

Psychiatric Manifestations of Right Hemisphere Infarctions

BRUCE H. PRICE, M.D., AND MARSEL MESULAM, M.D.¹

Five right-handed patients (aged 45 to 78 years) developed acute psychotic disturbances in conjunction with infarcts in the right hemisphere. Their presentation was marked by agitation, inattention, suspiciousness, paranoid delusions, hallucinations, and lack of appropriate concern. Several of these patients initially received primary psychiatric diagnoses. Although neurological findings indicative of right hemisphere involvement could also be elicited, these were generally overshadowed by the more dramatic behavioral alterations. The electroencephalogram and computerized axial tomography were positive in most cases. These cases demonstrate that the possibility of a right hemisphere lesion needs to be entertained in patients who present with an atypical psychotic episode.

We treated five right-handed patients whose clinical presentation raised the possibility of primary psychiatric disease but whose test results also indicated infarcts in the right hemisphere. One purpose of this report is to alert the physician to the psychiatric presentations of cerebrovascular disease; another is to advance some thoughts on the potential anatomical substrates of these conditions.

Case Reports

Case 1

A 66-year-old right-handed engineer with no prior neurological or psychiatric disease but with a history of adult onset diabetes mellitus, chronic obstructive lung disease, and alcoholism, suddenly became restless and sleepless. He fixated on numbers and money and was convinced that he would win the lottery so that "all my children would be set free for life." He lost 30 lbs over the ensuing month and was hospitalized eventually, where he remained agitated and accused the nurses of trying to poison him. In addition, he was convinced he had terminal cancer and would soon die. The admitting diagnosis was psychotic depression. The medical and neurological exams were free of diagnostic abnormalities. The EEG was unremarkable, but a computerized axial tomography (CAT) scan revealed a right parietal infarction. He was treated with imipramine, haloperidol, benztropine, and psychotherapy, but his agitated and delusional state persisted. Over the next several months he received other diagnoses, including major depression with suicidal potential and panic reaction.

Approximately 3 months later, he experienced two episodes of transient left upper extremity sensory-motor symptoms. On examination at that time, his blood pressure was 180/120 mm Hg. He was oriented but mildly inattentive and did not appear to show concern for his condition. Spontaneous gait demonstrated a diminished left arm swing. A minimal left pronator drift, mild weakness of the left wrist extensors and interossei, brisk left upper extremity deep tendon reflexes, and left-sided extinction upon double simultaneous tactile stimulation were seen. Impaired visual-spatial skills were also demonstrated. Routine admission studies were normal. A repeat EEG showed focal right posterior temporal and occipital slowing. The CAT scan at this time demonstrated a small lacunar infarct in the right anterior internal capsule as well as the previously seen larger infarct in the right posterior parietal region (Figure 1, left). His behavioral difficulties gradually remitted over 3 months. Though his mild left body findings persist, he has experienced no further episodes and has returned to his previous job with success over the past 2 years. He remains only on antihypertensive and antiplatelet medications.

Comment. It is likely that the infarction in the right parietal region seen in the first CAT scan was responsible for the initial psychotic behavior, although the temporal relationship between these two events remains unresolved. The additional lacunar stroke several months later brought him to neurological attention. It is interesting that this second cerebrovascular event was not associated with a new psychotic episode.

Case 2

A 35-year-old right-handed woman office manager with no prior medical or psychiatric history experienced the abrupt onset of left hemiparesis and slurred speech which cleared over 3 weeks. Birth control pills were implicated. They were withdrawn, and she had

¹ Section of Neuroscience and Behavioral Neurology, Charles A. Dana Research Institute, Beth Israel Hospital, 330 Brookline Avenue, Boston, Massachusetts 02215. Send reprint requests to Dr. Price.

The preparation of this manuscript was supported in part by the Javits Neuroscience Investigator Award. The authors want to thank Leah Christie and Rick Plourde for expert secretarial and photographic assistance.

