neuroleptic administration (2, 9). Our data indicate that genetic factors may be associated with the determination of these patterns and their clinical correlates.

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Cardiac Arrest During ECT Modified by β-Adrenergic Blockade

Paolo Decina, M.D., Sidney Malitz, M.D., Harold A. Sackeim, Ph.D., John Holzer, M.D., and Stuart Yudofsky, M.D.

A hypertensive patient with a history of diabetes and ischemic heart disease was given propranolol before ECT and experienced cardiac arrest after subconvulsive electrical stimulation. The authors suggest exercising caution when combining β-adrenergic blockade and ECT.

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Beta-adrenergic blockade has been used to attenuate the sympathetically mediated cardiovascular changes associated with electrically induced seizures (1–3). These changes follow the initial parasympathetic response (e.g., bradycardia, hypotension), mostly evident immediately after electrical stimulation, and are usually limited to a transient increase in sinus rhythm rate, cardiac output, and blood pressure. The most common complications are premature atrial and ventricular contractions and exaggerated hypertension. These are clinically benign. Rare but potentially lethal complications are ventricular tachyarrhythmias and myocardial ischemia secondary to an increase in myocardial oxygen consumption. The incidence and severity of these complications appear to increase in the presence of certain variables relating to the patient's condition, such as preexisting cardiovascular illness and old age, and certain variables relating to treatment conditions, such as oxygenation and premedication (4).

Anecdotal evidence supports the efficacy of propranolol and other β blockers in the treatment of ECT-related tachyarrhythmias and exaggerated hypertension (1–3) and, at least in theory, in the prevention of myocardial ischemia that may occur in patients with ischemic heart disease (5). To our knowledge, the oral or intravenous administration of β blockers as a pre-ECT medication has not been reported to be associated with adverse side effects, but in the case reported here the use of intravenous propranolol immediately before ECT in a patient with pretreatment anxiety and a history of ischemic heart disease was associated with a reversible cardiac arrest.

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CASE REPORT

Ms. A was a 68-year-old woman who was suffering from her sixth episode of severe major depressive disorder. Her past depressive episodes had been refractory to pharmacotherapy and psychotherapy but partially remitted with ECT. Each episode lasted approximately 2 years and was followed by complete remission and return to normal functioning. Because the depressive symptoms of the current episode had not responded to an outpatient trial of pharmacotherapy, Ms. A was hospitalized to received ECT.

Her medical history included a myocardial infarction with a brief hospitalization when she was 63. Diabetes mellitus was discovered at that time and had been treated since then with low doses of insulin. The results of admission laboratory tests were normal except for a fasting blood sugar level of 337 mg/dl and an ECG that showed the signs of the anteroseptal myocardial infarction and nonspecific ST-T wave abnormalities. The results of a physical examination were unremarkable except for a cataract in one eye. A second ECG, done before the beginning of ECT, was virtually identical to the one obtained on admission. Her fasting blood sugar values gradually and steadily decreased to 208 mg/dl after she resumed regular intake of NPH insulin (15 U).

The morning of the first scheduled treatment Ms. A exhibited pretreatment anxiety; her pulse rate was 100 beat/min (baseline=60–70). Her blood pressure was 180/120 mm Hg (baseline=120/80–130/85). After unsuccessful attempts to control her anxiety with reassurance and support, we decided to proceed with the treatment with Ms. A's consent. Before anesthesia induction 1 mg i.v. of propranolol was administered and the standard administration of atropine was omitted. Intravenous pentothal, 100 mg (1.8 mg/kg), and succinylcholine, 30 mg (0.5 mg/kg), were used to induce general anesthesia and muscle relaxation, respectively. From the onset of anesthesia 100% oxygen was given through a mask with positive pressure. The treatment was continuously monitored with single-channel ECG and EEG. A bidirectional brief-pulse electrical stimulus (pulse width=1.5 msec, frequency=20 Hz, duration=1 second) was delivered bilaterally, from a constant-current (800 mA) ECT device (MECTA), but no seizure occurred. The stimulation, however, was followed by 5 seconds of progressive slowing of sinus rhythm ending in arrest. Thump pacing was promptly instituted, and regular sinus rhythm resumed after a total of 15 seconds of asystole. Ms. A awoke uneventfully from the anesthesia shortly thereafter and exhibited complete amnesia for the event.

