

A mysterious physical and mental decline

Matthew Macaluso, DO, Christine Skotzko, MD, and Maria Rueda-Lara, MD

Since Mr. C developed intermittent fever, hematuria, and fatigue 2 months ago, his short-term memory has diminished so much that he forgets to eat. What's going on?



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HISTORY 'Not himself'

Mr. C, age 69, presents to the emergency department complaining of intermittent fever of about 100°F, hematuria, headache, weakness, fatigue, and decreased appetite over 2 months. Testing shows acute renal failure, elevated C-reactive protein, and increased sedimentation rate. The attending internist admits Mr. C with a working diagnosis of temporal arteritis and acute renal failure, administers corticosteroids for headache, and orders a right temporal artery biopsy, which shows no signs of vasculitis.

Family members report that Mr. C has not been himself—he has become increasingly withdrawn and “emotionless.” Mr. C's wife says her husband has needed help with dressing and eating because of short-term memory loss over 9 months. She says he has lost 20 to 30 lb.

The patient's cognitive function appears to have worsened since he developed these physical symptoms. Mrs. C also reports that he has had weakness and fatigue for 8 months.

One month earlier, the patient was admitted to a different hospital and treated for 2 weeks with IV antibiotics for fever of unknown origin. Results of lumbar puncture and extensive rheu-

matologic, infectious disease, urologic, and gastroenterologic evaluations were normal.

The internal medicine physician requests a psychiatric consultation. During our interview, Mr. C is cooperative, shows no signs of acute distress, is well groomed and dressed appropriately, and maintains eye contact. Speech rate and volume are low, with normal articulation and coherence, diminished spontaneity, and paucity of language. Mrs. C tells us her husband was lively and talkative before his recent illness. His mood is euthymic, and he is pleasant and cheerful during the evaluation.

Mr. C's symptoms suggest:

- delirium caused by a medical condition
- Alzheimer's dementia
- dementia caused by a medical condition
- mood disorder secondary to a medical condition

The authors' observations

Initially, we suspect an underlying medical condition is causing Mr. C's psychiatric symptoms.

Mr. C's wife reports that her husband stopped drinking 2 years ago after his family expressed concern about his health. Mr. C's past alcohol use could not be quantified. He has not abused illicit drugs and has no personal or family history of dementia, trauma, or psychiatric or neurologic disorders.

Dr. Macaluso is chief resident, department of psychiatry and behavioral sciences, University of Kansas School of Medicine, Wichita. Dr. Skotzko is director of psychosomatic medicine, Morristown Memorial Hospital, Morristown, NJ. Dr. Rueda-Lara is assistant professor, department of psychiatry, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway, NJ.

continued

Clinical Point

Mr. C's cognitive function appears to have declined since he developed fever, hematuria, headache, weakness, and fatigue

Table

Mr. C's laboratory findings

	Value	Normal range
WBC	15.1	4.8 to 10.8 cells/ μ L
Hb	9	13.8 to 17.5 g/dL
Hct	25.9%	40% to 54%
MCV	89.7	80 to 94 fL
BUN	119	7 to 18 mg/dL
Cr	12.1	0.7 to 1.3 mg/dL
Na	125	136 to 145 mmol/L
K	6.5	3.5 to 5 mEq/dL
HCO₃	13.5	22 to 29 mmol/L
ESR	125	30 mm/hr

WBC: white blood cell; Hb: hemoglobin; Hct: hematocrit; MCV: mean corpuscular volume; BUN: blood urea nitrogen; Cr: creatinine; Na: sodium; K: potassium; HCO₃: bicarbonate; ESR: erythrocyte sedimentation rate

EVALUATION Impaired memory

Mr. C is afebrile during the initial physical examination, but fever returns within several days. Neurologic examination is normal, and negative rapid plasma reagin rules out syphilis. Vitamin B₁₂ and folate levels are normal, as is thyroid function. Other laboratory findings are outside normal limits (*Table*).

