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Seasonal Hypomania in a Patient with Cold Urticaria

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The clinical and biochemical disturbances of a patient with seasonal hypomania and cold urticaria are described and discussed with reference to histamine metabolism in mental disorder.

Allergic disorders have often been reported in association with mental disturbance, although interpreting the relationship is more complex than has often been assumed (Rix *et al*, 1984). Shared biochemical features have been suggested in recent work on the behavioural associations of histamine and antihistamines (Hough & Green, 1984). Histamine acts through two classes of receptors, both of which are affected by antidepressants and neuroleptics (Kanof & Greengard, 1978). Antagonism of the type designated H1 causes sedation, whereas unbalanced antagonism of the H2 type, produced by cimetidine, has been linked with psychiatric manifestations, which are often affective in nature (Crowder & Pate, 1980; Hubain *et al*, 1982; Titus, 1983).

This report describes a case of intermittent cold urticaria, occurring in close relation to unipolar affective disturbances over several years. There are no reports in the literature over the past two decades of any similar case, or of any recognised psychiatric morbidity associated with cold urticaria. It is estimated that about 0.4% of the population are affected by cold urticaria at some time in their lives (Champion *et al*, 1969).

Case History

Presentation of cold urticaria

The patient, a caucasian male born in 1961 first became ill in 1972, when he collapsed after swimming. During each subsequent winter he experienced episodes of diffuse

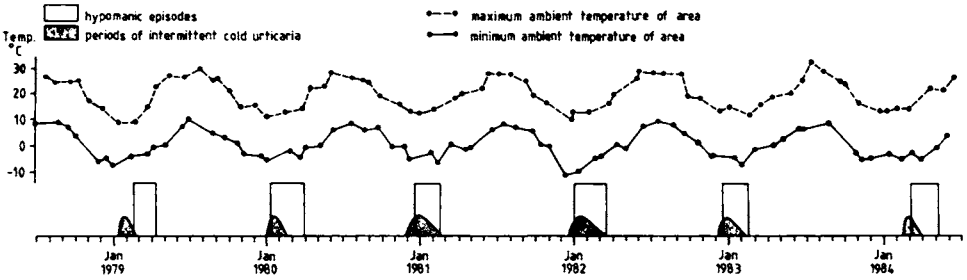

FIG. 1 The chronological relationships of hypomanic episodes, cold urticaria, and temperature extremes in the patient's area of residence.

swelling affecting his hands and face, often accompanied by headaches, from exposure to the cold.

In 1975 he was examined at St John's Hospital, London where dermatographia and a marked urticarial reaction to ice were noted. The following tests were normal or negative: immune globulin E, cryofibrinogen, cryoglobulins, C_3 and C_4 complement components, serum protein electrophoresis, lupus cells, anti-nuclear factor, rheumatoid factor, Wasserman reaction, and stool microscopy for ova and parasites. A diagnosis of idiopathic cold urticaria was made.

Psychiatric presentation

In the severe winter of 1978, when the episodes of swelling commenced, the patient (then aged 17) began to talk incoherently about electronic forces and of a plan he had to construct a magnetic train. Growing restlessness culminated in a sudden outburst of bizarre excitement, and at psychiatric examination a preoccupation with an electronic activity which fused mind and body was noted. On the day he was admitted to the psychiatric unit, a disturbance arose in which he jumped from one bed to another while stripping off his clothes.

Psychiatric assessment and observation

The patient complained that thoughts were crowding his mind, which tired him and prevented him from achieving his objectives, and that sounds seemed very loud. He heard the incoherent voices of a crowd talking to him and had a vague notion that someone was trying to harm him. His talk was coherent, though circumstantial, and he was markedly distractable. His mood was one of moderate euphoria, with transient feelings of dysphoria and marked irritability. Apart from impairment of concentration, his cognitive functions were intact. No abnormality of premorbid personality was elicited. There was a history of a single episode of severe depression in a maternal aunt. On physical examination no significant abnormality was found, but there were scratch marks on his hands and face in keeping with recent urticaria.

During his first week on the ward he was awake for most of the night, when he would bang his head on the wall or roam about and shout. He climbed chairs and attempted to throw himself on to the floor, likening himself to an Olympic swimmer, and he smashed the glass of a door. During this time he was given a daily dose of 15 mg of trifluoperazine and up to 250 mg of chlorpromazine. He improved gradually during five weeks of in-patient treatment. A diagnosis of mania was made.

A month later, at follow-up, he was doing well and his medicines were reduced. Shortly afterwards he stopped his treatment, and did not return to the clinic because he remained well.

Clinical Course

Dermatological follow-up

The patient's next contact with St John's Hospital was in early 1981, when he was readmitted for further routine tests.

Following the application of an ice cube to his arm, blood samples from the antecubital fossa produced circulating histamine, reaching a maximum level of 9 ng/cm^3 after 14 minutes. He was placed on a cyproheptadine, which he used intermittently.

Psychiatric follow-up

Since the first psychiatric admission the patient has shown annual hypomanic episodes, occurring only during the winter. His parents noticed that they built up over three or four weeks, after periods of unusually severe exposure to the cold. Although the psychiatric admission was delayed in 1984, it occurred during severe cold weather, when he spent several days working outdoors to repair his car. The onset was preceded by marked urticaria. Fig. 1 shows the chronological relationship between the two conditions.

