# ANOREXIA, WEAKNESS, RESTLESSNESS AND PARKINSONISM ASSOCIATED WITH HYPOKALEMIA FOLLOWING RADIOACTIVE IODINE THERAPY

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In a series of 52 hyperthyroid patients treated with varying doses of radioactive iodine, we have observed in 10 of the patients symptoms very suggestive of a thyrotoxic aggravation — a worsening of the exophthalmos, tremors, irritability, increased weight loss and hyperhydrosis. This aggravation usually appeared within the first two weeks following therapy and generally associated with elevation of the protein bound iodine values. Exacerbation of the hyperthyroid state following radioactive iodine therapy has been described in the literature and has occasionally been referred to as the "thyroxine release syndrome."

This paper, however, deals with a set of symptoms observed in four of the 52 patients — symptoms which we feel are apart from those in the thyroxine release syndrome. The uniformity of the signs and symptoms presented by the four patients, the consistency in the time of appearance and the correspondence of the biochemical observations in all the patients excited our curiosity. It is possible that the four cases are those of a delayed, severe or atypical thyroxine release syndrome. They seem more likely to be what many would call cases of thyroid storm or thyroid crisis — a vague and ill defined syndrome which has defied understanding.

## CASES

CASE No. 1: L.M., 47 years old, female, Filipino, married, developed exophthalmos, irritability, loss of weight and blurring of vision of six weeks' duration. She also had all the signs and symptoms of hyperthyroidism. She was given 6.8 millicuries of RAI. There was marked improvement after the treatment.

Three weeks after the treatment, she developed anorexia, marked weakness, restlessness, insomnia, dizziness, intention tremors, mask-like facies and Parkinson-like movements.

Laboratory results:

Blood sugar (2-10-58) — 112 mg. per cent
Cholesterol (2-10-58) — 180 mg. per cent
Protein bound iodine (12-10-57) — 4.0 gamma per cent
( 2- 8-58) — 2.9 gamma per cent
( 9-26-58) — 3.3 gamma per cent
Sodium (2-7-58) — 141 meg/L
Potassium (2-7-58) — 3.1 meg/L
Blood pressure — normal.

CASE No. 2.: P.B., 47 years old, male, Filipino, married, businessman, had all the typical signs of toxicity (palpitation, hyper-irritability and fine tremors). He was seen by an outside physician and was given 9 millicuries. There was immediate improvement after the treatment with marked diminution of the signs and symptoms.

Four weeks later, he developed anorexia, marked weakness, coarse tremors, sweating and insomnia. This weakness was first noticed in the lower extremities, so much that the patient could not stand up. It later progressed to complete paralysis of the upper and lower extremities. Auricular fibrillation which disappeared two weeks after RAI therapy recurred and the patient showed Grade V failure on admission.

Laboratory results (10-7-58):

Sugar ---------- 104 mg. per cent
NPN ---------- 34 mg. per cent
Uric Acid ---------- 3.5 mg. per cent
Cholesterol ---------- 226 mg. per cent
Protein-bound iodine ---- 5.1 gamma per cent
Sodium ---------- 144 meq/L
Potassium ---------- 2.2 meq/L
Chlorides ---------- 99 meq/L
Blood pressure ---------- normal

CASE No. 3.: B.B., 44 years old, male, Filipino, married, lawyer, had an enlarged thyroid, exophthalmos and all the typical signs of toxic goiter for the past 6 years. A month ago, he

was given RAI therapy — 6.8 millicuries. There was marked improvement immediately after the treatment, both symptomatically and objectively. There was regression of the exophthalmos; palpitation, restlessness and irritability were markedly diminished.

Three weeks after the treatment he developed auricular fibrillation, marked weakness, anorexia, restlessness and insomnia. In addition, he showed Parkinson-like movements of the upper and lower extremities. He was admitted with a temperature of 37.5°C.; Blood pressure — 166/90; Pulse rate — 120; Respiration rate — 24.