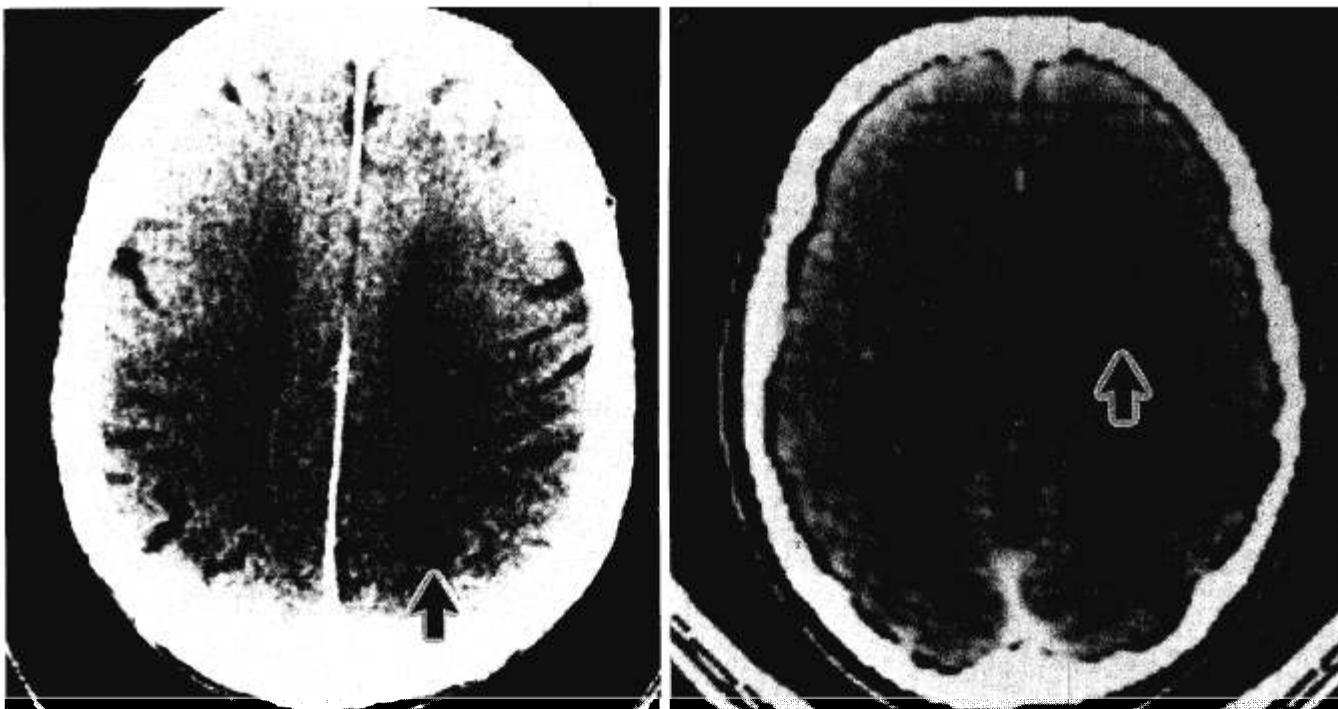


FIG. 1. CAT scans of patient 1 (left) and patient 2 (right). The left side of the head is on the left side of the scan. The arrowhead points to the site of infarction.

no further cerebrovascular events. She was essentially well again for 10 years when, at the age of 45, she experienced the first of four acute psychotic episodes over the ensuing 8 months. Each episode was accompanied by multiple visual and auditory hallucinations, such as seeing Shriner comic cars and faces in fireplaces. She had the delusions of being poisoned and killed, accompanied by feelings of panic and depression. The episodes began and ended rather abruptly and lasted from 1 day to 1 week. She required psychiatric hospitalization and received various diagnoses, such as acute schizophrenia, schizoid personality, and atypical depressive disorder. She continued to function well between psychotic episodes.

