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Case Conference

Resistant Bipolar Disorder

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A 66-year-old farmer's wife had been admitted 31 times over eight years, suffering from manic depression. A variety of treatments for depressive episodes led to hypomania, and a case conference was held to discuss treatment.

Affective disorder is generally considered to have a reasonably good immediate prognosis, with episodes of illness and various prophylactic regimes maintaining euthymia. It can prove frustrating for both patient and physician when euthymia proves impossible to sustain. We present a record of a case conference held on 4 May 1988 in Royal Cornhill Hospital, Aberdeen, to discuss such a case.

As part of the Grampian Rotational Training Scheme in Psychiatry a case conference is held each week. The aim is to discuss cases of educational and clinical interest, and the conferences are attended by members of the university department, consultants, junior staff, psychologists, students, and other professionals connected with the case. The chair rotates through various consultants. The format usually consists of a case presentation, an interview with the patient (either live or on videotape), followed by discussion.

Objectives

The principal aims of the conference in question were to consider the treatment efficacy to date, and to suggest future treatment possibilities for a lady with treatment-refractory manic–depressive illness.

Presentation of case

Psychiatric history

Mrs G is a 66-year-old married lady whose first presentation to the psychiatric services was in 1954 with a diagnosis of puerperal depression after the birth of her first child. She had incised her abdomen and perforated her small and large bowel with a pair of scissors. She responded well to electronculsive therapy (ECT). She was again admitted and responded to ECT following the birth of her second child in 1955. The birth of her third child did not precipitate a recurrence, and there was no further contact with psychiatric services until 1973, when she was admitted in a hypomanic state. She had three admissions in 1973 and was commenced on lithium. She had a brief admission in 1978, a two-month admission in 1979, then 31 admissions over the next eight years, usually lasting one or two months.

In 1980 she was commenced on flupenthixol (1 mg b.d.) for 18 months. In 1983 she was commenced on carbamazepine for one year; this was discontinued after a number of falls and a Colles' fracture. Lithium was restarted in 1984, and in 1985 carbamazepine was reintroduced in combination, but discontinued after more falls. Carbamazepine blood levels were 7–10 mg/l and lithium 0.2–0.9 mmol/l. She has been on thyroid replacement therapy since 1981. Episodes of depression have been treated with a variety of antidepressants: amitriptyline, nortriptyline, dothiepin, clomipramine/L-tryptophan/lithium combination, and ECT. These were usually discontinued shortly after improvement, owing to the onset of hypomania.

Admissions were usually preceded by a period when the patient would remain in bed, sometimes for eight weeks, and occasionally they would be preceded by overactivity and irritability. Between admissions her mood is not stable; most of the time she is reported to be depressed, doing very little for herself, then there are sudden episodes when she will arrange everything, talk to everybody, and drive around the countryside (occasionally deliberately on the wrong side of the road). When hypomanic she often makes extravagant suicide threats, although there has been only one recent parasuicide, by overdose, in 1982. There is no suggestion of abuse of alcohol or any other drug.

Personal history

Mrs G was the second of five siblings. Her father was a farmer and she has lived all her life in the farming community of Aberdeenshire.

She had an unremarkable birth, infancy, and childhood. She reports that she was a happy child and an average scholar, leaving school at the age of 16 to work on the family farm. She was engaged briefly at the age of 20, but remained with her parents until marrying her present husband (also a farmer) at the age of 30. It appears that her marriage was at first happy and stable, but naturally it has been considerably disrupted by her many years of mental ill health.

During periods of well-being, she has worked as a 'farmer's wife', coping well. She has one son, who lives at home and will take over the farm when Mrs G's husband retires, and two daughters, one of whom lives on a nearby farm and one who is a nurse.

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Family history

Her father committed suicide by hanging at the age of 53, when Mrs G was 16. He had not had contact with psychiatric services. Her mother died aged 57 from heart disease. Her elder brother died in 1985 in a long-stay psychiatric ward. He was diagnosed as schizophrenic.

