

PSYCHOSIS IN HYPOPARATHYROIDISM

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INTRODUCTION

RECENTLY there has been a resurgence of interest in the subject of hypoparathyroidism and it has become increasingly clear that psychiatric symptoms may frequently be found in patients with hypoparathyroidism, even where no evidence of tetany is present. It is significant that in a survey, in the Cardiff area, of 82 patients who had had a thyroidectomy, Davis *et al.* (1961) found that mental symptoms (defined as a feeling of uneasiness, tension and anxiety, sometimes with attacks of panic, often with depression) occurred in 66 per cent. of 26 patients whose plasma calcium was below 9·3 mgms./cent, in 51 per cent. of 31 patients whose plasma calcium lay between 9·3 and 9·8 mgms./cent. and in 35 per cent. of 23 patients whose plasma calcium was above 9·8 mgms./cent. They estimated that at least 24 per cent. of the patients showed partial parathyroid insufficiency, and that this apparently accounted for many minor but disabling symptoms, particularly depression and lassitude. They found that often these symptoms could be cured by the administration of calcium.

Coincident with the publication of the findings of Davis *et al.* we had a patient admitted to our care in whom the clinical picture was that of a psychosis arising in the setting of hypoparathyroidism. We feel it of value to report this case, with some review of relevant publications, as we can find no previous case of psychosis of this type in the British literature.

CASE REPORT

Mrs. A., a 61-year-old widow, with no previous history of psychiatric abnormality, was admitted 6 weeks after she had had a sub-total thyroidectomy. She had developed a thyroid swelling one year previously, and had made an uneventful recovery from her operation, being discharged from hospital after 7 days. The histology of the gland showed no evidence of toxicity or malignancy. On her return home from hospital she appeared well for 7 to 10 days, and then became anxious and depressed. She was afraid to be left alone and developed mild anorexia. She complained at this time of occasional cramping in her hands, found that she had difficulty in gripping objects and noticed that occasionally her hands felt numb. Over the next three weeks her condition worsened, and she became overtly depressed. Her appetite was poor, she had difficulty in sleeping, and she frequently wept. In the week immediately preceding her admission to hospital she became confused, and her memory for recent events was markedly impaired. She could not remember her grandchildren's names, misidentified her relatives, and was unable to recollect when friends had called to visit her home. She was agitated, refused all food, and there was a suggestion that she had had occasional choking attacks. At this stage her admission as an informal patient was arranged by her general practitioner.

On admission she was noted to be an ill-looking woman, who was markedly depressed. She was unable to give a coherent account of her illness, and her memory for recent events was grossly impaired. She wept frequently and was acutely miserable. She showed disorientation for time and place, and thought she was still in her home. She had no delusions or hallucinations. Physical examination shows a fluctuating bilateral carpo-pedal spasm with *main d'accoucheur*. Both Chvostek's and Trousseau's signs were positive. There was no evidence of hypothyroidism, cardiac or renal failure or neurological disease. Within 12 hours of admission the patient had two grand mal seizures (there was no previous history of epilepsy) and following the second seizure she complained of a choking sensation. A provisional diagnosis of hypoparathyroidism was made and the following investigations were carried out:

Serum calcium, 4.4 mgms./cent.

Serum inorganic phosphate, 5.4 mgms./cent.

Alkaline Phosphatase, 14 units.

E.C.G. normal.

No urinary abnormality detected.

EEG showed paroxysmal dysrhythmia, with a considerable amount of fast activity: low frequency activity of 6 to 7 cycles per second, associated with random spiking was also noticed.

Immediate treatment was given with intravenous and intramuscular calcium gluconate. Parenteral injections of calcium gluconate and high potency Vitamin D were continued until the patient could take oral calcium. Within 48 hours the signs of tetany had diminished considerably, and treatment was continued with oral calcium and Vitamin D. The confusional state, which had previously been continuous, now became intermittent and her depressive symptoms lessened. Within 5 days the patient's memory had completely returned and she was fully orientated for time and place, her depressive symptoms were much improved, she was no longer so miserable, her appetite had increased, and she slept well. Coincident with the improvement in her mental state there had been a gradual rise in her serum calcium, which was now 6.4 mgms./cent. Over the next few weeks the patient's condition returned to normal, with a total disappearance of all psychiatric symptoms. Her electroencephalogram showed a corresponding improvement with a return to more normal rhythms. At the time of discharge, eight weeks after admission to hospital, her serum calcium was 9.2 mgms./cent., and she is now being maintained as an out-patient on oral calcium and Vitamin D. Psychological testing on discharge showed no evidence of intellectual deterioration.

