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Case Conference

Changing Interactions Between Bipolar Affective Disorder and Anoxic Brain Damage

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A manic-depressive young woman received mild brain damage from anoxia after attempting suicide by hanging. The case conference was held to elucidate whether her subsequent symptoms were functional or organic, and what courses of treatment should be tried in this very refractory case.

Objectives

This is a report of a case conference in neuropsychiatry held at the Institute of Psychiatry on 17 November 1988. The case illustrates the difficulties of distinguishing the relative importance of interacting neurological and psychiatric abnormalities in a patient who has both, but in whom communication is impaired. The conference was asked to help the presenters come to diagnostic and therapeutic conclusions. The case also illustrates the strengths and weaknesses of modern neurological investigative techniques.

Presentation of case

Miss A, an 18-year-old single Caucasian student, was admitted to her catchment area general psychiatric hospital on 13 February 1988, under Section 2 of the Mental Health Act 1983, with mania. Her symptoms had escalated over several days, having been preceded by an episode of depression. Her illness proved difficult to treat despite appropriate use of neuroleptics and lithium. During the month after admission she became severely depressed, then manic again after tricyclic antidepressants were started, and then again depressed. Electroconvulsive therapy (ECT) was commenced, but after the third treatment she attempted suicide by hanging herself from a shower rail with her dressing-gown cord, on 15 March 1988. When found, she was pulseless and cyanosed, with dilated pupils, but she was rapidly resuscitated by an experienced medical team from the general medical wards. The maximum time she had been unobserved was ten minutes, so her anoxia would have been relatively brief.

Following a few days in intensive care, she was taken via a general medical ward to a neurological unit, where she was admitted two months after the hanging. Her persisting problems were mutism, dystonia, dyspraxia, urinary incontinence, and poor self-care. She was assessed for rehabilitation but considered unsuitable because of "manipulative behaviour" (reflecting, we suspect, variability in performance of tasks) and lack of motivation. She was then transferred to a psychiatric unit three months after the hanging attempt. Although psychiatric staff did not observe significant depression, noting normal sleep and appetite, and the absence of diurnal variation in behaviour, they started her on tricyclic antidepressants, without apparent benefit. She was transferred for a neuropsychiatric assessment on 1 September 1988, nearly six months after the hanging, to address the question of therapy in the light of the relative importance of neurological and psychological factors in her presenting condition.

Family history

Her mother, aged 45, has a history of recurrent depression, requiring hospital admission once in the past. A paternal aunt in Ireland has been diagnosed as schizophrenic, and her maternal grandfather is said to have had 'emotional difficulties' after World War II. Her elder sister is depressed and treated with a tricyclic antidepressant, although she has never been admitted, and a younger sister is reported as being depressed with difficulty coping at school.

Both parents are Catholics of Irish origin, but have lived in England since marriage. The father, aged 47, is a buildings officer, who works at the hospital where his daughter hanged herself. Miss A has always been the 'apple of her father's eye', as 'near perfect as a daughter could be'.

Personal history

Birth and developmental milestones were unremarkable, and childhood was happy. She was very intelligent, obtaining 13 'O' levels, and she was studying for 'A' levels with the intention of going to university to read law. She performed badly at interview for the University of Cambridge, was rejected, and became depressed, this being the first hint of psychiatric difficulty. Four months later she was admitted to hospital, as described.

She had no history of drug or alcohol abuse. Premorbidly she was hard-working, conscientious, reasonably outgoing, at times stubborn. She had male friends but no special boyfriend.

Present condition

Miss A was co-operative and able to follow simple commands, although, left to her own devices, she tended to sit or lie and do little. She was episodically incontinent of urine. Every few minutes she grimaced, closing her eyes

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tight shut and pouting, and often turned her head fully to left or right for a few seconds. She then returned to normal eye contact. Her speech was almost non-existent, with occasional (appropriate) one-word or two-word replies to questions. Her mood was very difficult to assess. Her face was usually expressionless; there were no obvious biological disturbances, nor was she overactive or tearful. Nothing suggested she was having psychotic experiences. Cognition was also hard to assess. On the rare occasions she had answered questions, she had sometimes been orientated in time and place, sometimes not. She knew her birthdate and could write her name and address on request. Memory was otherwise untestable. She had a severe defect in initiative and marked difficulty with dressing, eating and washing.