Discussion

This patient, with proven idiopathic acquired cold urticaria, was manic on presentation and typically hypomanic during each subsequent psychiatric dis-

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turbance; the clinical features were observed and documented by one of us during three of the six episodes recorded here.

The onset of cold urticaria prior to the disturbed behaviour was observed by the patient's parents, who lived with him throughout the period in question. Selective recollection may have affected the accuracy of their observations, although for most occasions examples could be given of everyday activities leading to greater cold exposure just before the disturbances. The parents were not aware of any early affective changes which could have been responsible for increased cold exposure.

In cold urticaria, a massive release of histamine is detected in the circulation (Kaplan & Beaven, 1976) and in the urine (Granerus *et al*, 1969), which is generally undetectable in other types of urticaria due to its rapid tissue uptake. There has never been substantiation of the view once held that parenteral histamine might benefit man by increasing cerebral blood flow and capillary permeability (Simpson & Kline, 1961). On the contrary, histamine release may correspond with a systemic reaction which includes light-headedness, a sensation of tightness in the chest, transient hypotension, and fainting. These effects may be expected to contribute to any emotional distress associated with cold urticaria, and were reported by our patient in relation to acute episodes, although during in-patient treatment his recorded pulse and blood pressure readings were normal.

Elucidating possible aetiological factors in individual examples of regular cyclical affective disorders is difficult (Jenner & Damas-Mora, 1983). Although our patient's clinical picture could have resulted from the remarkable coincidental concurrence of two independently seasonal conditions, it appears more likely to be due to provocation of one by the other, or to a shared aetiological factor.

There is evidence to suggest that histamine crosses the blood-brain barrier in animals (Crossland & Mitchell, 1956; Snyder *et al*, 1964), although this has not been shown in man. Endogenous release of hypothalamic histamine may be markedly increased during cold exposure (Taylor & Snyder, 1971), and its intraventricular injection in rats results in catalepsy and hypothermia (Pilc & Nowak, 1979). Besides histamine there are other products of mast cell degranulation, such as prostaglandin D_2 and the leukotrienes, and one of histamine's metabolites, imidazoleacetic acid, when given parenterally to rats, has been shown to cause increased exploratory behaviour, hyperactivity, ataxia, and catalepsy (Marcus *et al*, 1971). Increased levels of conjugated imidazoleacetic acid have been found in the urine of schizophrenic patients (Kobayashi & Freeman, 1961).

Finally, the effects of cyproheptadine should be considered. It is the drug of choice for cold urticaria (Wanderer *et al*, 1977), and has a greater therapeutic effect than other drugs with a more powerful antihistaminic action, probably due to its influencing the kinin system at tissue level. Cyproheptadine is also a serotonin antagonist, which has encouraged the suggestion that its use might be associated with psychiatric disturbance (Pearce *et al*, 1977). However, in our case cyproheptadine was only introduced after the first three psychiatric episodes, and it was taken irregularly for subsequent attacks of cold urticaria. The patient's family observed that in the short term the drug exerted a beneficial calming effect on the mood disorder, but it is not known if its overall effect could have been to contribute to the onset of some of the episodes.

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Priapism and Psychotropic Medication

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Priapism is a rare but serious adverse effect of psychotropic drugs resulting from their peripheral alpha-adrenoreceptor blocking action. Two patients developed this during treatment with oral phenothiazines: one was treated surgically with a venous shunt, and the second case resolved after intracavernosal injection of an alpha-adrenoreceptor stimulating drug.

Priapism is a pathologically prolonged and painful penile erection, usually unassociated with sexual desire or intercourse. It is caused by obstruction of the venous drainage from the corpora cavernosa, while that from the corpus spongiosum and glans penis remains unaffected. Priapism, therefore, can be clinically differentiated from a normal erection in that only the corpora cavernosa are turgid, the corpus spongiosum and glans penis being quite flaccid (Wasmer *et al*, 1981). Prompt diagnosis and treatment are essential, or the resultant stasis will lead to thrombotic changes and ultimately to fibrosis of the corpora cavernosa, and thus to permanent erectile impotence. This can be restored only partially by implantation of a penile prosthesis—a difficult and sometimes unsuccessful operation (Pryor, 1982).

The usual treatment of priapism is surgical, initially involving aspiration and saline irrigation of the corpora cavernosa, the creation of a temporary fistula between these and the corpus spongiosum and, if the venous drainage is still unsatisfactory, a corpus cavernosum saphenous shunt (Pryor, 1982). Recently, there have been encouraging preliminary results for injection of metaraminol, an alpha-adrenoceptor stimulating drug, directly into the cavernosal space (Brindley, 1983, 1984; Stanners & Colin-Jones, 1984).

Priapism may occur at any age, being most frequent in the third and fourth decades, and may arise in a wide variety of circumstances; it often occurs on waking, but only occasionally following prolonged sexual stimulation. Some 30–40% of affected cases have the condition recurrently; about half are idiopathic. The remainder are associated with diverse factors, which can be grouped into three main categories: local pathology of the pelvis—a direct obstructive effect; blood dyscrasias, especially sickle cell disease, which facilitate thrombosis by increasing