Laboratory results:

| | (10-25-58) | | (10-10-58) | | (10-25-58) |
|---|---|---|---|---|---|
| Sugar | 105 mg. per cent | Ca. | 9 mg. per cent | | 9 mg. per cent |
| NPN | 47 " " " | Na. | 127 meq/L | | 127 meq/L |
| Creatinine | 2.2 " " " | K | 3.2 " | | 2.3 " |
| Cholesterol | 207 " " " | | | | |
| Protein-bound iodine | | | 16.6 gamma per cent | | 12.5 gamma per cent |
| Blood pressure — normal | | | | | |

CASE No. 4.: E.P., 53 years old, female, Filipino, nurse, married, has been having toxic symptoms for the past 6 months. Exophthalmos was noted 2 months ago. She received 7.62 millicuries of RAI.

Four weeks later, she developed anorexia, marked weakness, restlessness and intention tremors, particularly of the lower extremities. She was anoretic and unable to sleep. Tremors progressed to classical Parkinsonism with typical mask-like facies. This set of symptoms subsided after 10 days. The patient is now obviously well.

Laboratory results:

| | (10-22-58) | (11-3-58) | (11-24-58) | (11-7-58) |
|---|---|---|---|---|
| Sodium | 135 meq/L | 148 meq/L | 153 meq/L | pH blood 7.4 |
| Potassium | 4.4 " | 3.2 " | 4.4 " | |
| Chlorides | — | — | 104 " | |
| Sugar | — | — | 111 mg. per cent | |
| Cholesterol | — | — | 253 " " " | |
| Calcium | — | — | 12.2 " " " | |
| Phosphorous | — | — | 3.2 " " " | |
| P.B.I. | 11.4 gamma per cent | 16 gamma per cent | 12 gamma per cent | |

| | (11-11-58) | (11-13-58) | (11-14-58) |
|---|---|---|---|
| Urinary 17-ketosteriods | 5.6 mg./24 hrs. | 7.5 mg./24 hrs. | 3.26 mg./24 hrs. |
| Blood pressure — normal | | | |

## DISCUSSION

These four cases have been investigated with particular emphasis on various biochemical parameters among which were: protein-bound iodine, cholesterol, blood sugar, calcium-phosphorous, pH (blood), uric acid, serum electrolytes, urinary 17-KS and 17-OH steroid excretion, and electrocardiographic examinations.

Calcium-phosphorus values seem to be perfectly normal and no physical signs (Chvostek's, Trousseau's, Erb's) suggestive of hypoparathyroidism were demonstrable in any of the patients. Blood sugar values in all the patients were completely normal. Cholesterol values were perfectly within the normal range in all the cases. Protein-bound iodine was elevated within the first two weeks in two cases with progressive diminution within the 3rd week. The values at the time the symptoms were observed, however, ranged from elevated to low values. The serum electrolyte results were interesting. Sodium was normal in all the cases, but potassium values were persistently low, ranging from 2.2 to 3.5 meq/L at the period when the symptoms were most evident. Curiously, the lowest potassium value observed (2.2 meq/L) was in the patient with quadriplegia. Chlorides were perfectly normal. The blood pressure was normal in all the cases.

## COMMENTS

Aside from the obvious background of a severe thyrotoxic disease and equally obvious measures to suppress it, we have no definite idea what produces this set of symptoms and how it is produced. We can only suggest that whatever it is, it seems to be intimately or remotely related with potassium metabolism. One instinctively wonders if the adrenal cortex might be the culprit. There are, however, no clinical signs that may suggest an increased or decreased adrenocortical activity; 17-KS and 17-OH steroid excretion was normal. Moreover, we wonder why all these symptoms have not been more frequently observed after surgical removal of the gland. There is also the possibility that the development of the symptoms depend on the retention in the body of substances resulting from the destruction of the

gland rather than from the sudden removal of such substances from the body. Another possibility is that some of the radioactive iodine introduced may produce radioactive metabolic by-products which act on liver cells and result in the production of the symptoms. The level of radioactivity alone, however, does not seems to be a very important factor, for two reasons; (1) we have given much bigger doses for patients with cardiovascular complaints without observing this phenomenon and (2) the syndrome appears when radioactivity detectable in the liver is almost negligible. The marked anorexia observed with these patients suggest that the liver is somehow involved. It is also possible that these patients may have from the very onset some form of sub-clinical Parkinsonism. Even in such a situation, however, one can not ignore the fact that some biochemical event occurring in these patients has contributed to making this Parkinsonism clinically manifest.

