Suid-Afrikaanse Tydskrif vir Geneeskunde : South African Medical Journal

Kaapstad, 13 Mei 1961 Deel 35 No 19 Volume 35 Cape Town, 13 May 1961

HYPERTHYROIDISM ASSOCIATED WITH HYPOPOTASSAEMIC PERIODIC PARALYSIS

B. GOLDBERG, M.D. (RAND), M.R.C.P., *Johannesburg*, and A. M. BARNETT, M.B., B.CH. (RAND), *Durban*

The association of hyperthyroidism with hypopotassaemic periodic paralysis is extremely rare. Since the first description nearly 60 years ago[1] only 40 cases have been described. In 1955, Linder[2] reviewed the literature and found 35 case reports to which he added 3 further cases. Subsequently Overholt *et al.*[3] and Anderssen and Wigmostad[4] have each described single cases. The object of this paper is to report another instance of this rare association. As far as we are aware it is also the first case to be associated with a positive thyroid auto-antibody test.

CASE REPORT

A 53-year-old European man, an advertising executive, was seen for the first time at 10 a.m. on 10 March 1958. Ten hours previously he had woken and found he was unable to sit up or move his limbs. During the previous 2½ years he had experienced frequent episodes of weakness and stiffness of his legs. In March 1956, 2 months after recovering from a severe bout of gastro-enteritis, he suddenly collapsed while walking and was so weak that he was unable to lift himself up. Similar attacks, which were transient, recurred 2 or 3 times daily for about 10 days and then disappeared spontaneously. During the next 2 years milder attacks of weakness and stiffness of the legs occurred. He was particularly liable to an attack if he sat in one position for more than 15 minutes, when he would find great difficulty in rising. Attacks could be prevented by changing his position at frequent intervals and were alleviated by exertion which 'loosened him up'.

Apart from these mild episodes he had woken on 3 occasions with attacks of weakness similar in distribution, but milder than the present episode. He had always recovered spontaneously by the following morning. The proximal muscles of the limbs were more severely affected and he had not experienced any ocular, bulbar, respiratory or sphincter disturbance. There were no particular precipitating factors, but the attacks tended to occur in the evenings, during weekends or when he was anxious. For the past 35 years he had passed frequent, loose stools on several days of each week. In 1932 a laparotomy had been performed because of this, and his appendix had been removed. He did not use purgatives and had never noticed any relation between exacerbations of his diarrhoea and the episodes of weakness or paralysis. During the past year he had become nervous and shaky, sweated excessively, and had lost 10 lb. in weight. The remainder of the history was not contributory.

Examination showed an anxious, sweaty, middle-aged man with warm extremities. The heart rate was 120 per minute and the blood pressure was 120/60 mm.Hg. Apart from a grade 1 apical systolic murmur there were no findings of note in the heart, chest or abdomen. The thyroid gland was slightly enlarged, smooth and firm. No bruits were heard over it. The cranial nerves and fundi were normal and there were no signs of bulbar or respiratory weakness. The patient was unable to sit up and there was symmetrical weakness of all limbs, most marked proximally. The hands and feet could be flexed and extended, but no other limb movements were possible. Muscle tone was moderately reduced and the tendon reflexes were absent. The affected muscles felt normal. There was no wasting, fasciculation or sensory loss. Rectal examination was normal.

Investigations at this time gave the following results: haemoglobin 16·2 G. per 100 ml.; haematocrit 50 vols. %; ESR (Wintrobe) 5 mm. in 1 hour; leucocytes 13,700 per c.mm. with a normal differential count; serum sodium 141 mEq. per litre; and potassium 2·7 mEq. per litre. Urine examination was normal.

No immediate treatment was given and within 3 hours spontaneous improvement began. Eight hours later the patient could walk with difficulty. At this time potassium chloride was given in doses of 15 gr. *t.d.s.* and was continued for 2 days. He was then well without any weakness. A tachycardia of 100 per minute and a fine tremor of the fingers were present.

