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(Accepted 2 June 1977)

Typhoid catatonia responsive to ECT

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British Medical Journal, 1977, **2**, 357-359

Summary

Twelve patients with typhoid fever presented with a catatonic syndrome that persisted after other signs of the fever had disappeared. The syndrome was distinct from the delirium seen in typhoid fever and did not have the characteristics of an affective or schizophrenic illness. Electric convulsion therapy produced rapid and lasting improvement.

Introduction

Catatonia is often seen in schizophrenia, but it may also occur in the course of other diseases.¹⁻⁵ The many publications on typhoid fever, make only scant reference to its psychiatric manifestations. Thus Pathania and Sachar⁶ described 340 cases of enteric fever in Punjab. They mentioned delirium in the acute stages of the disease but gave no details of any other psychiatric complications. Gadeholt and Madsen⁷ described 2647 cases that occurred in Bergen over five decades, in which there was a 1% incidence of "psychosis," including paranoia, melancholia, hysteria, and delirium. Stuart and Pullen⁸ in New Orleans during 1939-44 reported that stupor occurred in the acute phase of typhoid in 72.8% of cases and that a "psychosis" persisted in 1.9% after all other evidence of the disease had passed. Osuntokun *et al*⁹ described the neurological complications of 959 Nigerian patients. Five had initially been diagnosed as schizophrenic and the diagnosis of typhoid was made later, either during their hospital stay or at necropsy, but there was no description of a catatonic syndrome persisting after the fever had subsided.

We cannot find any detailed description of persisting catatonia other than a single case described briefly by Bleuler.¹⁰ The patient, a physician, had "neurasthenia" at 29. At 31, after typhoid fever, he became catatonic. At 47 he was apparently "cured" and resumed his practice. He was well for the next two years.

In our experience a persisting catatonic syndrome is a fairly

common complication of typhoid fever, and we report 12 cases seen in India.

Present series

During 1974-6, 238 patients were admitted to the Christian Medical College Hospital with typhoid fever. Of these, 45 showed gross behavioural disturbances, which in 32 cases necessitated psychiatric examination. Though most of these patients had typical delirium, 12 presented with a catatonic syndrome that persisted after the fever had resolved and their physical condition had returned to normal. These 12 patients are the subject of this report.

Of the 12 patients, 11 were aged 17-24 years, and one was a 7-year-old (table). The slight preponderance of men was typical of admissions to the hospital, and they came from various socioeconomic backgrounds. All the patients were brought to the hospital because of high fever and behavioural change, in many cases insomnia and restlessness or excitement, and in others withdrawal, muteness, strange movements of limbs, or posturing. The duration of fever before admission varied up to 12 days. In most cases there were few definite physical findings apart from the fever. Two patients had moderate splenomegaly. In some cases pathogens were grown in blood culture, and in every case the Widal test gave a positive result. One patient underwent electroencephalography (EEG), which showed excessive diffuse slow-wave activity.

In most cases psychiatric examination showed a typical catatonic picture of withdrawal and mutism, which in several progressed to stupor, the patients being apparently awake and aware of their surroundings but unable to respond to spoken or written communication. Some patients were excited rather than withdrawn and reacted irritably or aggressively. In two cases excitement alternated with mutism and withdrawal, and many patients exhibited catatonic posturing and waxy flexibility. Volitional symptoms such as negativism and automatic obedience, were apparent in some patients but ambivalence and ambitendency were not seen. Clinical features of delirium were not observed; so far as could be ascertained the patients were orientated and aware of their surroundings and did not experience the frightening delusions and hallucinations that occur in delirium. They also denied alteration of mood.

In the first two or three cases phenothiazine alone had little or no effect. Electric convulsion therapy (ECT), however, produced a rapid response in every case in which it was used. In some cases three or four sessions were enough to obtain a remission, and no patient received more than seven. All patients improved, and most were completely recovered after two or three weeks.

