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Postmortem Behavior of Serum Thyroxine, Triiodothyronine, and Parathormone

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ABSTRACT: Comparison of thyroxine, triiodothyronine, and parathormone levels in antemortem and postmortem sera was done by radioimmunoassay. In all but one of twelve cases, thyroxine levels irregularly declined after death, but this was statistically significant in only five patients. Triiodothyronine was assayed in eleven patients; two levels fell, six rose, and two remained unchanged as late as 17.75 h after death. One patient had a decline in hormone level, followed by an elevation. Five of the eleven patients assayed for parathormone maintained stable levels for as long as 17.75 h after death. Five levels showed an elevation, and one, a decline followed by an elevation. The erratic behavior of triiodothyronine and parathormone after death may be due to conversion from thyroxine or from heterologous forms of parathormone, respectively. It was noted that hormone levels from the inferior vena cava tended to be higher than those from femoral veins, with diffusion of hormone from decomposing glands in the neck as a possible cause.

KEY WORDS: pathology and biology, hormones, postmortem examinations

Knowledge of the postmortem behavior of serum hormones has two potential, related applications: the estimation of the time of death and the assessment of the hormonal status in life. When the time of death is to be estimated, autopsy must reveal no morphological basis for antemortem endocrine dysfunction. If the status of hormone levels during the life of the patient is to be determined, the time of death must be accurately known.

Coe [*1*] has previously reported on serum thyroxine and thyroid-stimulating hormone. He found that thyroxine tends to fall irregularly after death, but thyroid-stimulating hormone remains fairly stable for one or two days postmortem.

We assayed antemortem and postmortem sera from twelve autopsied patients at St. Luke's Hospital for thyroxine and from eleven patients for triiodothyronine and parathormone (COOH-terminal moiety). Our interest was particularly directed towards triiodothyronine and parathormone. Because the structure of the former varies from that of thyroxine by the absence of a single iodine atom, it seemed possible that degradation of thyroxine after death might lead to increased serum triiodothyronine. Similarly, because of

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the immunoheterogeneity of parathormone [2] and because we measured only a portion of the intact molecule, we thought anomalous behavior might also be found with this assay.

Method

The twelve patients in the study consisted of six males and six females, with ages ranging from 44 to 87 years. The terminal illness in each instance was of a chronic nature (cancer, congestive heart failure, bronchiectasis, lung abscess, bullous emphysema, and nonlethal carbon monoxide poisoning), with the exception of one individual (Patient 4), who died ten days after a myocardial infarction. The time of death of each was known to within 10 min, except for one case where the possible error was 15 min. Postmortem intervals varied from 2.75 to 23.75 h. Antemortem blood specimens were retrieved from blood drawn for other purposes within the 48 hours before the patient died, except for some instances in which death was anticipated and the blood already obtained during the final hospitalization. One patient lacked sufficient serum for the determination of the antemortem parathromone level, while in another case only enough serum for thyroxine assay was available. Postmortem sera were obtained from the inferior vena cava. Two patients also had blood drawn before autopsy from either femoral vein. All specimens were spun and frozen for later assay. Radioimmunoassays of serum thyroxine and triiodothyronine were carried out with kits provided by Kallestad Laboratories (Chaska, Minn.), using the method of Hales and Randle [3]. The COOH-terminal moiety of the parathomone molecule was assayed by a similar radioimmunological procedure with kits from Cambridge Nuclear Corporation (Billerica, Mass.). At least 85% of circulating immunoreactive parathormone in living subjects consists of such carboxyl-terminal fragments of the intact molecule, with the remaining antigen composed of NH_2-terminal parathormone [4]. The assays were performed with duplicate specimens, except for four samples in which duplicate parathormone assays could not be done because of a lack of serum. There was satisfactory agreement with controls and between duplicate samples. Statistical analysis was done with a Hewlett-Packard Model 9830A computer.