Urine is cloudy with 2+ protein, 3+ blood, and trace leukocyte esterase. The presence of protein and blood suggests a glomerular disease such as a glomerulonephritis.

A positive leukocyte esterase test results from the presence of white blood cells, either as whole cells or as lysed cells. An abnormal number of leukocytes may appear with upper or lower urinary tract infection or in acute glomerulonephritis.

Chest radiography shows increased bilateral pulmonary vasculature, which can indicate pulmonary hypertension.

Mr. C shows variable and incongruent affect and mood, often shifting from labile to blunted. He denies depressed mood. At times he is disinhibited and makes inappropriate remarks. His thought processes are decreased but generally logical and goal-directed. Mr. C reports no hallucinations or suicidal thinking. He has concrete

reasoning with regard to his medical condition and linear associations with fair to poor insight/judgment. He exhibits intact impulse control and is oriented to person, place, and time.

Mr. C has fair attention and concentration but impaired recent memory. He cannot recall yesterday's events without help.

Mr. C's Mini-Mental State Examination score of 21/30 suggests markedly impaired executive functioning and cognitive deficits. The attending psychiatrist recommends brain MRI.

The authors' observations

Mr. C shows markedly impaired cognitive function without significant impairment of attention and concentration despite his progressive deterioration and increasing disability. Urine toxicology shows no illicit substances. Given his lack of a previous mood disorder and his family's description of him as formerly vibrant and cheerful, he likely does not have a mood disorder.

Based on the history of events, including the symptom pattern, we rule out delirium. We suspect that Mr. C has dementia secondary to a general medical condition. His symptoms seem to be directly related to his medical complaints and do not have a waxing and waning course. The internal medicine physician orders additional laboratory tests.

TESTING Kidney, lung damage

Over 5 days, Mr. C's intermittent low-grade fevers continue. Laboratory tests are negative for HIV antibody, hepatitis panel, and antinuclear antibodies (ANA). C-reactive protein is elevated at 27.8 mg/dL (normal range, <8 mg/dL). Oliguria persists, and creatinine remains elevated at 12.1 mg/dL (normal 0.7 to 1.2 mg/dL). Initial antglomerular basement membrane (anti-GBM) antibody titer is negative, but a second titer is positive. Mr. C also is positive for perinuclear-staining antineutrophil cytoplasmic antibody (pANCA) but negative for cytoplasmic-staining ANCA (cANCA) with normal C3 and C4 levels.

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Renal ultrasound is normal, but preliminary renal biopsy shows rapidly progressive glomerulonephritis. The internist immediately starts dialysis, cyclophosphamide at 1.5 mg/kg, and prednisone, 1 mg/kg. The pathology report on the renal biopsy describes extensive crescentic glomerular destruction, with inflammatory cells present.

Ten days after admission, Mr. C develops hemoptysis, and chest radiography shows increasing alveolar infiltrates. The attending internist consults pulmonary and critical care services.

The consultant suspects a pulmonary-renal syndrome because of bilateral alveolar infiltrates (diffuse alveolar hemorrhage). The internal medicine team continues high-dose corticosteroids, followed by plasmapheresis.

Brain MRI shows subacute to chronic infarcts involving the right basal ganglia and corona radiata and mild to moderate small vessel ischemic changes. Old areas of hemorrhage are noted within both cerebellar lobes, left temporal lobe, right basal ganglia, right parietal lobe, and right frontal lobe.

During follow-up interviews, Mr. C often cannot recall recent dialysis or plasmapheresis and reports no physical symptoms. His short-term memory continues to deteriorate; he would forget to eat if not cued by family or nursing staff. He shows global cognitive deficits and is increasingly withdrawn and flat.

Mr. C's medical findings suggest:

- isolated CNS vasculitis
- systemic lupus erythematosus
- another medical condition

The authors' observations

Mr. C's overall condition and medical test results suggest Goodpasture's syndrome—also called anti-GBM disease—a rare autoimmune condition characterized by rapid destruction of the kidneys and hemorrhaging of the lungs (*Box, page 58*).¹⁻⁵ We diagnose Goodpasture's syndrome based on Mr. C's anti-GBM antibody and pANCA findings combined with crescentic glomerular destruction on renal biopsy.