Seven patients were followed up 6-24 months after discharge. All had maintained their improvement and were functioning normally. There had been no recurrence of symptoms and there was no evidence of a persisting psychiatric disorder. The following two cases are described in detail.

CASE 1

This 20-year-old man was admitted to hospital with a history of moderately high, continuous fever for two weeks and withdrawal and abnormal behaviour

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Details of patients with typhoid catatonia

Case No	Sex and age	Result of Widal's test	Psychiatric symptoms	Treatment	Response to treatment	Follow-up
1	M 20	<i>S typhi</i> 1/320; <i>S typhi</i> H 1/20; <i>S paratyphi</i> BH 1/80	Stupor; waxy flexibility; posturing	ECT × 3	Excellent	Completely normal at one year
2	M 23	<i>S typhi</i> 1/320	Withdrawal; stupor; waxy flexibility	ECT × 6	Great improvement	No psychiatric abnormality at 6 months
3	F 18	<i>S typhi</i> 1/320	Excitement; stupor; negativism	ECT × 4; chlorpromazine	Great improvement	Normal and active at 8 months
4	M 7	<i>S typhi</i> 1/320	Mute; stuporous	Chlorpromazine	Gradual improvement	Normal at 2 years
5	F 23	<i>S typhi</i> 1/320	Mute; posturing	ECT × 5; chlorpromazine	Improved	No abnormalities found at 15 months
6	M 19	<i>S typhi</i> 1/640	Mute; posturing	ECT × 5; trifluoperazine	Greatly improved	Psychiatrically normal at 1½ years
7	F 17	<i>S typhi</i> 1/640	Extreme withdrawal; periods of excitement; mute	ECT × 7	Full recovery	Psychiatrically normal at 14 months
8	M 21	<i>S typhi</i> 1/640	Withdrawal; posturing; negativism	ECT × 4; chlorpromazine	Full recovery	
9	F 24	<i>S typhi</i> 1/320; <i>S typhi</i> H 1/40; <i>S paratyphi</i> BH 1/20	Mute; withdrawn; periods of excitement	ECT × 5; chlorpromazine	Great improvement	
10	F 20	<i>S typhi</i> 1/320	Stuporous; waxy flexibility	Chlorpromazine	Gradual improvement	
11	M 18	<i>S typhi</i> 1/640	Mute; posturing; automatic obedience	ECT × 6; chlorpromazine	Excellent	
12	M 19	<i>S typhi</i> H 1/320; <i>S typhi</i> 1/40; <i>S typhi</i> BH 1/20	Extreme withdrawal; mute	ECT × 4; chlorpromazine	Great improvement	

for 10 days. He had never before had a psychiatric illness and was usually cheerful and well adjusted. There was no family history of psychiatric illness.

Physical examination showed nothing abnormal apart from a temperature of 40°C. He was noticeably withdrawn and posturing and was negativistic, responding to questions only occasionally. He was, however, fully orientated to time, person, and place. There were no delusions, hallucinations, thought disorder, or depression. Investigations showed: haemoglobin 13.5 g/dl; WBCs $6 \times 10^9/l$ (6000/mm³; neutrophils 55%, lymphocytes 45%); erythrocyte sedimentation rate (ESR) 24 mm in first hour; positive Widal test result (*Salmonella typhi* 1/320, *S typhi* H 1/20, *S paratyphi* BH 1/80); *S typhi* in blood culture; cerebrospinal fluid (CSF)—WBCs $2 \times 10^6/l$, protein 0.7 g/l, glucose 3.7 mmol/l (67 mg/100 ml), chloride 131 mmol(mEq)/l; and excessive slow-wave activity on EEG.

The patient was treated with chloramphenicol and his temperature became normal after one week. His withdrawal, posturing, and negativism, however, persisted. Over the next week three ECT sessions were given. There was a rapid response and he became progressively more communicative. Three weeks after admission he was normal except for a slight deficit of recent memory, which was attributed to ECT. One year later there was no evidence of any psychiatric abnormality.