Follow-up cardiologic evaluations revealed no sequelae from the accident. Nevertheless, ECT treatment was interrupted in favor of further pharmacotherapy and psychotherapy. After 4 more months of treatment without any symptomatic improvement, all psychotropic medications were discontinued and Ms. A was referred back for ECT. The results of an ECG repeated before beginning treatment were virtually identical to the ones obtained 4 months earlier, before the first ECT trial, and her fasting blood sugar had further decreased and stabilized around 160–180 mg/dl while she was taking NPH insulin (15 U). This time she did not manifest pretreatment anxiety. She was premedicated with atropine (0.5 mg i.m. and 0.4 mg i.v.) and then given methohexital, 40 mg (0.7 mg/kg), and succinylcholine, 30 mg (0.5 mg/kg). Electrical stimulation of sufficient intensity to elicit a generalized seizure was administered during the course of treatment (pulse width=1.5 msec, frequency=60 Hz, duration=1 second). Ms. A tolerated a course of 13 treatments very well; she had no further significant cardiologic complications and experienced a good remission of the depressive syndrome.

DISCUSSION

The use of propranolol with this patient was justified by the presence of two clinical conditions presumed to increase the risk of serious complications secondary to the sympathetic stimulation associated with electrically induced seizures. The patient's anxiety state, characterized by tachycardia and hypertension, heightened the risk of cardiac complications posed by the preexisting ischemic heart disease. Propranolol was indicated for the management of cardiac symptoms associated with anxiety (6), as well as for the attenuation of the hypertensive and tachycardiac response, to reduce the risk of myocardial ischemia and ventricular ectopy. Atropine was omitted to avoid further blood pressure elevation (7). Ironically, the use of propranolol may have contributed to the cardiac arrest by exacerbating the parasympathetic response associated with the subconvulsive stimulation.

Cardiac arrest is a well-documented, although rare, complication of ECT and is not necessarily related to β blockade. Indeed, it may be argued in this case that the likelihood of a cardiac arrest was heightened by the lack of preventive use of atropine, the subconvulsive intensity of the electrical stimulation, or the use of pentothal. Although not exclusively, each of these conditions has been associated with cardiac arrest (5). In particular, Pitts and associates (8) demonstrated that methohexital causes many fewer cardiac irregularities during ECT than pentothal. Nonetheless, experimental data support the notions that an adrenergic mechanism is involved in the phenomenon of vagal escape (9) and that in the presence of sympathetic blockade a shock-induced activation of the autonomic nervous system can lead to a parasympathetic-mediated cardiac arrest (10). In view of these data, it seems probable that propranolol was involved, at least in part, in the pathogenesis of the asystole.

This case illustrates the occurrence of asystole associated with the use of intravenous propranolol in combination with ECT and indicates the need to exercise caution in using such a combination. In particular, the prophylactic use of β blockade in patients with ischemic heart disease with or without pretreatment anxiety should not be implemented until the risk/benefit ratio of such a combination has been carefully assessed.

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A Case of Mania Secondary to Vitamin B_{12} Deficiency

Frederick C. Goggans, M.D.

A case of mania apparently secondary to vitamin B_{12} deficiency appeared without other overt clinical features of pernicious anemia and resolved with B_{12} replacement. Six months later, the patient was receiving monthly B_{12} injections and his mental status remained normal.

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Secondary mania is defined as a manic syndrome of organic etiology with clinical features indistinguishable from those of primary mania (1). Numerous factors—including various drugs and toxins, metabolic disturbances, and infectious and neoplastic disorders—have been associated with secondary mania (2, 3). Although many psychiatric symptoms have been associated with B_{12} deficiency, I present here the first report, to my knowledge, of the full manic syndrome secondary to B_{12} deficiency.