We feel justified in describing the set of symptoms as a syndrome for a number of reasons:

1. If it is a thyroid storm, then we may have here some biochemical data relative to a heretofore very vague syndrome.
2. In view of the almost classifical Parkinsonism that is observed, a study of the syndrome, may help considerably in elucidating the heretofore obscure problem of Parkinsonism.
3. In view of the consistent hypokalemia, one wonders at the wide possibilities for investigation.

## SUMMARY

This paper covers our observation on four cases which we feel might represent some unusual observations in connection with thyrotoxicosis and radioactive iodine therapy. They present principally in the form of anorexia, marked weakness occasionally progressing to complete quadriplegia, restlessness, tremors later on progressing ·Parkinson-like movement, and auricular fibrillation. These symptoms come on or about the 3rd or 4th week after therapy and are especially observed in the severely thyrotoxic cases, regardless of whether or not they have received previous antithyroid therapy. The salient features of these cases can be summarized as follows:

1. All the cases uniformly presented marked weakness. Two cases showed classical Parkinson-like movement and mask-like facies.

2. The syndrome appeared uniformly on the 3rd or 4th week after therapy.

3. All the patients presented significant hypokalemia corresponding to the severity of the manifestations.

4. All the cases were severely thyrotoxic. Two were rendered euthyroid with Tapazole while the others did not have any antithyroid preparation.

5. Calcium-phosphorus values were normal in all.

6. Cholesterol values were normal in all.

7. Protein-bound iodine values showed no relation to the symptoms. Some presented elevated, others normal, while still others depressed PBI values.

8. Blood pH in a few was normal; this makes the possibility of alkalosis and acidosis coming into the picture quite unlikely.

9. Blood sugar was normal in all.

10. Serum sodium and chlorides were normal.

11. 24 hour 17-KS and 17-OH steroid excretion was within the normal range.

12. All the symptoms lasted from one to four weeks with spontaneous improvement in all cases.

## ACKNOWLEDGMENTS

Acknowledgment is hereby made to Dr. Mario Gutierrez of the Department of Medicine, P.G.H., who helped take care of the cases; to Dr. Angel Florentin, also of the Department of Medicine, who did the urine 17-KS and 17-OH studies; to Mrs. Serapia Roque-Rubio, who did the serum electrolyte studies; and to the numerous patients of the Thyroid Clinic who wholeheartedly cooperated in the investigations.

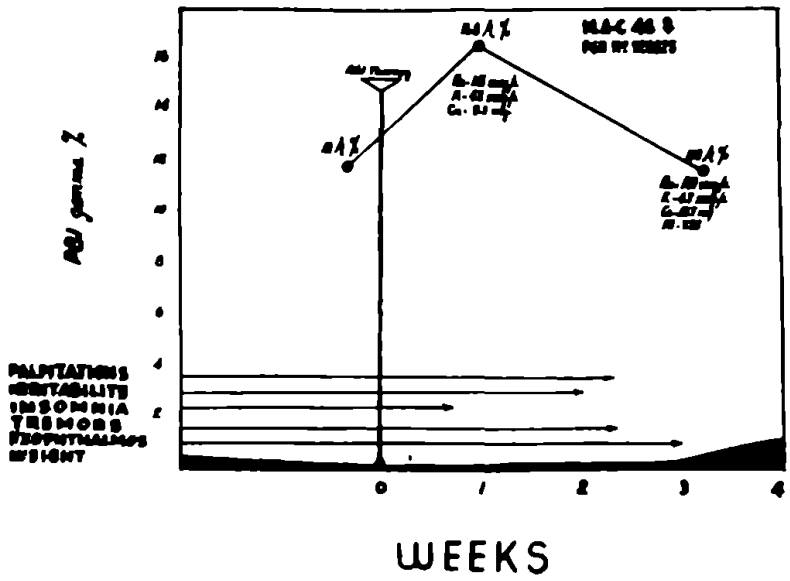


Fig. 1 A Case of Thyroxine Release Syndrome.