Neurological examination 1 year later revealed the presence of brisk deep tendon reflexes and slowness of individual finger movements on the left, as well as impaired visual-spatial skills. A CAT scan revealed an old infarct in the white matter of the right frontal region (Figure 1, right). An EEG showed paroxysmal independent bitemporal epileptiform activity during drowsiness and sleep. She was placed on phenobarbital and has had no recurrences over the subsequent 2 years.

Comment. Since there is no evidence of recurrent stroke, it is likely that the psychotic episodes represented seizure phenomena. This is supported by her epileptic EEG and the apparent beneficial response to an anticonvulsant. Although the EEG focus was in the temporal lobes, this may well represent daughter

foci secondary to electrical instability around the zone of the frontal infarction (Morrell, 1969; Morrell, in press; Morrell, *et al.*, 1975). Naturally, the possibility that this woman had additional limbic lesions or a totally independent condition of temporal lobe epilepsy cannot be ruled out.

Case 3

A 61-year-old right-handed woman was admitted to the psychiatry ward for agitation, anorexia with weight loss, suicidal ideation, and inappropriate behavior, such as threatening to kill her husband, pulling down all her house plants, and attempting to set her house on fire. Past medical history was remarkable for atherosclerotic cardiovascular disease, chronic obstructive lung disease, left mastectomy for carcinoma, one transient episode of left monocular blindness, and another involving left upper extremity numbness and weakness.

During the hospitalization she was noted to be confused and incontinent. Neurological exam revealed brisker left upper extremity reflexes, left upper extremity clumsiness, and left dystonic posturing with stressed gait. She was markedly inattentive and disoriented, showed a lack of appropriate concern, was perseverative, and had impaired visual-spatial skills. A CAT scan was unremarkable, and the EEG showed a mildly slow background of 7 Hz. No toxic or metabolic causes could be determined. She was discharged

on haloperidol, isosorbide, digoxin, dipyridamole, theophylline, and nitroglycerin.

She was readmitted 5 months later due to her husband's inability to care for her at home. She was still mildly inattentive and displayed left-sided extinction during double simultaneous visual stimulation. Her visual-spatial skills remained impaired. A repeat CAT scan showed no change, but the EEG showed paroxysms of right posterior temporal sharp theta waves with occasional involvement of homologous areas in the left. Her behavior improved spontaneously, and she has experienced no recurrence.

Comment. The abrupt onset of a confusional state accompanied by psychotic features, incontinence, and left-sided motor findings makes the diagnosis of an idiopathic affective disorder highly improbable. It is more likely that the behavioral picture resulted from structural injury to the right side of the brain.

Case 4

A 78-year-old right-handed woman with long-standing hypertension and a recent subendocardial infarct became abruptly confused and was admitted to the hospital. She refused to drink for fear of being poisoned, would take off other patients' surgical head dressings, and would intermittently scream "My family thinks I have Hitler's papers under my head People are out to kill me I am Hitler ... I'm covered with worms." On occasion, she became assaultive towards family members and staff. These spells were mixed with periods of relative lucidity.

Neurological exam revealed inattentiveness, perseveration, lack of appropriate concern, mild left hemiparesis, and tactile extinction on the left. Impaired visual-spatial skills and dysgraphia were also noted. Toxic and metabolic factors were ruled out. The CSF examination was unremarkable. A CAT scan was normal. The EEG showed intermittent rhythmic sharp theta waves of medium to high voltage, with phase reversal in the right parietal region. A trial of diphenylhydantoin did not result in clinical improvement. During one of her agitated delusional episodes, she fell and sustained a pelvic fracture. Haloperidol was needed for behavioral management. Over the 1 year since onset, she has remained confused, with episodic exacerbations of her agitated and delusional behavior.