CASE REPORT

Mr. A, an 81-year-old man, was admitted to the hospital with a 1-week history of irritable mood associated with hyperactivity, decreased need for sleep, grandiosity, sexual indiscretion, and reckless and agitated behavior. He felt that his home town was planning a day of celebration in his honor to which several Hollywood personalities were invited. Also, he became so physically energized that six younger men were required to restrain him at the time of admission to the hospital. Mr. A had no personal or family history of psychiatric disorder. He did not have any history of major medical disorders, and he had not been taking any medication before admission.

On admission Mr. A was oriented in all spheres but was easily distractible. He was agitated, loud, and pressured and denied any mental or physical disorder. He had no delusions or hallucinations other than those already mentioned.

Administration of 5 mg of intramuscular haloperidol resulted in marked clinical improvement. Oral haloperidol, 5 mg b.i.d., was continued during the evaluation phase of his hospitalization. The results of general physical and neurological examinations were entirely within normal limits. His hematocrit was 42.4%, his hemoglobin level was 13.8 g/100 ml, and his white blood count was 5,000 cell/cm^3. His red blood cell morphology was normal. His mean corpuscular volume was 85.1 μm^3. No hypersegmented neutrophils were noted on the peripheral blood smear. The results of general blood chemistries, a thyroid function test, and a comprehensive drug screen were within normal limits. His CAT scan was normal. The initial serum vitamin B_{12} level was 116 pg/ml (normal=200–900). A repeat level was 96 pg/ml. Folate levels were within normal limits. The EEG showed borderline slowing with intermittent 4–6-cycle/sec theta activity bicentrally. A Schilling test was positive; antibodies to both parietal cells and intrinsic factor were present.

Mr. A was treated with daily vitamin B_{12} replacement, 1000 μg i.v., for 1 week, then with weekly injections at the same dose. Haloperidol was tapered and discontinued during the first week of hospitalization. Mr. A returned to a completely normal mental status by the end of daily B_{12} replacement therapy. His serum B_{12} level at that time was 1054 pg/ml. Six months after discharge his mental status was still normal and he was receiving monthly B_{12} injections from his general physician. He had returned to full work activities. A repeat EEG at that time was entirely normal, and his vitamin B_{12} level was 3444 pg/ml.

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DISCUSSION

This patient's history fulfills the criteria for secondary mania insofar as the full manic syndrome was present and there was no coexisting delirium or prior history of affective disorder. Also, none of the currently recognized secondary causes of mania was present.

Although Mr. A's early improvement could have been related to factors other than B_{12} replacement, his continued clinical remission outside of the hospital while he was receiving B_{12} alone, coupled with complete normalization of his EEG, argues that B_{12} deficiency was the most likely cause of his psychiatric disorder. Although a literature survey produced no prior cases of the full manic syndrome secondary to B_{12} deficiency, this could be related in part to the nature of past diagnostic procedures, which tended to classify most excited psychotic states as schizophrenic rather than manic.

The most common psychiatric symptoms associated with B_{12} deficiency are organic mental syndrome, violence, paranoia, and depression (4). In a review of 15 cases that met specified criteria for B_{12}-responsive psychosis, Zucker and associates (4) noted that euphoria, grandiosity, and overactivity each occurred in 7% of the cases. Nevertheless, even their review, which was published after the adoption of *DSM-III* and the emergence of the concept of secondary mania, failed to present a case report in which the manic syndrome was fully present in the absence of delirium or recognized as the predominant pattern of abnormal behavior.

Although involvement of the CNS is common in B_{12} deficiency, this case emphasizes that psychiatric manifestations can occur in the presence of low serum B_{12} levels but in the absence of the other well-recognized neurological and hematological abnormalities of pernicious anemia. Evans and associates (5) recently reported two cases of patients with schizophreniform organic psychosis secondary to B_{12} deficiency. In both of their cases as well, no hematological or spinal cord abnormalities were observed and B_{12} replacement led to clinical remission. My case is different in that, unlike the patients in that report, Mr. A also had positive Schilling test and detectable antibodies to both parietal cells and intrinsic factor. Thus, the diagnosis of pernicious anemia was unequivocal in Mr. A's case.

This case not only adds B_{12} deficiency to the list of conditions that can present as a secondary manic syndrome, but it also supports other recent reports that psychiatric symptoms may antedate the other major manifestations of pernicious anemia.

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