Physical examination

General examination was normal. In the neurological examination, cranial nerves (as far as these could be tested), muscle tone, power, reflexes, and plantar responses were all normal, as was fundoscopy. She had a movement disorder characterised by pouting movements of the lips, choreiform and dystonic movements of the hands, especially when accompanying normal tasks such as shaking hands. She exhibited forced blinking and had choreiform movements affecting orbicularis oculi bilaterally, suggesting blepharospasm.

Her gait was wide based and accompanied by dystonic arm and hand movements. She had general incoordination. Some movements appeared manneristic. She showed a disorder of visuomotor co-ordination and range-finding such that she could perform the finger–nose test when the examiner's finger was in front of her, but not when pointing laterally; when going through a doorway or sitting in a chair, she felt for the outlines with her hands before passing through or sitting down, as if unable to localise them in space otherwise. The blink reaction to visual threat was absent. Frontal lobe examination was impossible. She exhibited no cortical release reflexes.

Investigations

Routine biochemical and haematological investigations were normal. She had had three electroencephalograms (EEGs). On 28 March 1988 (two weeks after the hanging) there was generalised slowing (2–4 Hz) over both hemispheres, with no response to auditory stimuli, suggesting a prominent anoxic disturbance. On 24 May 1988 the record had improved, and showed irregular activity at 7–8 Hz, with slowing over the right hemisphere. On 30 September 1988 there was rhythmic activity at 9–10 Hz, although often 6–7 Hz, with runs of irregular theta activity in the left temporoparietal area, generalised episodes of sharp waves, and some sharp forms in the right temporal area; this was abnormal.

Computerised tomography (CT) of the brain on 10 July 1988 showed mild prominence of the sulci frontally, and the left Sylvian fissure was wider and deeper than normal. Single-photon emission computerised tomography (SPECT) on 20 September 1988, using technetium-labelled HMPAO, was normal. Magnetic resonance imaging (MRI) on 1 November 1988 was initially reported as normal, but on review was thought possibly to show slight cortical atrophy, especially frontally, and the basal ganglia were darker than normal, suggesting iron or calcium deposition, as may be seen in Hallervorden–Spatz disease.

Interview

An edited video of Miss A, made on 13 October 1988, was shown. Also present were Miss A's mother and a family friend.

DR JACOBSON (*consultant neuropsychiatrist*): Sit down in the middle chair.

Miss A does so, feeling the outlines before sitting in the chair.

DR JACOBSON: Can you tell me how you are?

Miss A looks around, stares, blinks, and grimaces.

DR JACOBSON: Can you point at the camera?

Miss A does so.

DR JACOBSON: Point to your mother.

Miss A does so.

DR JACOBSON: Pick up a pen off the table.

Miss A does nothing. Dr Jacobson repeats the instruction.

Miss A does nothing.

DR JACOBSON: Point to the pen.

Miss A picks up the pen.

DR JACOBSON: Put the pen on the yellow paper.

Miss A turns her head and grimaces. Dr Jacobson repeats the instruction three times. She finally obeys the instruction.

Dr Jacobson holds up a piece of paper with the written instruction "Clap your hands". Miss A looks at the paper, sighs, grimaces, looks at her mother, yawns, then eventually whispers "Clap your hands".

DR JACOBSON: Can you put your arms out in front of you?

Miss A does nothing, despite several repetitions of the instruction. Dr Jacobson initiates the motor act by lifting Miss A's left arm. She holds both arms out.

DR JACOBSON: How are you feeling?

Miss A stares vacantly.

DR JACOBSON: Good or bad?

Miss A does not respond.

DR JACOBSON: Can you pick up the small piece of paper and give it to your mother?

Miss A does nothing. Dr Jacobson repeats the instruction, and with no response from Miss A, initiates the required movement. She performs the task once the movement has been initiated.

DR JACOBSON: Can you write your name on the paper?

Miss A writes her name legibly, then adds her address and telephone number.

DR JACOBSON: Can you do up the buttons on your jumper?

Miss A does nothing. Dr Jacobson repeats the instruction several times with no response, then initiates the required movement by placing Miss A's hand on the button. She performs the action well, once the movement has been initiated.

DR JACOBSON: We have finished now; you can get up and go.

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Miss A remains seated. Dr Jacobson pushes lightly to initiate the movement. She gets up and walks out of the room.