One week after the onset, X-ray examination of the heart and lungs was normal, as was the electrocardiogram. Blood urea was 23 mg. per 100 ml.; plasma CO_2-combining power 24; serum sodium 144, potassium 4·9 and chlorides 108 mEq. per litre. Serum proteins were 7·8 G. per 100 ml., of which albumin was 3·5 and globulin 4·3 G. per 100 ml. Urine examination on several occasions showed random specific gravities between 1016 and 1020 and pH ranged between 4·9 and 5·5; no abnormal constituents were present. The serum protein-bound iodine (PBI) was 9·3 µg. per 100 ml.; the I^{131} uptake at 5 and at 24 hours was 100% and the conversion ratio was 79%. The salivary sodium/potassium ratio was 1:1. An attempt was made to provoke an attack of paralysis by the ingestion of 150 G. of glucose, but this was unsuccessful. Intravenous pyelogram, barium meal and barium enema were all normal. On a normal diet the faecal fat was 2·6 G. in 24 hours and the serum calcium and phosphorus were 9·8 and 2·4 mg. per 100 ml. respectively.

On 4 April 1958 treatment with methimazole, 10 mg. *t.d.s.*, and potassium chloride, 15 gr. *t.d.s.*, was begun. One month later the patient was clinically euthyroid and the potassium chloride was stopped. The dose of methimazole was reduced to 5 mg. *t.d.s.* and continued for a further 11 months. Within 2 weeks of starting treatment he felt well and had no recurrence of stiffness, weakness or paralysis. This improvement has been maintained for more than 2 years and all signs of hyperthyroidism have disappeared; the serum PBI in September 1958 was 3·4 µg. per 100 ml. In June 1958 he had a severe bout of diarrhoea lasting 4 days, but this did not cause any muscle weakness or hypopotassaemia. In 1960 it became possible to have tests for thyroid antibodies performed in Johannesburg. His serum showed a positive gel-agar precipitation test; the final titre was 1:8. The tanned red-cell agglutination test was negative.

DISCUSSION

Hypopotassaemia, regardless of aetiology, frequently causes muscle weakness or paralysis. This paralysis often has a typical distribution, affecting mainly the proximal muscles of the limbs. The affected muscles may swell and feel firm. The tendon reflexes are diminished or absent.[5] Chronic potassium depletion often causes renal dysfunction, characterized by polyuria, nocturia, hyposthenuria and inability to produce urine with a low pH. It is often associated with a metabolic alkalosis.[6]

Hypopotassaemia may result from excessive losses of potassium ions through the gastro-intestinal or urinary

tracts or from alterations in the distribution of potassium within the body. Although chronic diarrhoea may have contributed to the hypopotassaemia in this patient, his rapid spontaneous clinical recovery, the absence of renal impairment and the subsequent normal serum levels without potassium supplements, suggest that there was no depletion of the body's stores of this ion. His subsequent progress has shown complete relief of muscular symptoms despite an unchanged bowel habit. Primary hyperaldosteronism[7] was also considered unlikely, in view of the normal blood pressure and salivary electrolyte ratio and the absence of evidence of chronic potassium depletion. 'Potassium-losing nephritis' was excluded by the normal urinary sediment, pH and concentrating powers, and the normal blood urea and CO_2-combining power. The absence of chronic potassium depletion also made this diagnosis seem unlikely. It seemed probable that the hypopotassaemia was due to a shift of ions from the extra- to the intracellular phase.

Periodic paralysis is an uncommon condition manifested by recurrent episodes of muscle weakness and stiffness. Cardiac and respiratory involvement has occurred only rarely. The majority of cases are familial, but a few sporadic cases have been described. The sporadic and familial types differ in certain respects. The familial type usually begins at puberty and has a slight male preponderance. Treatment is usually unsatisfactory, but the condition tends to remit in middle-age.[8] The sporadic type usually begins after the age of 40 and is found almost exclusively in males. The prognosis of sporadic cases associated with thyrotoxicosis is good, since cure of both conditions is often achieved when the hyperthyroidism is controlled. Factors which provoke attacks are common to both the familial and sporadic types and include exertion, prolonged sitting, sleep, and meals rich in carbohydrates.