All twelve patients were clinically euthyroid and free of parathyroid disease. Serum calciums, or calcium/albumin ratios, and serum phosphates were normal in the eleven patients assayed for parathormone. Several patients had received glucocorticoid medications within the previous two months, and one each had been taking an androgen and diphenylhydantoin. These agents are known to affect thyroid hormone levels by their influence on thyroxine-binding globulin [5]. At autopsy, two patients had adenomatous goiters. In two other patients, the neck was not examined. In a further two cases, the parathyroids could not be found. All remaining cases had normal anatomy.

Results

The results are listed in Table 1 and indicate the concentrations of each of the three hormones from the twelve patients.

Serum Thyroxine

All but four of the twelve patients had normal antemortem thyroxine levels. The four (Patients 6, 7, 9, and 12) with levels well below normal had triiodothyronine-uptake assays (Mallinckrodt, Inc., St. Louis, Mo.) performed. These were in the commensurate "hyperthyroid" range, indicating low thyroxine-binding globulin, from medications or chronic illness, as the cause of the diminished thyroxine value [6].

Our data confirmed Coe's finding [1] in that eleven of the twelve patients demonstrated an irregular decline in their serum thyroxine levels after death. In Coe's series, 21 of 22 cases

TABLE 1—*Postmortem intervals and serum hormone concentrations (thyroxine, triiodothyronine, and parathormone).*

Patient	Site and Time of Sampling (Hours Postmortem)[a]	Thyroxine,[b] μg/dl		Triiodothyronine,[c] ng/dl		Parathormone,[d] pg/ml	
		Antemortem	Postmortem	Antemortem	Postmortem	Antemortem	Postmortem
1	IVC, 2.75	5.9	2.1[e]	57.8	<25[e]	416.7	443.5
2	IVC, 4.0	4.9	3.6	...	...	...	...
3	IVC, 4.1	4.6	4.0	<25	63.8[e]	828.9	1563.1
4	IVC, 4.25	6.7	7.7	127.1	236.9[e]	332.9	1008.9[e]
5	IVC, 6.5	6.8	6.0	56.2	354.2[e]	638.0	1087.1[e]
6	IVC, 7	2.5	1.8	<25	<25	850.6	852.9
7	IVC, 7.25	2.8	2.7	<25	64.2[e]	449.0	1532.2[e]
8	IVC, 12.5	7.1	5.0	54.0	39.5[e]	647.3	840.0
9	IVC, 17.75	2.4	1.8[e]	<25	<25	960.7	1181.0
10	IVC, 23.75	6.4	5.3[e]	71.9	371.6[e]	1269.6	1830.1[e]
11	LFV, 3.75	5.4	3.4[e]	54.3	26.5[e]	no specimen	473.9
	RFV, 11.75	...	3.4	...	44.8	...	428.5
	IVC, 20	...	5.3[e]	...	212.1[e]	...	1389.0[e]
12	RFV, 5	3.8	2.2[e]	<25	<25	318.3	213.2[e]
	LFV, 14.25	...	2.1	...	<25	...	260.4
	IVC, 15	...	3.2	...	44.2[e]	...	988.3[e]

[a]IVC = inferior vena cava; RFV = right femoral vein; and LFV = left femoral vein.
[b]Normal range, 5.0 to 12.0 μg/dl.
[c]Normal range, 90 to 200 ng/dl.
[d]Normal range, up to 450 pg/ml (most hyperparathyroid patients have levels over 600 pg/ml).
[e]Statistically significant alteration (>2 standard deviations) from previous level.

showed this pattern. However, in only five of our twelve was the decline statistically significant. The shortest postmortem interval before such a decline was 2.75 h, while the longest interval with unaltered thyroxine levels was 12.5 h. Patient 11, the sole case wherein a statistically significant elevation occurred, developed this elevation in blood from the inferior vena cava 8.25 h after blood from a femoral vein had shown a decline from the antemortem value.