Progress

While on the ward, considerable variability in Miss A's functional abilities was noted. On some days she did little for herself, requiring assistance to eat, dress, wash, and go to the toilet. On other days she was much more able to do these things for herself. There was no detectable pattern to this. Her speech had always been confined to one-word or two-word utterances, which were infrequent. In view of the possibility of underlying depression, masked by her neurological status, we started treatment with antidepressants. We chose protriptyline because of its potentially alerting properties, and she was able to tolerate maximal doses.

On 20 October 1988, the ward charge nurse reported the observation that Miss A's pupil size exhibited bursts of rapid changes, showing marked dilation and constriction against constant illumination, and that Miss A appeared intermittently not to be paying attention. This observation was confirmed by medical staff. At this point we decided that there was sufficient evidence for a seizure disorder to warrant a trial of anticonvulsants. Until now we had been advised by our neurological colleagues that Miss A had no evidence of seizures. We, however, felt that partial complex seizures of frontal lobe origin could explain some of her symptoms; we therefore prescribed carbamazepine.

Within a week there was a dramatic improvement in her performance. She was much better at eating, dressing, washing, and going to the toilet, and there was virtual resolution of grimacing, pouting, blinking, and head-turning. The pupillary changes were no longer observed. Her speech also improved, with more frequent utterances involving sentences of up to eight words, grammatically and contextually appropriate. All these observations were made as objectively as possible, using a specially designed form. This form broke down aspects of daily living into component parts, allowing a score for each component, depending on the degree of independence of task completion. Thus "Getting up/Washing" had 21 separate components, each of which was scored. The improvement in total scores following the introduction of carbamazepine was obvious and convincing.

This improvement lasted three weeks, but her performance then began to fall off in a very different way. She became overtly depressed, looking sad, crying at times, and saying on more than one occasion "I feel dead". Although her performance on the rating scale deteriorated, there was no return of grimacing, pouting, blinking, head-turning, pupillary changes, or episodic loss of attention; the slight improvement in frequency and quantity of speech was sustained. Most recently she had begun to refuse food and drink.

Conference discussion

DR COLLINS (*lecturer in psychiatry presenting case*): Miss A has a severe bipolar affective disorder which was difficult to treat. As a result of anoxic brain damage she has dementia with some frontal lobe features. She also temporarily had symptoms consistent with ischaemic dysfunction in the watershed zone between the posterior and middle cerebral artery territories, namely the visual range-finding abnormalities. This had been labelled hysterical. She also has dystonia, associated with MRI abnormalities in the basal ganglia.

We are unsure to what extent her current state is 'neurological' or 'psychological'. Although there is a very strong organic 'feel', the investigations show only slight abnormalities. To what extent does a continuing mood disorder affect her performance? Is it possible that the suicide attempt incidentally ameliorated the mood disorder?

We would propose that she has been suffering from partial complex seizures, of frontal lobe origin, possibly for months, and that her dramatic response to carbamazepine reflected treatment of this, with the unfortunate consequence that her mood disorder paradoxically worsened.

DR JANOTA (*consultant neuropathologist*): May I first comment on the MRI scan? I have discussed this already with Dr Hoare [consultant neuroradiologist], who has seen the films. The diagnosis of Hallervorden–Spatz disease is impossible on the basis of the scan alone. In that condition there is iron deposition in the basal ganglia, associated with dystonia. However, the onset is in childhood, and we have heard no evidence of any problems until after the hanging attempt.

DR COLLINS: We too discounted Hallervorden–Spatz disease. I would be interested to know whether the appearances, implying iron or calcium deposition, could result from an anoxic episode eight months previously.

DR JANOTA: The basal ganglia are vulnerable to anoxic damage. I do not know precisely what changes would be expected eight months after an anoxic episode, but it seems likely that anoxia is the cause of the scan findings in this case. I am not dissuaded by the minor abnormalities on the scans from suspecting severe anoxic brain damage in this patient. Anoxic lesions, in my experience, may be widespread, causing severe neurological dysfunction (in this case dementia) without producing much change on CT or MRI scans.

DR ELWES (*senior registrar in neurology*): I agree that the abnormality in the basal ganglia is a result of anoxia. The abnormality correlates with the clinical picture of dystonia. I am not, however, at all persuaded by the arguments for frontal lobe seizures. I think that everything described by you and shown on the video represents dystonia. The EEG does not provide evidence for an ictal disturbance, although EEG telemetry would be a better way of assessing this. If others thought seizures likely, then telemetry might be worth doing, but I do not think you have made a sufficient case.