Previous medical history

The only medical history of note is hypothyroidism, treated with thyroxine since 1982. Other blood parameters are within normal limits, and there is no evidence of neurological abnormality on physical examination.

Pre-morbid personality

Mrs G was described as friendly, capable, and intelligent, an 'ordinary housewife' who managed the farm finances competently. Now her husband reports 'endless swings', with only two months of near normality in the past two years.

Mental state examination

Mrs G's mental state obviously fluctuates greatly. She looks rather older than her years, but has no abnormal movements or mannerisms. On the day of the conference she had just returned from a visit home and was mute but fully conscious; she was eating nothing, drinking only with persuasion, and refusing medication. At times she becomes preoccupied with her financial situation (which is healthy), but she has not suffered from frank depressive delusions. Hallucinations have not been documented. Recent testing has not uncovered any deficits in her cognitive functioning.

Interview

The interview was recorded on videotape two weeks before the conference. At that time Mrs G had been in hospital for 15 weeks and had been treated with lithium and thyroid replacement. She had stopped her lithium before admission. During her admission she had slowly improved. The following comprises excerpts shown to the case conference.

DR THOMAS (*registrar in psychiatry presenting case*): How old were you when you first had difficulties?

MRS G: The first time that I can mind was when my son was born, antenatal depression or something, but I dinnae mind a'thing about it.

DR THOMAS: How old would you have been?

MRS G: Just over 30; 32 or so.

DR THOMAS: Had you had any problems with taking to your bed before then?

MRS G: No, this taking to my bed wasn't to start with, it was after a while.

DR THOMAS: So after your son was born you went into hospital for a bit but you can't remember a lot about that.

MRS G: No, I cannae mind. I was in the infirmary at first, then I was in Kingseat, but I cannae mind a lot about it; there's a lot of years I cannae really remember a lot about. The girls going to school – it must have been when the girls were old enough to start getting the meals that I started going to my bed.

DR THOMAS: Can you remember what you were like at the time you came into hospital this time?

MRS G: Dr McCance [the patient's consultant] she said, "You're on the go again".

DR THOMAS: I know that in the past you've had times when you've been on the go too much, and other times when it's been the opposite problem. Do you notice the difference between the two?

MRS G: I ken myself that I go like that, but I don't think I realise that I'm going too much, as I say when I'm doing too much, I've nae feelings for anybody. My husband's inclined to tell me that I can tell a'body what to do, and I suppose that's right enough because he doesn't say things that aren't true.

DR THOMAS: When you're feeling down, do you tell people what to do then?

MRS G: No, no, I'm not telling then, I maybe think, just lying there. If you're just lying there for weeks, your thoughts are nae right thoughts, something comes up, and it's all out of proportion, and I suppose sometimes I dinnae drink enough or eat enough, and I come in here not feeling well because I've not been eating or drinking and that's why I say it's maybe up to myself to do more. Mercy, Dr McCance has done a'thing she knows.

DR THOMAS: What's the longest length of time you've been in hospital?

MRS G: This time. This is about three months – I don't think I've been in that long.

DR THOMAS: And over the past two to three years, what's the longest length of time you've been at home?

MRS G: Let's see, maybe a month, something like that; a month functioning properly, and then weeks in my bed. I think if I remember right Kathy Urquhart [the community psychiatric nurse] said I'd been eight weeks in bed. My husband just left me there. Well I dinnae ken. I suppose I was ill.

DR THOMAS: Say five or six years ago, were you keeping better then?

MRS G: Aye, aye.

DR THOMAS: As you know, one of the things we're having to think about is how we can keep you well for longer than a month, and, as you say, the time you're keeping well for seems to be getting shorter. Have you any ideas yourself?

MRS G: No. I think it needs to come from myself, kind of control myself better, and if I see something that bothers me, dinnae let it bother me, leave the rest of them alone. You ken what I mean? They've their own worries and let them alone. Just try and keep myself on an even keel.