Comment. This elderly patient without prior psychiatric history was at high risk for stroke. The abrupt onset of psychotic behavior was associated with neurological and EEG findings that point to a right hemisphere lesion.

Case 5

A 76-year-old right-handed male plumber without prior psychiatric history suddenly became confused.

He was unable to drive to his son's house for Thanksgiving, became increasingly inattentive and irritable, but remained indifferent to his difficulties, merely complaining of a stuffy nose. On admission, he was inattentive, perseverative, and impaired on visual-spatial tasks. Left-sided visual extinction was elicited during double simultaneous visual stimulation, and a left pronator drift was also noted. During the hospitalization, he thought there was a plot against him and refused all tests and medications. He was agitated and combative, repeatedly dressed and attempted to escape, and claimed there was no reason for him to be there. He stated that he was in a prison or hotel and that "you are all murderers you're torturing me I want to call the police." He would continually disturb other patients, make inappropriate verbal and physical sexual gestures, and felt he was going to die. Tests for toxic and metabolic causes were negative. An EEG showed 6 Hz background slowing without focal features. A CAT scan revealed no focal lesions. The echocardiogram and Holter monitor were normal, as were noninvasive carotid studies. Past medical history was remarkable for a myocardial infarct and congestive heart failure. The left-sided body findings cleared over the next month, but his behavioral and cognitive difficulties remained.

Comment. This patient had an atypical psychiatric presentation in conjunction with findings suggestive of a right hemisphere lesion.

Discussion

We have described five right-handed patients between the ages of 45 and 78 years who attracted psychiatric attention in conjunction with signs of structural injury to the right hemisphere. Although focal findings were present, the intensity of the behavioral changes far exceeded the abnormalities noted in the examination of cognitive and sensory-motor functions. Some of the patients were initially diagnosed as having agitated depression or other psychotic conditions. An alternative diagnostic consideration was toxic metabolic encephalopathy. No patient had a prior psychiatric history, but cardiovascular risk factors were commonly present.

Many of these patients experienced agitation, inattention, persecutory delusions, hallucinations, lack of appropriate concern, and mood disturbances, which included dysphoria, hypomania, generalized anxiety, and panic. These behavioral manifestations did not fit any well-established primary psychiatric entity, especially in view of the age of onset and the absence of an obvious precipitating life experience. All patients also had some cognitive and sensory-motor impairment consistent with right hemisphere injury. How-

ever, these could easily be overlooked in the context of the more salient psychiatric features. Either the CAT scan or the EEG provided confirmation of a structural lesion in the right hemisphere in several of the cases.

Except for case 2, the behavioral disorders most likely coincided with the stroke onset. The hallucinations, agitation, and confusion persisted in cases 4 and 5. Only case 2 was attributable to a seizure disorder 10 years after her stroke.

The emergence of severe psychiatric manifestations as a consequence of organic brain disease is well known in clinical practice. However, in most such cases, metabolic or toxic encephalopathies are usually implicated (Wolff and Curran, 1935). In fact, the term organic psychosis was once popular as a synonym for toxic metabolic encephalopathy. Our patients show that similar behavioral syndromes can also emerge in conjunction with focal brain disease. Accurate diagnosis in such cases is of obvious benefit to institute appropriate management.

Patients similar to ours have been described previously. In 1979, Guard *et al.* reported 10 patients with right temporal softening secondary to strokes or trauma. The clinical presentations were characterized by disorientation, agitation, inattention, flight of ideas, and blunted intellect. Four had visual hallucinations, six displayed visual-spatial difficulties, one had symptoms suggestive of a manic-depressive illness, and six had focal left-sided neurological findings. The EEGs, brain scans, angiograms, and dichotic listening tests helped to confirm the diagnosis in all cases.