DR COLLINS: How do you explain the response to carbamazepine?

DR ELWES: As well as being an anticonvulsant, carbamazepine is also used in affective disorders and probably has a non-specific psychotropic effect. More particularly it is used in paroxysmal dystonias in childhood. I think

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her improvement in praxis represents removal of the impairment her dystonia was causing.

DR JACOBSON (*chairman*): What about the more general question of brain damage?

DR ELWES: I think she has evidence of anoxic brain damage clinically, in the form of dysphasia, dyspraxia, and frontal lobe symptoms such as lack of initiative and urinary incontinence. I am surprised that there is nothing more dramatic on the scans.

DR REVELEY (*consultant psychiatrist*): I am very struck by the severity of her bipolar affective disorder. Am I right in thinking that this was so before the hanging?

DR COLLINS: Yes, this is documented in the case notes. She received very large doses of neuroleptics, lithium, and antidepressants, but remained psychotic and behaviourally disturbed. This was why ECT was started.

DR REVELEY: I think it is possible that affective disturbance is more important than at first appears. Obviously the issue of epilepsy needs to be resolved and I feel that it would be reasonable to perform EEG telemetry. If there is no evidence in support of frontal lobe epilepsy, then I think her depression should be vigorously treated. In the face of failure of tricyclic antidepressants, I would recommend ECT.

PROF. LISHMAN (neuropsychiatrist): As this case unfolded, I thought we were going to hear an account of a predominantly psychiatric disorder, with a finale of successful response to psychiatric treatment. I am therefore surprised at the more 'neurological' direction the presentation has taken, and have to say that I disagree with this emphasis.

I have seen several patients with evidence on scans of severe brain damage who perform much better than Miss A in their speech, praxis, communication, and movement. I believe Miss A has at most mild to moderate brain damage. I am struck that the CT scan might even be passed as normal, although I accept the balance of expert opinion that there is probably mild cortical atrophy. Similarly the MRI scan is remarkable for the lack of abnormality, apart from in the basal ganglia. I think it is most unlikely for her to have severe brain damage without there being more to see on the scans.

When I saw the video, I was struck by Miss A's posture, with slumped shoulders and head bowed forward – the picture of dejection. I think she is severely depressed and that this is the major reason for her severe functional deficits. I would recommend a course of ECT with some urgency, in view of her recent refusal of food and drink.

Regarding Dr Collins' interesting suggestion of a diagnosis of frontal lobe epilepsy, I remain unconvinced. I do not know the significance of varying pupil size in patients with anoxic brain damage, but do not think it provides evidence of seizure activity in the absence of other paroxysmal clinical features. I would also expect evidence of epilepsy on the EEG. I agree with Dr Elwes that she is displaying typical dystonia, and that her beneficial response to carbamazepine does not result from its anticonvulsant action.

If this strategy is not successful, I might consider abreaction.

DR COLLINS: We did in fact perform abreaction on Miss A, although I omitted it from the presentation. Under intravenous diazepam Miss A was able to communicate occasional appropriate 'Yes' 'No' answers. She said her name, but little else. At one point she made a joke, referring to the fact that a nurse had the same first name as she did; when the nurse said "I am called A too", Miss A pointed at a third nurse and, with a smile, said "A three". While under abreaction, there was no grimacing, pouting, or other abnormal movement. No further information was obtained.

PROF. LISHMAN: My final suggestion, if ECT fails to produce a good response, is to consider using L-dopa. Some patients with frontal lobe symptoms, especially lack of initiative, may respond to dopaminergic stimulation.

DR JACOBSON: We have considered using bromocriptine, but are worried about possible side-effects, particularly on Miss A's dystonia.

DR BINNIE (*consultant clinical neurophysiologist*) was unable to be present at the conference, but he subsequently watched the video, having noted the comments of other participants in the discussion. He made the following comments:

A very wide range of ictal phenomena can occur in epilepsy of frontal lobe origin, and some of these are so bizarre as to invite a psychiatric explanation, notably bimanual, bipedal seizures with hand-clapping, stamping, rocking, and pelvic thrusting, etc. However, the pouting, grimacing, and blepharospams shown do not fall within the range of bizarre behaviour commonly seen with mesial frontal seizures, and seem more readily explicable as part of this patient's more general movement disorder. I do not know the significance of the rapidly fluctuating pupil size in this context, but it would not appear particularly suggestive of epilepsy. A response to carbamazepine, as seen here, often confuses rather than clarifies the differential diagnosis between epilepsy and a psychiatric disorder, because of its known psychotropic effects. The lack of epileptiform activity in the interictal EEG contributes little to the diagnostic assessment; patients with seizures of mesial frontal origin often exhibit no interictal EEG abnormality and, indeed, ictal changes are often confined to brief runs of generalised slow activity, the significance of which may be overlooked unless simultaneous video recording is performed.