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DR THOMAS: I know Dr McCance has mentioned the idea of an operation, a brain operation. Have you had any thoughts on that?

MRS G: It's an awfy thought. Ach, I'm 66, and no, I dinnae think so. I'd like to do it more myself.

Conference discussion

DR OSWALD (*chairman, consultant psychiatrist*): Are there any comments on the video? There was one thing that struck me – when she was well she had no insight that there was an endogenous component to her illness, that she seemed to think that if only she could cope better with her environment then she would be better.

DR TROTTER (*consultant psychiatrist*): I wonder if that's the case. I don't think that she was euthymic – I thought that she was still mildly depressed, and that she was being self-deprecatory.

DR McCANCE (*Mrs G's consultant*): I think you're right, but her condition was relatively good.

DR TROTTER: Has her medication been changed in the last three weeks?

DR McCANCE: She's been out on pass and stopped taking her medication and been in her bed. She remains well now for a matter of days before she's depressed.

DR THOMAS: In a part of the video that I did not show she said quite specifically that she stops taking her medication when she starts getting depressed, not the other way round.

DR EAGLES (*consultant, psychiatric tutor*): Can we assume that her compliance with medication while she's in hospital is what we think it is?

DR THOMAS: Her lithium levels while in hospital are reasonable, although as an out-patient they vary widely, as do the thyroid tests.

DR OSWALD: I wonder if it might be worth thinking more about that, since the only study that has suggested that thyroxine is effective in the prophylaxis of manic–depressive illness (Stancer & Persad, 1982) also suggested that it tends to be particularly effective in post-partum illnesses, so there may be a link there. That was a small study; they looked at ten patients refractory to lithium prophylaxis and found that by adding thyroxine, five out of ten were reasonably well maintained.

DR EAGLES: I think the important thing about their study was that thyroxine was not just returning patients to euthyroid levels – you had to give them three or four times the normal replacement dosage, 0.3 or 0.5 mg per day. There is also evidence that rapid cyclers are more prone to become thyroid deficient on lithium than are non-rapid cyclers (Cho *et al*, 1979; Cowdry *et al*, 1983) and that's odd. There must be some link between thyroid and rapid cyclers.

DR OSWALD: Probably everyone accepts that lithium has very little effect in up to a quarter of bipolar patients (Dunner *et al*, 1976) and particularly rapid cyclers tend to respond poorly (Roy-Byrne *et al*, 1984). That certainly seems to be the case with this lady if we define rapid cyclers as people with three or more affective illnesses in one year. Even when lithium does not prevent affective illness, it can often reduce the severity and/or frequency of the illness, and although that does not seem to be the case recently, there is a suggestion that it did in the early stages.

I wonder whether we have given up on carbamazepine too quickly, and whether we have been trying to get the carbamazepine levels too high. Most reports have assumed that we ought to reach the sort of levels we need in epilepsy (Okuma *et al*, 1981) but it may be that much lower blood levels have a prophylactic action.

PROFESSOR ASHCROFT (*professor of mental health, Aberdeen University*): Whatever drug you use there is going to have to be some attempt to tackle the compliance problem.

DR CALDER (*senior registrar in psychiatry*): Would there be grounds for compulsorily admitting this lady for say six months, to see the pattern?

DR TROTTER: This lady's illness seems to fall into four decades. In the 1950s she had two serious episodes of depression with biological precipitants in the form of childbirth, then she disappeared in the '60s, but came back in the '70s although by and large maintained on lithium, and then things began to worsen in the 1980s, and I wonder if we can see what has happened to her in the past eight years, not as a series of depressive relapses, but as one continuing depressive episode that we need to tackle properly, even if it means detaining her.

DR McCANCE: The difficulty with having her in hospital is that her husband is unwilling to agree because she will hold it against him.

DR MATTHEWS (*registrar in psychiatry*): Looking at it from the four separate decades, has there been some significant change in her home life or social circumstances that is continuing to precipitate episodes of depression?