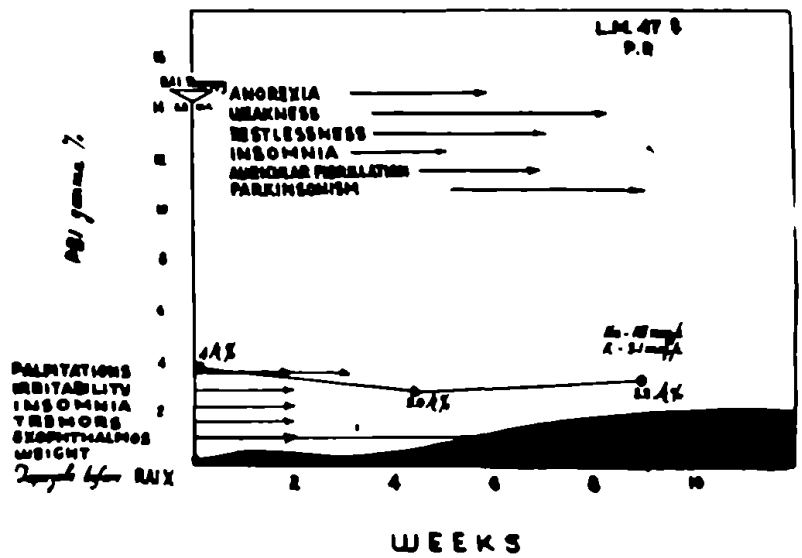


Fig. 2 Case No. 1.

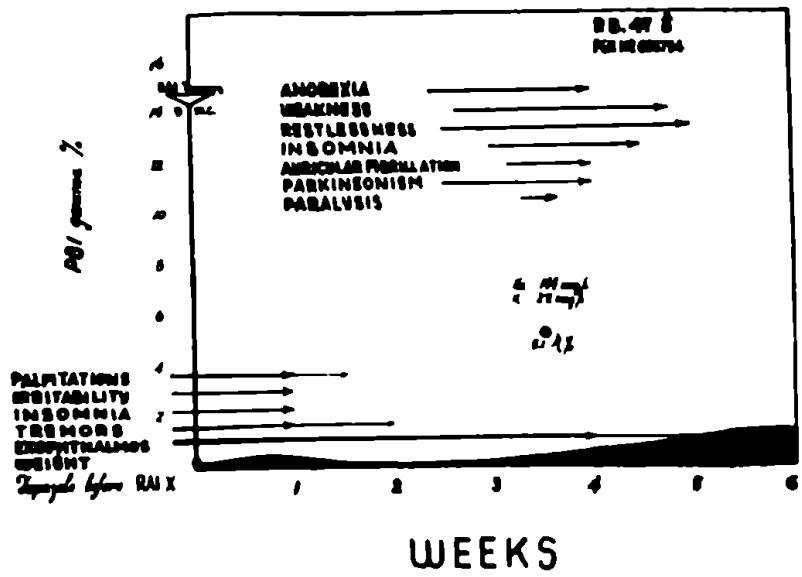


Fig. 3 Case No. 2.

