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A Case of Overt Hypothyroidism with Cardiac Autonomic Neuropathy with Contradictory Findings in Autonomic Reactivity: Interesting Case Report.

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ABSTRACT

A 62-year-old lady of hypothyroidism whose autonomic function was evaluated revealed contradictory findings on sympathetic reactivity testing. She had co-morbidities of diabetes and hypertension and we performed the full battery of basic autonomic functions and the results showed severe loss of cardiac autonomic tone which was expected as well as loss of parasympathetic reactivity. However sympathetic reactivity testing showed fall of 24 mm Hg of SBP in lying to standing test and rise of 38 mm Hg DBP in Hand grip test. The former suggests loss of sympathetic reactivity while the latter suggests increased sympathetic reactivity.

Keywords: hypothyroidism, neuropathy.

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INTRODUCTION

Hypothyroidism is an endocrinological condition with different aetiologies characterized by reduced metabolic rate which leads to decreased body temperature, intolerance to cold and dry skin. [1]An accumulation of extracellular matrix with mucopolysaccharides causes characteristic clinical features of non-pitting myxedema such as enlarged tongue, hoarseness, joint stiffness and entrapment syndromes. Constipation, loss of hair and anaemia are also seen. Apart from these, there is also an alteration in Autonomic functions. [1] Although both the limbs of the autonomic function system are affected in hypothyroidism, major change is observed in the Sympathetic limb. Adrenergic activity is reported to be markedly decreased leading to bradycardia and other cardiovascular autonomic sympathetic responses. Thyroid hormones are synergistic with catecholamines in increasing metabolic rate, heart rate, motor activity and excitation of central nervous system. [1] Thyroid hormones are known to enhance the number of beta adrenergic receptors in the heart. [2] Hypothyroidism in rats blunts the arterial baroreflex and alters the relative contribution of systems that maintain resting blood pressure and heart rate with a predominant sympathetic influence at rest which compensated for the lower intrinsic heart rate of hypothyroid rats, and the blunted arterial baroreflex would reduce the capacity to maintain blood pressure in situations that require reflex activation of the sympathetic system like stress or exercise. [3] Inukai et.al studied the relationship between hypothyroidism and parasympathetic nervous system and observed that in marked hypothyroidism there are hypofunctional abnormalities in the parasympathetic system in association with a reduction in the levels of serum T4 and T3 [4]

In summary, hypothyroidism causes increased sympathetic discharge to maintain resting blood pressure in the face of decreased heart rate and also causes a decrease in parasympathetic tone. With reference to these changes, we present an interesting case which presented to our lab.

Case: Mrs X was referred to our Autonomic Function Lab, Department of Physiology from Endocrinology OPD of AIIMS Jodhpur with a clinical history of Diabetes Mellitus type 2 having this primary disease for 10 years also associated with Hypertension and Hypothyroidism. She was referred to the lab for evaluation of Autonomic Functions. We evaluated both cardiovascular autonomic tone and reactivity. A standard battery of autonomic reactivity testing was undertaken. Upon evaluation we found that she had severely decreased Heart Rate Variability (HRV) with marked loss of autonomic tone. On reactivity testing there was a severe loss of Parasympathetic reactivity (according to Ewing's criteria) with postural hypotension in Lying to Standing test with a fall of 24 mm Hg. In view of this it was surprising to note a rise of 38 mm Hg in Diastolic blood pressure when we performed the hand grip test. The results of cold pressor test was a 16 mm Hg rise in diastolic blood pressure.

DISCUSSION

Hypothyroidism is characterised by a decreased sensitivity and down regulation of adrenergic receptors which are required for normal sympathetic reactivity and tone. This is in light of the fact that thyroid hormone is required for the production of adrenoceptors probably by transcriptional activation of gene expression of these proteins or by causing increased expression of these receptors on the cell membrane. However, there is a paradoxical increase in adrenaline in spite of sympathetic withdrawal which probably reflects the effort of the physiological system to compensate for the decreased sensitivity and number of receptors seen in hypothyroidism. In our patient, in view of the dramatic fall in blood pressure in lying to standing test, we would have expected a subnormal or at the very most a normal response to the hand grip test which involves the pressor reflex. However, this was not the case as we recorded a 38 mm Hg rise in diastolic blood pressure. This highlights the importance of factors other than the increase in sympathetic outflow which occurs when our posture changes from lying to standing such as the peripheral venous pump, competent valves and rise in abdominal pressure for maintaining the blood pressure. Another major factor which could explain the observed finding is the presence of hypertension in our patient as it is well known that hypertension causes reduced sensitivity of the baroreceptors in the carotid sinus due to increased stiffness. Since the pressor reflex involves a different afferent limb (metabo- and mechano-receptors within muscle spindle) compared to the baroreflex we can surmise that the efferent limb involving the sympathetic response to stimuli is intact as even the cold pressor elicited the expected blood pressure changes. However, the dramatic rise in blood pressure in the handgrip test remains unexplained. The cardiovascular changes in