DR McCANCE: She moved out of the main farmhouse, and the son moved in, but I do not think that caused any great trauma. She inherited quite a lot of money, and that caused some problems. Her children are doing very well.

PROFESSOR ASHCROFT: Could anyone make a case for stopping all drugs and seeing what happens? At least then you start off on a baseline and you can take it from there.

DR EAGLES: I would support that because I don't think over recent years there is any evidence that lithium has helped her and certainly Wehr *et al* (1988) suggest that lithium can occasionally make rapid cyclers worse, and there are many reports in the literature of tricyclic antidepressants also making them worse (Wehr & Goodwin, 1987).

DR CALLENDER (*consultant psychiatrist*): There are reports of relapse being precipitated by lithium withdrawal (Mander & Loudon, 1988). This lady has repeatedly been in episodes of relative or absolute lithium withdrawal and although in retrospect it is difficult to say whether this caused relapse or vice versa, perhaps it would be better to withdraw it.

PROFESSOR ASHCROFT: There are drug therapies that she has not had. Monoamine oxidase inhibitors (MAOIs) are worth considering. The other thing which she's not had which other people would try in rapid cycling patients is valproate.

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DR McCANCE: The other thought I had is to use intramuscular flupenthixol, to overcome possible non-compliance.

PROFESSOR ASHCROFT: The other thing about rapid cyclers is that sometimes they benefit from a change of environment, or even a change of ward. It is nothing whatever to do with the standard of care on a ward, but a switch of people looking after them seems to sometimes produce a change. Also there are one or two units that specialise in the treatment of resistant depression, for example Professor Eccleston's in Newcastle, and if someone has as bad a history as this, perhaps we should be thinking of asking them if they would take her. They are used to treating this sort of illness; they would run through the different therapies, and would not take her for just a short time. They do claim a high success rate, but it is very difficult to run controlled trials on this sort of patient.

DR OSWALD: I think they would be faced with exactly the same problem. Could we ask Stephen Bell here whether there is anything the psychologists might offer to improve a patient's compliance.

MR BELL (*top-grade clinical psychologist*): In such patients, I don't think so.

DR MATTHEWS: Does it not strike anyone as a little odd that after having recurrent illnesses, on the evidence of the video, she has no insight whatsoever that she can be helped in any way by physical treatment.

PROFESSOR ASHCROFT: To a certain extent, she is right. I think that starting afresh may be our only hope of changing attitudes. I would push for that and I would not feel a failure in doing so.

DR OSWALD: I wonder if there is nothing more we could do locally to improve her compliance. At our day hospital we have a group we refer to as the 'Health Talks Group', and one of its main functions is talking about taking your pills.

DR McCANCE: She lives a long way from the hospital.

DR CALLENDER: It's important to remember simple things like one-day dosing where possible, avoidance of multiple medication, and so on.

DR CALDER: She will not be more compliant unless we increase her insight. Surely we have to take control of this lady in a formal way, with a second opinion, so we can monitor whether she takes her tablets, and if she does not and she becomes ill, then we can say it is through non-compliance. At the moment it is only assumption.

DR McCANCE: Not entirely – she has relapsed in hospital on tablets. She does take them when she is in, but whether they are the right tablets is of course questionable.

DR OSWALD: I was hoping to discuss whether psychosurgery might be an appropriate intervention.

DR TROTTER: I do not think that you have been able to prove that she does not respond to a variety of treatments. I think she would be sent back to you fairly quickly by any psychosurgeon saying try A, B, C, D, and E first.

DR THOMAS: There is the report by Poynton *et al* (1988) suggesting that psychosurgery can be used to ameliorate manic–depressive illness.

DR McCANCE: There have been two reports of nine cases (Lovett & Shaw, 1987; Poynton *et al*, 1988), not generally startlingly good, but occasional ones *have* been startlingly good: 22% very good results in bipolars, 67–70% in unipolars, over a four-year follow-up in the bipolars. I did send a bipolar lady for stereotactic subcaudate tractotomy and she has done remarkably well, so that obviously has an effect on me. In the bipolar ones it seems to control manic spells better than depressive episodes, which was contrary to what had been thought by Pippard (1955).