Levine and Finkelstein (1982) reported eight patients with the acute onset of psychotic behavior 1 month to 11 years after right temporoparietooccipital stroke or trauma. As in the case of our patients, the onset was abrupt, and the clinical manifestations included hallucinations, delusions, agitation, a fluctuating course, mild left body findings, impoverished visual-spatial skills, and an absence of prior psychiatric history. They suggested that the pathophysiology of the psychosis may be related to epilepsy. Peroutka *et al.* (1982) reported a similar patient who presented with hallucinations and delusions 2 days after a right temporoparietooccipital infarction. Although the elementary neurological examination of this patient was normal, diminished visual-spatial skills were demonstrated. The EEG was not epileptic. Only two of our six patients (case 2 and perhaps case 4) had epileptiform activity on the EEG. Therefore, epilepsy does not appear to constitute a necessary feature in patients with this syndrome.

Levine and Grek (1984) recently reported nine cases of delusions following right hemisphere infarction and

concluded that delusions depend more on premorbid brain atrophy than on the exact location or size of the infarct. Since none of our patients had significant brain atrophy on CAT scan, this is also unlikely to constitute a necessary relationship. The fact that patient 2 was only 45 years old and otherwise mentally intact also rules out the possibility that a background of age-related cognitive decline is essential for the emergence of these syndromes.

There are other settings in which cerebrovascular disease may present predominantly as a behavioral or psychiatric syndrome. For example, some right hemisphere infarcts may give rise to an isolated confusional state without the florid psychiatric symptomatology described in these patients (Mesulam, *et al.*, 1976). In patients with medial temporooccipital lesions in either hemisphere, severe agitated delirium may emerge, but these are almost invariably associated with marked visual field deficits (Horenstein, *et al.*, 1967, Medina, *et al.*, 1977). In still other patients, acute left prefrontal lesions may present as apathy and withdrawal (Mesulam, 1979). Furthermore, the initial presentation of Wernicke's aphasia is characterized by what appears to be an incoherent word salad in a patient who may have no primary neurological findings. Many such patients may also show intermittent agitation and suspiciousness, so that an adequate examination of language may not be possible during the acute phase (Benson and Geschwind, 1975). In such patients, the demonstration that axial commands can be followed perfectly while limb commands cannot be performed is diagnostic of the condition. Thus, even when elementary sensory-motor findings are hard to detect, subdued, or even absent, there are several settings in which the clinician must suspect the presence of cerebrovascular disease when faced with a patient in whom the clinical picture appears to be dominated by psychiatric symptomatology.

It is interesting that each of our patients as well as those of Guard *et al.* (1979), Levine and Finkelstein (1982), and Peroutka *et al.* (1982) had right hemisphere injury. It is not clear if this indicates that damage to the right hemisphere is more closely associated with this type of psychiatric disturbance or whether similar disturbances are equally frequent after left hemisphere injury but become masked by the prominent aphasic symptoms. Our initial impression, shared by several other investigators as well (Gainotti, 1979), is that right hemisphere injury is more frequently implicated than left hemisphere injury as the cause of salient psychiatric disturbances. It would be useful to find out what proportion of individuals with right hemisphere infarcts develops psychotic symptoms. Furthermore, it is of interest to determine if this indicates a unique lesion site or,

perhaps, a set of special vulnerabilities in the form of preexisting brain disease or psychiatric profile. Our cases do not support advanced age, atrophy, epilepsy, or concomitant left hemisphere dysfunction as necessary prerequisites.

The pathophysiology of the psychotic behavior in our patients is obscure. The brain is not only the organ of cognition, perception, and action but also that of affect and thought. The proper balance among thought, experience, and affect is indispensable to mental health. It is not surprising that certain lesions of the brain can disrupt this balance in a way that may lead to severe behavioral disturbances which appear to represent psychotic episodes. Usually, the limbic parts of the brain are implicated in psychiatric disease. However, many patients with the type of acute psychotic symptoms described in this report have lesions located in frontal, parietal, or lateral temporal cortex. Recent evidence indicates that the high-order association areas in the prefrontal and posterior parietal regions receive direct, monosynaptic limbic system inputs (Barbas and Mesulam, 1981; Mesulam, *et al.*, 1977). It is conceivable, therefore, that lesions in such areas of the brain disrupt the interaction between high-order association cortex and limbic structures and that the behavioral manifestations of this include psychotic episodes.