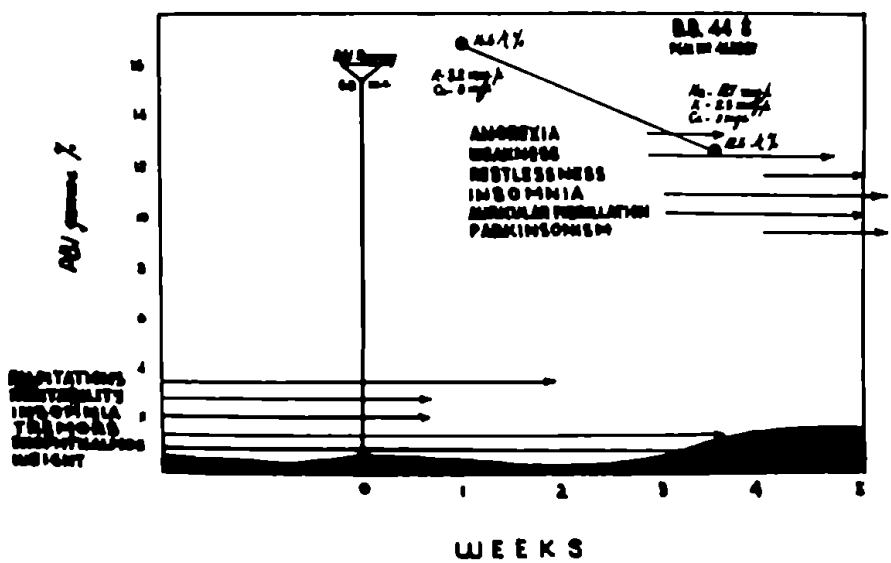


Fig. 4 Case No. 3.

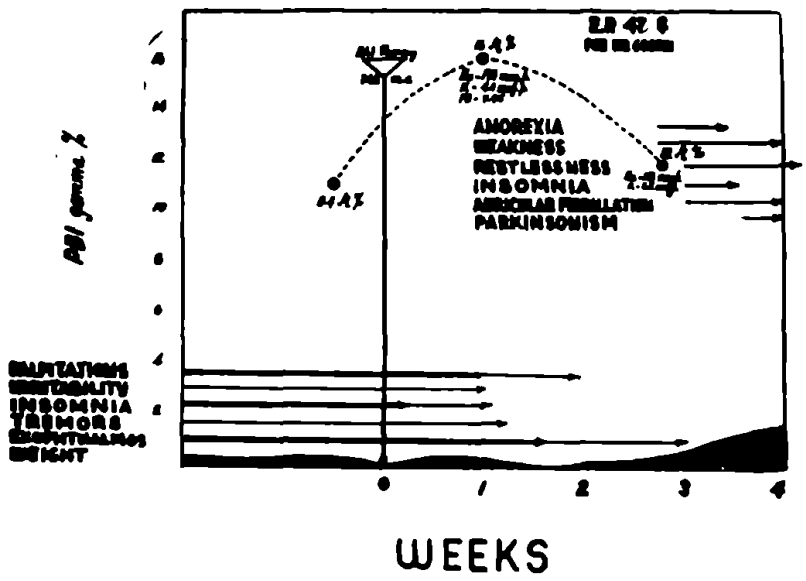


Fig. 5 Case No. 4.

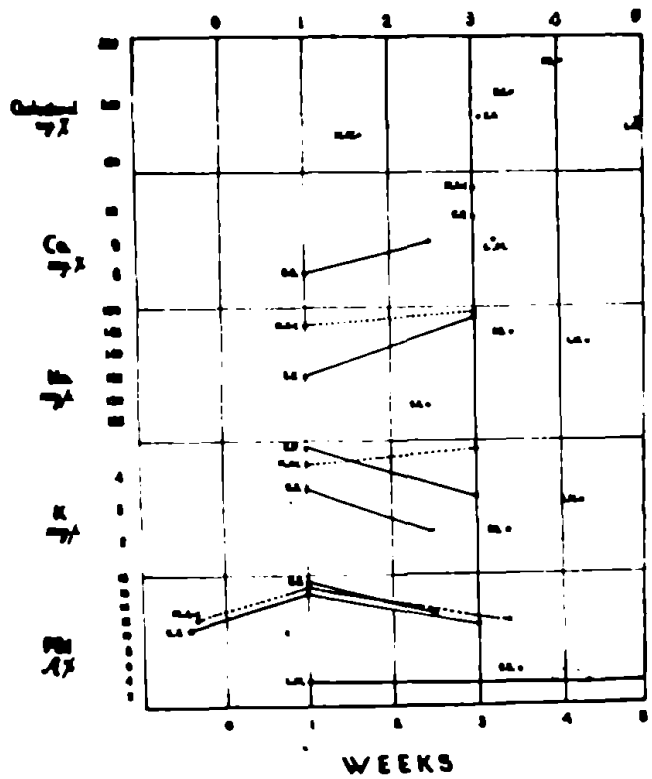


Fig. 6 Changes in Laboratory Findings.