DR OSWALD: Certainly we could not proceed without her full approval, and she seemed very reluctant. MAOIs are an interesting suggestion – people have tended to use clorgyline rather than phenelzine, a type A MAOI. It has fewer side-effects but it too has been reported to induce mania in a substantial minority of patients. Maybe we can turn to Dr McCance and ask whether she has gained anything from this discussion.

DR McCANCE: I think it is extremely helpful to hear other people's ideas. I think the thyroxine is well worth trying. I am a little doubtful about the MAOIs, having seen her high so often. Valproate seems worth a trial and depixol by intramuscular injection is another that I would consider. I would also consider her going to somebody else's ward, but have known her for a very long time, so I have a certain affection for her, and I think she has for me. Finally, I think I probably should admit her compulsorily. I want to be able to keep her in hospital, although for somebody who has been ill so much I feel if she has a few days when she feels well it seems a shame to keep her in hospital.

Addendum

After the case conference Mrs G was detained under Section 18 of the Mental Health Act (Scotland) 1984 and has been in hospital for one year. Her lithium was discontinued and she had been tried without medication other than thyroid replacement and on intramuscular flupenthixol. Her mood remains predominantly depressed with short episodes of near euthymia. Her willingness to comply with prophylactic medication remains unchanged. Her mood has been such that it is not felt that she could have been maintained out of hospital.

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References

CHO, J. T., BONE, S., DUNNER, D. L., *et al* (1979) The effect of lithium treatment on thyroid function in patients with primary affective disorder. *American Journal of Psychiatry*, **136**, 115–116.

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COWDRY, R. W., WEHR, T. A., ZIS, A. P., *et al* (1983) Thyroid abnormalities associated with rapid cycling bipolar illness. *Archives of General Psychiatry*, **40**, 414–420.

DUNNER, D. L., FLEISS, J. L. & FIEVE, R. R. (1976) Lithium carbonate prophylaxis failure. *British Journal of Psychiatry*, **129**, 40–44.

LOVETT, L. M. & SHAW, D. M. (1987) Bipolar affective disorder after stereotactic tractotomy. *British Journal of Psychiatry*, **151**, 113–116.

MANDER, A. J. & LOUDON, J. B. (1988) The clinical sequelae of lithium discontinuation. *Lancet*, *ii*, 15–17.

OKUMA, T., INANAGA, K., OTSUKI, S., *et al* (1981) A preliminary double blind study on the efficacy of carbamazepine for treating manic depressive illness. *Psychopharmacology*, **73**, 95–96.

PIPPARD, J. (1955) Rostral leucotomy: a report of 240 cases personally followed up after 1.5–5 years. *Journal of Mental Science*, **101**, 774–787.

POYNTON, A., BRIDGES, P. K. & BARTLETT, J. R. (1988) Resistant bipolar affective disorder treated by stereotactic subcaudate tactotomy. *British Journal of Psychiatry*, **152**, 354–358.

ROY-BYRNE, P. P., JOFFE, R. T., UHOLE, T. W., *et al* (1984) Approaches to the evaluation and treatment of rapid-cycling affective illness. *British Journal of Psychiatry*, **145**, 543–550.

STANCER, H. C. & PERSAD, E. (1982) Treatment of intractable rapid-cycling manic depressive disorder with levothyroxine. *Archives of General Psychiatry*, **39**, 311–312.

WEHR, T. A. & GOODWIN, F. K. (1987) Can antidepressants cause mania and worsen the course of affective illness? *American Journal of Psychiatry*, **144**, 1403–1411.

——, SACK, D. A., ROSENTHAL, N. E., *et al* (1988) Rapid cycling affective disorder: contributing factors and treatment responses in 51 patients. *American Journal of Psychiatry*, **145**, 179–184.

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