Conclusion

Five right-handed patients developed psychotic features in conjunction with right hemisphere infarcts. Although subtle neurological signs could be elicited, their psychiatric features were most salient. Cardiovascular risk factors were usually present. Several patients received primary psychiatric diagnoses and inappropriate treatments. CAT scans and EEGs were helpful in most cases. In patients who present with an acute atypical psychotic episode, focal brain disease must be considered.

References

Barbas H, Mesulam M-M (1981) Organization of afferent input to subdivisions of area 8 in the rhesus monkey. *J Comp Neurol* 200:407-431.

Benson DF, Geschwind N (1975) Psychiatric conditions associated with focal lesions of the central nervous system. In S Arietti, N Reiser (Eds), *American handbook of psychiatry* (Vol IV). New York: Basic Books.

Gainotti G (1979) The relationships between emotions and cerebral dominance: A review of clinical and experimental evidence. In J Grzelier, P Flor-Henry (Eds), *Hemisphere asymmetries of function in psychopathology* (pp 21-34). New York: Elsevier.

Guard O, Delpy C, Richard D, Dumas R (1979) Une cause mal connue de confusion mentale: Le ramollissement temporal droit. *Rev Med* 40:2115-2121.

Horenstein S, Chamberlain W, Conomy J (1967) Infarctions of the fusiform and calcarine regions: Agitated delirium and hemianopia. *Trans Am Neurol Assoc* 92:85-89.

Levine DN, Finkelstein S (1982) Delayed psychosis after right temporo-parietal stroke or trauma: Relation to epilepsy. *Neurology (Minneapolis)* 32:256-273.

Levine DN, Grek A (1984) The anatomic basis of delusions after right cerebral infarction. *Neurology (Minneapolis)* 34:577-582.

Medina JL, Chokroverty S, Rubino FA (1977) Syndrome of agitated delirium and visual impairment: A manifestation of medial temporo-occipital infarction. *J Neurol Neurosurg Psychiatry* 40:861-864.

Mesulam M-M (1979) Acute behavioral derangements without hemiplegia in cerebrovascular accidents. *Primary Care* 6:813-821.

Mesulam M-M, Van Hoesen GW, Pandya DN, Geschwind N (1977) Limbic and sensory connections of the inferior parietal lobule (area PG) in the rhesus monkey: A study with a new method for horseradish peroxidase histochemistry. *Brain Res* 136:393-414.

Mesulam M-M, Waxman SG, Geschwind N, Sabin TD (1976) Acute confusional states with right middle cerebral artery infarctions. *J Neurol Neurosurg Psychiatry* 39:84-9.

Morrell F (1969) Physiology and histochemistry of the mirror focus. In HH Jasper, AA Ward, A Pope (Eds), *Basic mechanisms of the epilepsies* (p 357). Boston: Little and Brown.

Morrell F (in press) Secondary epileptogenic lesions in man: Extent of the evidences. In AV Delgado-Escueta (Ed), *Basic mechanisms of the epilepsies*. New York: Raven Press.

Morrell F, Tsuru N, Hoeppner TJ, *et al* (1975) Secondary epileptogenesis in frog forebrain: Effect of inhibition of protein synthesis. *Can J Neurol Sci* 2:407-416.

Peroutka SJ, Sohmer BH, Kumar AJ, Folstein M, Robinson RG (1982) Hallucinations and delusions following a right temporo-parietooccipital infarction. *Johns Hopkins Med J* 151:181-185.

Wolff HG, Curran D (1935) Nature of delirium and allied states. *Arch Neurol Psychol* 33:1175-1215.