Serum Triiodothyronine

Serum triidothyronine was assayed in eleven patients. Ten had subnormal levels in life; such findings, however, can result from a variety of causes, including chronic illness as was present in all ten, and are not sufficient in themselves to diagnose hypothyroidism [5]. Nine showed significant alterations in their postmortem samples: three patients had an initial decline in serum triiodothyronine levels and six an elevation. Two patients, with low levels in life, retained hormonal levels below the limit of reliable measurement (25 ng/dl). Decline in triiodothyronine was seen in samples obtained from 2.75 to 12.5 h after death; elevation, from 4.1 to 23.75 h after death; and unaltered levels were found as late as 17.75 postmortem. One individual (Patient 11), who had a decline in a femoral sample, and another (Patient 12), with low but unaltered triiodothyronine from the same site, later demonstrated significantly elevated values in their inferior vena cava specimens.

The rates of change of triiodothyronine levels were not uniform, and there was no apparent relationship to the patient's thyroxine level.

Serum Parathormone

Six patients had elevated parathormone levels in their blood during life. One (Patient 3) had been diagnosed as having sarcoidosis; one (Patient 8) had carcinoma of the pancreas, and another (Patient 6) had adenocarcinoma of the uterus, both potential sources of ectopic parathormone [7]. All six had normal serum calcium or a normal calcium/albumin ratio and were asymptomatic of parathyroid disease. The parathyroid glands of three of the six patients (Patients 6, 8, and 10) were examined at autopsy, and these were described as normal. It is possible that these cases are examples of overlap between normal and hyperparathyroid parathormone distributions. Five of the patients (Patients 5, 6, 8, 9, and 10) were 50 years of age or older; parathormone levels are, on the average, higher than the accepted normals in this age group [8]. In addition, part of the parathormone activity may be spurious, since this assay loses some precision as hormone levels climb into the elevated range.

Five of the eleven patients showed no significant alteration in serum parathormone level in postmortem intervals from 2.75 to 17.75 h. The remaining six cases included five with an irregular increase in the hormone in postmortem intervals from 4.25 to 23.75 h. The final case had a decline in the hormone level, as measured in a femoral vein, 5 h after death. Ten hours later, a sample from the inferior vena cava had an elevated level.

Conclusions

1. The serum thyroxine level tends to fall after death. In most cases, this fall is not of significant proportion in the first several hours postmortem. The erratic rate of decline precludes the use of this hormone in the estimation of the time of death, but it can possibly be of use in the determination of hyperthyroidism. In a previously published case report [9] the thyroxine level, still elevated several days after death, confirmed this diagnosis.

2. Serum triiodothyronine may rise or fall by various degrees after death. In some cases this behavior may be due to conversion from serum thyroxine. Serum triiodothyronine is of no apparent use either in estimating the time of death or in assessing the endocrine status during life.

3. Serum parathormone levels likewise show erratic alterations after death, possibly because of conversion of heterologous molecules to the COOH-terminal fragment measured. The assay is therefore of little use in predicting the time of death or in confirming the presence of hyperparathyroidism before death.

4. A total of six serial assays was carried out in two patients, the early specimens being drawn from the femoral veins and the last, from the inferior vena cava. In each instance, the specimen from the inferior vena cava showed an elevation of hormone level, be it thyroxine, triiodothyronine, or parathormone, over the preceding sample from a femoral vein. Five of these six elevations were statistically significant. It is therefore possible that diffusion of hormones from the decomposing glands in the neck reaches the inferior vena cava. It is recommended that all blood sampling for thyroid and parathyroid hormones be done from a peripheral site, such as a femoral vein.

Summary

Sera from twelve autopsied patients were assayed for thyroxine, and eleven sera were assayed for triiodothyronine and parathormone. An irregular decline in thyroxine was found, confirming earlier reports. Triiodothyronine and parathormone may rise or fall after death and should not be used for predicting endocrine status in life. Levels in samples obtained from the inferior vena cava tended to be higher than those from femoral veins, suggesting diffusion of hormones from decomposing glands into the former site.

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