I do not, therefore, think there is evidence that this young woman has epilepsy, but if the matter is sufficiently in doubt, it could be resolved by capturing some of the supposed ictal episodes during EEG and video telemetry.

Summary

Before the conference, the presenters considered that the aetiology of this patient's symptoms was more organic than functional. Although there was some disagreement among the discussants, the conclusion was that we should reconsider the possibility of a strong functional component to several of the symptoms. Our proposal that partial complex

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seizures of frontal lobe origin might explain some of the symptoms and signs was rejected.

Overall, we feel that this case illustrates the complexity of understanding what is happening where neurological and psychological symptoms coexist, particularly when verbal communication is so limited. The clinical management was extremely difficult, and although the case conference engendered several ideas on how to proceed, clear-cut answers were not immediately apparent, nor did the passage of time clarify the issue (see Addendum).

Addendum

As a result of the conference's recommendations, and because Miss A continued to refuse most food and drink, a course of bilateral ECT was started, comprising ten treatments over five weeks; carbamazepine was stopped, Miss A's mood lifted, and she again began to eat and drink, smile appropriately, and look after herself reasonably well. She hardly spoke at all however, and her dystonia recurred.

While awaiting admission to a neurological rehabilitation unit for physiotherapy and speech therapy, she became disturbed over Christmas and New Year. She became very restless and overactive, pacing and sometimes running around the ward, occasionally leaving the premises.

She slept very little and was at times sexually disinhibited, masturbating openly on the ward. We diagnosed mania. Despite progressively larger doses of neuroleptics (droperidol, up to 240 mg per day) and the addition of lithium carbonate (to a serum level of 1 mmol/l), her mania proved extremely difficult to control. We also tried less established treatments such as the addition of clonazepam, to no great effect.

By February 1989, she was on high doses of psychotropic drugs; self-care was very poor, and she was mute. We felt unable to assess her mental state accurately, and therefore withdrew all medication over two weeks. She then revealed (a) over-activity, minimal sleep, and occasional inappropriate behaviour, (b) relapse of dystonia, and (c) bursts of rapidly varying changes in pupillary size accompanied by a failure to pay attention to others. Reintroduction of carbamazepine and droperidol produced improvement in all three sets of abnormality, although her mood improved to a level no better than that following her course of ECT.

To complicate matters further, Miss A's younger sister became suicidally depressed and was admitted to another hospital. As the anniversary of Miss A's suicide attempt approached, the younger sister became increasingly ill, manifesting near mutism and refusal to eat and drink, with occasional episodes of bizarre posturing; her behaviour closely mirrored that of Miss A.

Presently both sisters remain in-patients, and the entire family has been engaged in family therapy. There has been no significant change in Miss A's condition over several months.

Theoretical note

The literature on the effects of non-fatal hanging is not extensive. Our patient clearly suffered a degree of brain damage, confirmed by the EEG evidence and by the more sophisticated brain scans. However, the degree of functional impairment was not matched by scan abnormalities. Our patient illustrates how difficult it can be to assess the contribution of functional illness to the overall picture in the presence of neurological dysfunction, especially where communication is impaired. Some features of behaviour may be labelled 'hysterical', when they in fact derive from organic disorder. For example, the visual range-finding difficulties, well described by Howard *et al* (1987) as deriving from lesions in the watershed zone between posterior and middle cerebral artery territories, were initially thought to be related to psychiatric disorder.

Partial complex seizures of frontal lobe origin may present with a range of bizarre behaviour (Quesney, 1986; Delgado-Escueta *et al*, 1987). The presenters were impressed by this possibility, and the combination of observations on pupil reactions and response to carbamazepine seemed to provide support to the idea that at least some of Miss A's behaviour might be epileptic activity. However, the conference rejected this suggestion.

Finally, we note that despite sophisticated neuroradiological investigations, there remained uncertainty as to the relative contribution of psychological and neurological factors to the behavioural dysfunction of Miss A.

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