CASE 2

This patient, a 23-year-old man, had had high fever, insomnia, and withdrawal for one week. There was no personal or family history of psychiatric illness. Examination disclosed an enlarged spleen and a temperature of 39°C. He was unkempt and withdrawn and exhibited posturing, waxy flexibility, and negativism, answering only when questioned repeatedly. He was fully orientated, his memory was intact, and there was no evidence of depression, delusions, or hallucinations. Investigations showed: haemoglobin 12.5 g/dl; WBCs $8 \times 10^9/l$ (neutrophils 51%, lymphocytes 49%); ESR 27 mm in first hour; CSF—no WBCs, protein 0.25 g/l, glucose 4.2 mmol/l (75 mg/100 ml), chloride 130 mmol(mEq)/l; and positive Widal test result (*S typhi* 1/320).

The patient was given chloramphenicol and betamethasone and became afebrile, but the psychiatric symptoms persisted until 10 days later when ECT was started. Six ECT sessions were given over two weeks with good results, and four weeks after admission he was communicative and did not show any psychiatric abnormality. Six months later he was completely asymptomatic.

Discussion

Muhangi¹¹ emphasised the importance in developing countries of recognising the association between organic and psychosocial factors in patients with psychiatric syndromes and reported four cases in which typhoid fever was associated with various psychiatric conditions. Our findings emphasise that delirium is not the only psychiatric manifestation of typhoid but that a catatonic syndrome may also occur that might easily be misdiagnosed as schizophrenia but responds well to treatment and has an excellent prognosis. Lengthy psychiatric hospitalisation is not required, but unrecognised and untreated it may persist for many weeks or months.

In the several reports of catatonia in acute brain disorders¹⁻³ the syndrome has occurred merely as part of a neurological

condition, with EEG abnormalities, seizures, or a delirious reaction that subsides with treatment of the underlying disease. Delirium occurs in typhoid as in any other acute fever, but it was not seen in our patients. The only evidence of neurological disorder was excessive slow-wave activity in the EEG in one patient. EEGs were not obtained in the other patients, and further research should include more exacting evaluation of the central nervous system. Nevertheless, also contrary to what is generally found in delirium, the catatonic syndrome persisted for long after the fever had subsided, liver function had returned to normal, and the patients' physical condition had apparently recovered.

We considered the possibility that our patients were in a depressive stupor. Catatonic stupor and the psychomotor retardation seen in severe depressive illnesses may be difficult to distinguish, and the response to ECT was similar to what might be expected in depression. There was, however, a striking lack of evidence of prior psychiatric illness in these patients and their families, and there was no evidence of any primary disturbance of mood. It would be of great theoretical interest if we could document a "symptomatic schizophrenia" related to typhoid. Eugen Bleuler described the condition of his patient, referred to above, as acute schizophrenia, but he included in this category many patients whom other psychiatrists would not call schizophrenic. In some ways our patients resembled schizophrenics: they were young, and their catatonic syndrome was similar to that seen in schizophrenia. There were none of the first-rank symptoms described by Schneider,¹² however, nor were there delusions, hallucinations, or any disorder of thinking or affect that is generally associated with schizophrenia. We were unable to conclude that typhoid catatonia represents a symptomatic schizophrenia or that it represents a true schizophrenic illness precipitated in susceptible people by severe physical illness.

Though ECT was dramatically effective, this does not help in defining the psychopathological basis of the syndrome. Good responses to ECT are expected in depressive illnesses and have been reported in schizophrenia. Roth and Rosie¹³ reviewed the use of ECT in various symptomatic and exogenous psychoses, including delirium. They pointed out that, because ECT is apparently therapeutic in such a wide variety of psychiatric disorders, its mechanism of action must be non-specific and so does not permit the formulation of any clear aetiological hypotheses in specific mental illnesses.