REVIEW

Hypoparathyroidism following thyroidectomy is a well-recognized but relatively rare condition. Its incidence in different series of patients varies between 3 per cent. (Cattell, 1949) and 5.8 per cent. (Lachmann, 1941). Wade (1960), in his study of 112 patients submitted to sub-total thyroidectomy, noted that 4.5 per cent. developed signs and symptoms of hypoparathyroidism; of these, 1.8 per cent. developed permanent hypoparathyroidism and 2.7 per cent. developed transient hypoparathyroidism at periods ranging from 2 to 14 days after operation.

Mental symptoms arising with tetany were originally described by Kussmaul in 1869. In 1920 Barrett reviewed the subject and noted that the mental symptoms commonly associated with tetany were "periods of stupor, with a dominant sad

mood and the expression of mild delusions of fear and sadness". In contrast with this, episodes of excitement with confusion, auditory hallucinations and marked apprehensiveness were also reported. Fünfgeld (1928 and 1943) noted that minor nervous disturbances frequently occurred in hypoparathyroidism, but that frank psychosis was rare. He described cyclical depressive illnesses with melancholia, and observed that in cases of tetany where the spasms were severe, mental disturbances occurred. Winterstein (1935) described three cases of tetany with atypical presentations, in all of whom mental symptoms were prominent. In one patient depressive symptoms had been present for at least 10 years, and in another patient depressive symptoms had been sufficiently severe to produce suicidal thoughts. In his third patient there had been frequent attacks of depression with a feeling of complete mental exhaustion. A response to treatment, with a relief of mental symptoms was obtained in all three patients. Barr *et al.* (1938) described two cases of hypoparathyroidism, one idiopathic and the other post-operative, in whom increased intracranial pressure and papilloedema were present. Following restoration of the serum calcium to normal levels, these symptoms disappeared. Similar observations were made by Sugar (1953), who found that anxiety, depression and typical psychosis might occur, in addition to epileptic fits, which, in association with papilloedema, might suggest an intracranial growth. Lachmann (1941) described epileptiform fits as an initial symptom of hypoparathyroidism. Three cases of parathyroid insufficiency with symmetrical cerebral calcification were reported by Eaton and Haines (1939) and these authors regarded symmetrical cerebral calcification, mental deterioration and convulsions as concomitant, but not necessarily inter-dependent, cerebral results of hypoparathyroidism. Greene and Swanson (1941) described five cases of psychosis in a series of 18 patients with hypoparathyroidism, who had been seen over a period of 9 years. In their survey of the condition they found only four previous cases in which an association of psychosis and tetany had been noted, and they considered that, in view of the high incidence of psychosis in their series, the complication occurs more frequently than is generally appreciated. The patients described by them were typical examples of toxic delirium, in which delusions and hallucinations developed. Anxiety, depression and a sense of impending disaster were common, but rarely of sufficient intensity to be classified as psychotic. They observed that psychiatric disturbances may be the first and only manifestation of parathyroid tetany, and they found that if a psychosis occurs, it usually arises within the first 3 to 4 months of the disease. In their cases improvement in the mental abnormalities arose 3 to 4 weeks after the serum calcium had returned to normal. They quote two cases described by Knospe (1938) in whom the mental symptoms persisted for several months after successful treatment of the parathyroid tetany. Dementia of several years' duration in association with epileptic fits was observed as the presenting feature of tetany by Scarlett and Houghtling (1944) and Robinson *et al.* (1954). Both those authors found that a relatively prompt and successful outcome occurred when treatment was instituted, despite the duration of the condition. De Mowbray *et al.* (1954) noted that symptoms of anxiety were prominent in two of their cases and as a result there was a tendency to hyperventilation precipitating further attacks of tetany. In two other cases of idiopathic hypoparathyroidism they found intellectual deterioration, impairment of memory and emotional instability. In a comprehensive review of the field of hypoparathyroidism they noted that mental changes were usually found to resolve within a few weeks after the serum calcium level had returned to normal, suggesting that they

