we have about the relationship between regional brain function (predominantly the septal zone) and sexual response. Copulatory behavior can be induced in primates \(^{16}\) and rats \(^{17}\) by stimulating the septal region.

Disinhibition syndromes involving hypersexuality have also been reported in humans who experienced damage to the orbitofrontal cortex. Starkstein and Kremer \(^{18}\) reviewed several studies that highlight the importance of the integrity of the orbitofrontal cortex and its associated circuitry, which projects to the septum, hypothalamus, and mesencephalon to maintain inhibitory control over such behaviors and eating, sexuality, and aggression. Despite the similarity in description between our patient’s disinhibition and that of individuals with orbitofrontal damage, our patient performed normally on several traditional neuropsychological measures of frontal lobe functioning. This finding was not surprising given the fact that many of these measures are relatively insensitive to damage in the orbitofrontal region; in fact, the Wisconsin Card Sorting Test is sensitive to dorsolateral prefrontal damage rather than orbitofrontal damage. \(^{19}\)

Humans who develop damage to the prefrontal cortex frequently exhibit defects in decision making despite intact intellectual skills. \(^{20}\) Similar to our patient, these individuals seem to make behavioral choices that are harmful, despite the knowledge that negative consequences may occur. To explore the possible neural basis for this defect, an experimental paradigm called the gambling task was developed by Bechara and colleagues. \(^{21}\) In this task, the subject is placed in a position of making choices that could result in either immediate short-term gains with long-term negative consequences or a net gain over time with a lower level of reward. The task was designed so that the solution to avoiding long-term negative consequences was easily acquired after several trials; thus, most healthy subjects showed no impairment in performing the task. However, studies \(^{22,23}\) using this paradigm revealed that subjects with ventromedial prefrontal damage were impaired on the gambling task, ie, they consistently made poor choices and took risks despite their knowledge that it would eventually lead to a negative outcome. In contrast, individuals with dorsolateral prefrontal damage consistently performed in the normal range on this task. Thus, it seems that this paradigm shows some promise in distinguishing between different types of prefrontal damage, and may explain why some individuals perform in the normal range on some frontal lobe measures despite the evidence of clearly disinhibited behavior. Additional research using this experimental task is warranted to develop normative data on more subjects and to further explore its utility in the diagnosis and treatment of individuals with prefrontal damage.

The complexity of the human sexual response and the neural basis for such response is poorly understood.
Arousal in humans is highly linked to structures with extensive frontal and limbic connections. Several changes in sexual behavior have been reported as a result of damage to the frontal cortex, hypothalamus, and amygdaloid nuclei. All of these regions have major anatomic connections to the septal region and, taken together, define a circuit of structures mediating sexual behavior. Sexual behavior may be increased or decreased depending on the site of tissue damage.

Hypersexuality and paraphilic behavior have been traditionally treated with counseling and pharmacotherapy, both of which were instituted without success in our patient. Some men have been treated with serotonergic drugs with limited success and with the antiandrogens medroxyprogesterone acetate and cyproterone acetate. However, 30 men with paraphilia all had a prompt reduction or total abolition of all paraphilic activities while being treated with triptorelin, a long-acting analogue of gonadotropin-releasing hormone that serves to reduce the serum testosterone level to low concentrations. Our patient had evidence of a low serum testosterone level, thereby suggesting that his behavioral alteration was not based on a peripheral endocrine derangement but rather on inflammatory demyelination in the hypothalamic and septal regions of the brain.

Multiple sclerosis can present with a host of cognitive and psychological changes, but the appearance of hypersexuality and paraphilia is uncommon. This report illustrates the important observation that specific areas of the brain, in particular the hypothalamic and septal regions, may be involved in mediating abnormal sexual behavior.

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