Published data on the catatonic syndrome in typhoid fever may be lacking because typhoid has been most extensively studied by physicians to whom psychiatric complications have been of secondary interest or because in developing countries, where it now most commonly occurs, systematic psychiatric

education has been neglected until recently. Parry¹⁴ suggested that catatonia may be a modern complication of typhoid fever in patients who have been effectively treated. Similar patients in an earlier era might well have died.

Ours was a selected group of patients referred because of the severe and unusual nature of their illness. Nevertheless, typhoid catatonia cannot be considered a rarity, and its recognition by physicians and psychiatrists is clearly important for effective treatment.

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(Accepted 30 March 1977)

Bleeding in renal failure: Is von Willebrand factor implicated?

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British Medical Journal, 1977, **2**, 359-361

Summary

Normal or increased concentrations of factor VIII procoagulant activity (VIIIc), factor VIII-related antigen (VIIIra), and factor VIII-von Willebrand activity (VIIIvWF) were found in the predialysis plasma of 10 out of 11 patients with chronic renal failure (CRF). All patients had a bleeding time longer than 15 minutes and platelet retention to glass beads lower than 40%. The only patient who had reduced concentrations of all three factor VIII complex components was subsequently shown to have von Willebrand's disease. In four patients with CRF, very low platelet retention, and slightly prolonged bleeding time none of the three factor VIII complex components were selectively modified in predialysis samples.

These findings suggest that the bleeding tendency common in CRF is not necessarily linked to defective plasma factor VIII-related activities.

Introduction

Uraemia is often complicated by a haemorrhagic diathesis. Extensive investigations have failed to identify with any certainty the cause of bleeding in chronic renal failure (CRF).¹⁻³ Different defects of platelet function described in patients with CRF have been attributed to one or more of the metabolites abnor-

mally accumulating in uraemic plasma.³⁻⁵ Nevertheless, platelet function values are often unchanged after dialysis and the usually prolonged bleeding time is only occasionally shortened, though results have varied.⁶⁻⁸

Recently Kazatchkine *et al*⁷ found a reduced amount of von Willebrand factor (ristocetin cofactor; VIIIvWF) in the plasma of patients with CRF and suggested that this was a possible cause of bleeding in this condition. The finding is of interest in view of the general opinion that VIIIvWF is necessary for controlling skin bleeding time and for normal platelet retention on glass beads.⁹⁻¹¹ Kazatchkine *et al* did not find that VIIIvWF concentrations were increased by dialysis.⁷

As part of a broader study on the causes of bleeding in CRF,⁸ we investigated VIIIvWF and the other factor VIII complex components (factor VIII procoagulant activity (VIIIc) and factor VIII-related antigen (VIIIra)) in a selected group of patients on long-term haemodialysis who had very prolonged bleeding times and very low platelet retention.

Patients and methods

Eleven patients with CRF (due to chronic glomerulonephritis in 10 and chronic pyelonephritis in one) who had been undergoing maintenance haemodialysis for one month to eight years were studied immediately before a routine dialysis—that is, 68 hours after the end of the last dialysis. These patients had bleeding times longer than 15 minutes and platelet retention on glass lower than 40% on several occasions before this study. The individual values obtained when blood was collected for factor VII measurements are shown in the table. Platelet counts were repeatedly found to be normal in each of these patients (range 170-300 × 10⁹/l).

Blood samples before dialysis were also obtained from four non-thrombocytopenic patients with CRF (chronic glomerulonephritis in three and chronic pyelonephritis in one) who had platelet retention lower than 40% but only slightly prolonged bleeding times (3 minutes 30 seconds to 5 minutes 45 seconds). The 15 patients with CRF were all receiving 12 m² hours per week of haemodialysis in thrice weekly sessions. The dialyser used was the Coil Kidney with cuprophane membrane. Blood flow was more than 300 ml/min and water flow was 500 ml/min.

Ten normal subjects (four women and six men aged 20-46 years) were also studied. Their bleeding times ranged from 2 minutes 30 seconds to 3 minutes 30 seconds, and they retained 56% to 98% of platelets on glass beads. The bleeding times in 30 normal subjects

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