were the direct result of hypocalcaemia. They also mention that mental retardation was recorded in a number of cases of idiopathic hypoparathyroidism arising in childhood. According to Wade (1960) early symptoms of post-operative hypoparathyroidism may be confined to paraesthesia or tetany, and in latent hypoparathyroidism acclimatization to the sub-normal calcium level may occur with a lessening in the severity of the tetanic symptoms. Insidious mental and ectodermal conditions may develop, however, despite a general impression that complete spontaneous recovery is the rule in post-operative hypoparathyroidism, and in the later stages of the untreated condition the principal symptoms may be epileptiform fits and psychoses of various types.

DISCUSSION

In our patient the appearance of frank psychotic symptoms in the presence of classical tetany, bearing a direct relationship to a previous thyroidectomy, rendered the clinical diagnosis straightforward. Rarely, however, in the post-operative psychosis can any such direct link be established between the mental symptoms and the preceding operation. Knox (1961) who estimated the incidence of post-operative psychosis as one in every 1,600 surgical operations, concluded that the "post-operative psychosis" did not exist as a distinct entity. Although considerable research has been carried out into the metabolic aspects of surgery, scant information exists about the role which biochemical disorders may play in the post-operative psychosis. Following thyroidectomy, however, psychiatric symptoms seemed clearly due to disturbed parathyroid secretion. The absence of such psychiatric symptoms prior to thyroidectomy and their emergence following operation argue against the possibility of negative calcium balance, occasionally seen in thyrotoxicosis, being the cause of these symptoms. Thyrotoxicosis is a rare cause of osteoporosis—rare because the thyroid disturbance is diagnosed and treated before bone changes develop. Excessive urinary excretion of calcium reflects the increased turnover of calcium with resultant negative balance. Whether this is due to a rise in glomerular filtration rate (Bradley, 1955) or to the occasional rise in thyrotoxicosis of plasma calcium (Kleeman *et al.*, 1958), the urinary excretion of calcium returns to normal in one to two weeks under treatment. It would seem unlikely that a lowered serum calcium due to pre-operative thyrotoxicosis would persist after uncomplicated thyroidectomy and produce chronic mental symptoms.

Hypoparathyroidism appears to provide a rare example of a direct relationship between a specific disorder of metabolism and mental symptoms, although emotional factors and constitutional pre-disposition are no doubt relevant in the development of the form which the psychosis takes. Confirmatory evidence of this relationship is seen in the relatively swift restoration to normality which usually occurs when the disorder of calcium metabolism is corrected, even if the mental symptoms have been present for a number of years. The nature of this biochemical relationship remains obscure. Barr *et al.*, who noted increased spinal fluid pressure during tetany with rapid subsidence following the restoration of normal serum calcium values, suggested that oedematous changes in the cerebrum or meninges might be operative in producing the psychiatric manifestations of tetany. Greene and Swanson suggested that mental symptoms arose from a failure of the brain to adjust to the acute chemical changes which were taking place. Gotta and Odoriz (1948) observed four EEG patterns in parathyroid deficiency:

- (a) Typical bursts of slow waves and spikes.
- (b) Continuous generalized dysrhythmia.

- (c) Slow waves, either single or in series.
- (d) A normal record.

but concluded that the EEG was not specific in this condition.

Howard and Ziegler (1942) and Prokop (1958) found that depressive illness was commoner in their patients after thyroidectomy and suggested that the operation had been mistakenly undertaken for psychiatric disorder. We consider, however, that the alternative suggestion, conveyed in a recent leading article in the *Lancet* (1961), namely that it is the thyroidectomy, with the incidental parathyroid damage, which produces the mental changes, is the most likely explanation. In view of the relatively high incidence of psychiatric symptoms reported recently by the Cardiff workers, it would seem of value to consider the possibility of diminished parathyroid function as being an aetiological factor in thyroidectomised patients presenting with nervous or mental symptoms.

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