Most investigators believe that periodic paralysis is due to changes in the muscle cells, although the precise chemical abnormalities have never been proved. A transient fall in serum-potassium levels during paralytic episodes has often been detected, but this finding has not been invariable.[9] This reduction is probably due to a shift of potassium ions into the muscle cells. Szent-Gyorgyi[10] suggested that the increased potassium concentration in the muscle cells prevented the combination of actin and myosin necessary for muscle contraction. Recently Grob *et al.*[11] have shown that in periodic paralysis, skeletal muscle responds abnormally to the administration of glucose and insulin. The ratio between intra- and extracellular potassium ions changes, with a resultant increase in the resting muscle membrane potential and diminished contractility. Conn *et al.*[12] related the muscle changes to alterations in sodium metabolism as well. They suggested that during paralytic episodes temporary hyperaldosteronism occurs with an increase in the sum of intracellular sodium and potassium ions. In their patients a low sodium diet could prevent induced or spontaneous attacks.

Apart from the cases previously mentioned, Okinaka *et al.*[13] discussed the association of thyrotoxicosis and periodic paralysis in Japan. Their report was based on questionnaires sent to 6,333 patients who had undergone thyroidectomy operations between 1937 and 1956. Among 1,250 males, 110 (8·9 %) were thought to have suffered from periodic paralysis before their operations. Only 0·4% of the female patients were similarly affected. The retrospective nature of this inquiry and the lack of personal observation raise doubts whether all these patients really suffered from hypopotassaemic periodic paralysis. Only cases treated surgically were considered and the exclusion of cases treated by other means may have created a falsely high incidence of this association. Nevertheless, this association of conditions is possibly commoner in Japan than elsewhere.

Although periodic paralysis is an uncommon syndrome, we feel that any patient who develops the sporadic form, particularly in middle-age, should be investigated to exclude hyperthyroidism. Where the conditions are associated, the paralysis is usually cured by successful treatment of the thyroid disease.

SUMMARY

A case of hypopotassaemic periodic paralysis associated with thyrotoxicosis is described. This association is very rare. Treatment of the hyperthyroidism produced a gratifying cure of the disabling muscular symptoms.

REFERENCES

1. Rosenfeld, quoted by Linder, M. A. (1955): *Loc cit.*[2]
2. Linder, M. A. (1955): Ann. Int. Med., **43,** 241.
3. Overholt, E. L., *et al.* (1957): A.M.A. Arch. Intern. Med., **100,** 132.
4. Anderssen, N. and Wigmostad, K. (1959): Brit. Med. J., **1,** 1389.
5. McArdle, B. *In* Ross, E. J., ed. (1959): *Clinical Effects of Electrolyte Disturbances,* p. 106. London: Pitman.
6. Relman, A. S. and Schwartz, W. B. (1956): New Engl. J. Med., **255,** 195.
7. Conn, J. W. and Louis, L. H. (1956): Ann. Intern. Med., **44,** 1.
8. Bickerstaff, E. R. (1953): J. Neurol., **16,** 178.
9. Tyler, F. H. *et al.* (1951): J. Clin. Invest., **30,** 492.
10. Szent-Gyorgyi, A. *Quoted in* Adams, R. D. *et al.* (1953): *Diseases of Muscle.* New York: Hoeber.
11. Grob, D. *et al.* (1957): Amer. J. Med., **33,** 356.
12. Conn, J. W. *et al.* (1957): Lancet, **1,** 802.
13. Okinaka, S. *et al.* (1957): J. Clin. Endocrinol., **17,** 1454.