Although few case reports have associated Goodpasture's syndrome with neurobehavioral changes, the apparent relationship of Mr. C's medical symptoms with the worsening of his cognitive impairment suggests a link.

Mr. C's MRI findings also might suggest CNS vasculitis, which affects small arteries of the cerebral and spinal cord leptomeninges and parenchyma, leading to CNS dysfunction.⁶⁻⁸ CNS vasculitis can result from primary nervous system involvement or from a secondary systemic process such as Goodpasture's syndrome.⁹

continued

Clinical Point

Rapid destruction of the kidneys and lung hemorrhaging characterize Goodpasture's syndrome

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Clinical Point

Be vigilant for a correlation between neurocognitive changes and the timing of medical symptoms

Box

Goodpasture's syndrome: A rare autoimmune disease

Goodpasture's syndrome, which afflicts <1 in 1 million persons, involves antiglomerular basement membrane (anti-GBM) antibodies that act against antigens in the kidneys and lungs.¹ Patients typically present with alveolar bleeding, rapidly progressive acute renal failure with proteinuria,¹ and pulmonary symptoms such as dyspnea and hemoptysis.²

Possible triggers include:

- viral upper respiratory tract infection (20% to 60% of patients)³
- exposure to hydrocarbon solvents (<5% of patients).^{3,4}

Mr. C was exposed to solvents during the 15 years he worked in a factory. Some researchers believe a noxious event among genetically susceptible persons damages basement membrane and exposes an antigen that triggers IgG auto-antibody production.^{3,4}

Malaise, weight loss, and fever are atypical in Goodpasture's syndrome but could suggest concomitant vasculitis.⁵

We rule out lupus because Mr. C is ANA-negative; this test has 99% sensitivity for lupus.¹⁰

OUTCOME Ongoing disability

Mr. C is hospitalized for 6 weeks. He receives cyclophosphamide, prednisone, and 10 sessions of plasmapheresis. We prescribe mirtazapine, 15 mg at bedtime, to treat mood symptoms. We chose mirtazapine because of

Related Resource

• Goodpasture's syndrome. National Kidney and Urological Diseases Information Clearinghouse (NKUDIC). <http://kidney.niddk.nih.gov/kudiseases/pubs/goodpasture>.

Drug Brand Names

Cyclophosphamide • Cytoxan, Neosar, others	Prednisone • Deltasone, Sterapred, others
Mirtazapine • Remeron	

Disclosure

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

the drug's sleep-restoring and appetite-stimulating properties.

Mr. C's fever resolves and pulmonary function soon improves, but his cognitive impairment persists. He has difficulties preparing meals, taking medications, and managing his money.

Mr. C is discharged with a referral to a psychiatrist. He continues taking mirtazapine and a lower dose of prednisone. He requires ongoing hemodialysis and assistance with activities of daily living.

The authors' observations

Prompt multidisciplinary intervention is critical when patients present with concurrent cognitive and medical symptoms. A thorough psychiatric evaluation can help piece together the illness' course. The psychiatrist's role in a multidisciplinary assessment is to:

- document neurocognitive changes
- verify them through collateral information

Bottom Line

For patients in whom neurocognitive symptoms may be caused by a medical condition, document and verify these symptoms and correlate them with the timing of medical symptoms. Seek collateral information from a patient's family to determine premorbid functioning and any temporal relationship between medical and cognitive symptoms.

- correlate these changes with the timing of medical symptoms.

Interview the patient alone, then seek collateral information to assemble the clinical picture and help establish premorbid functioning. Ask family members about the patient's cognitive function at home or at work and in high-risk situations such as while driving or operating machinery.

An underlying psychiatric condition can complicate the diagnosis. In these cases, careful interviewing and collateral information can help you discern the chronology of events.

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