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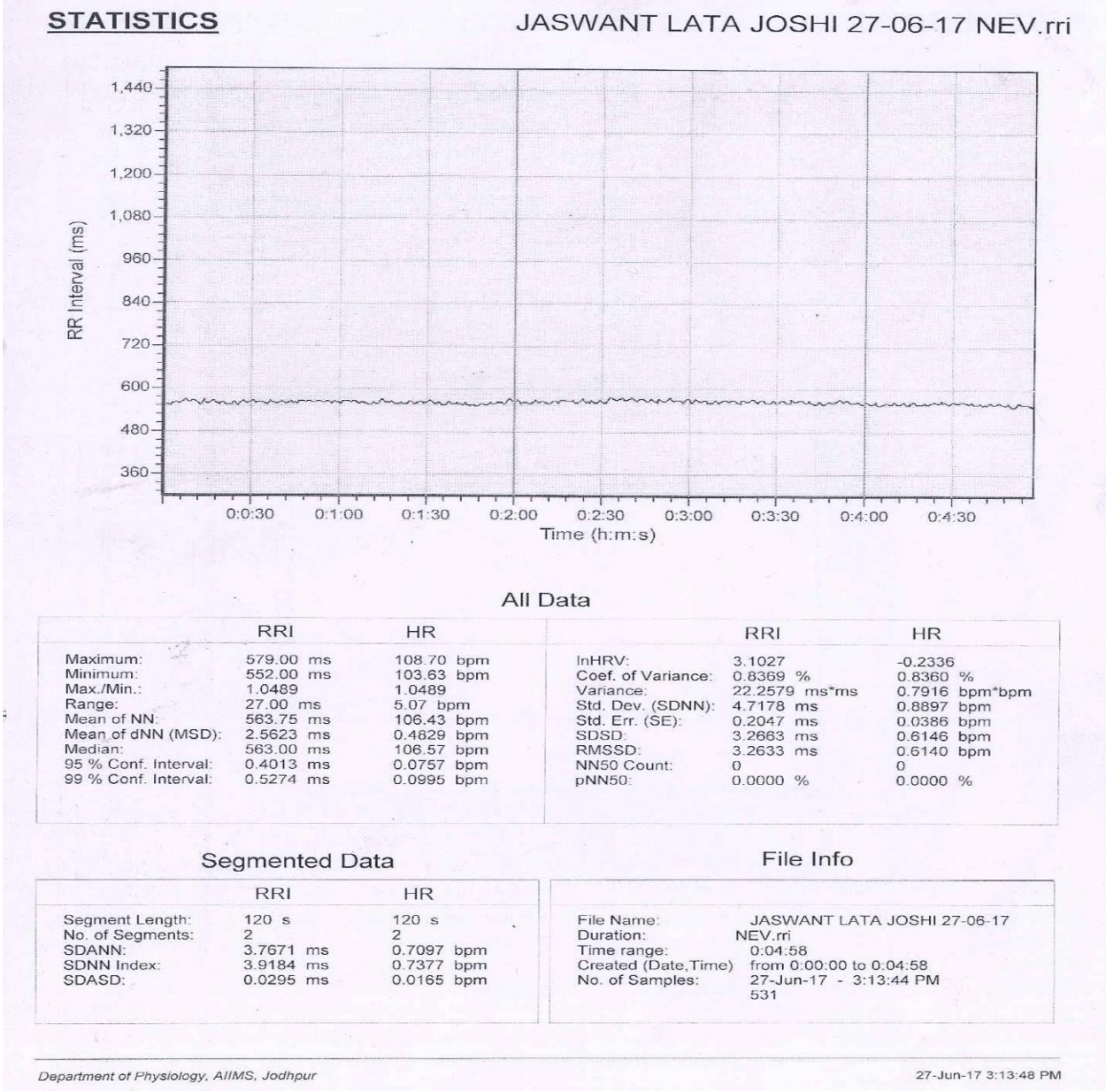
hypothyroidism which include reduced mean circulatory filling pressure, reduced heart rate and stroke volume are other contributing factors which can influence the cardiovascular autonomic response.



Poincare plot analysis

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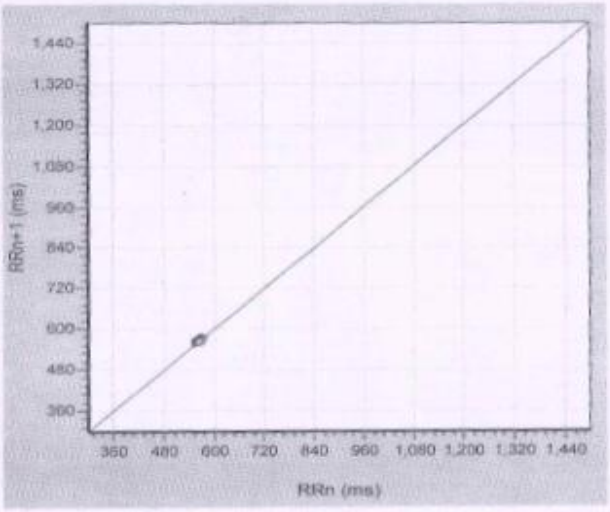
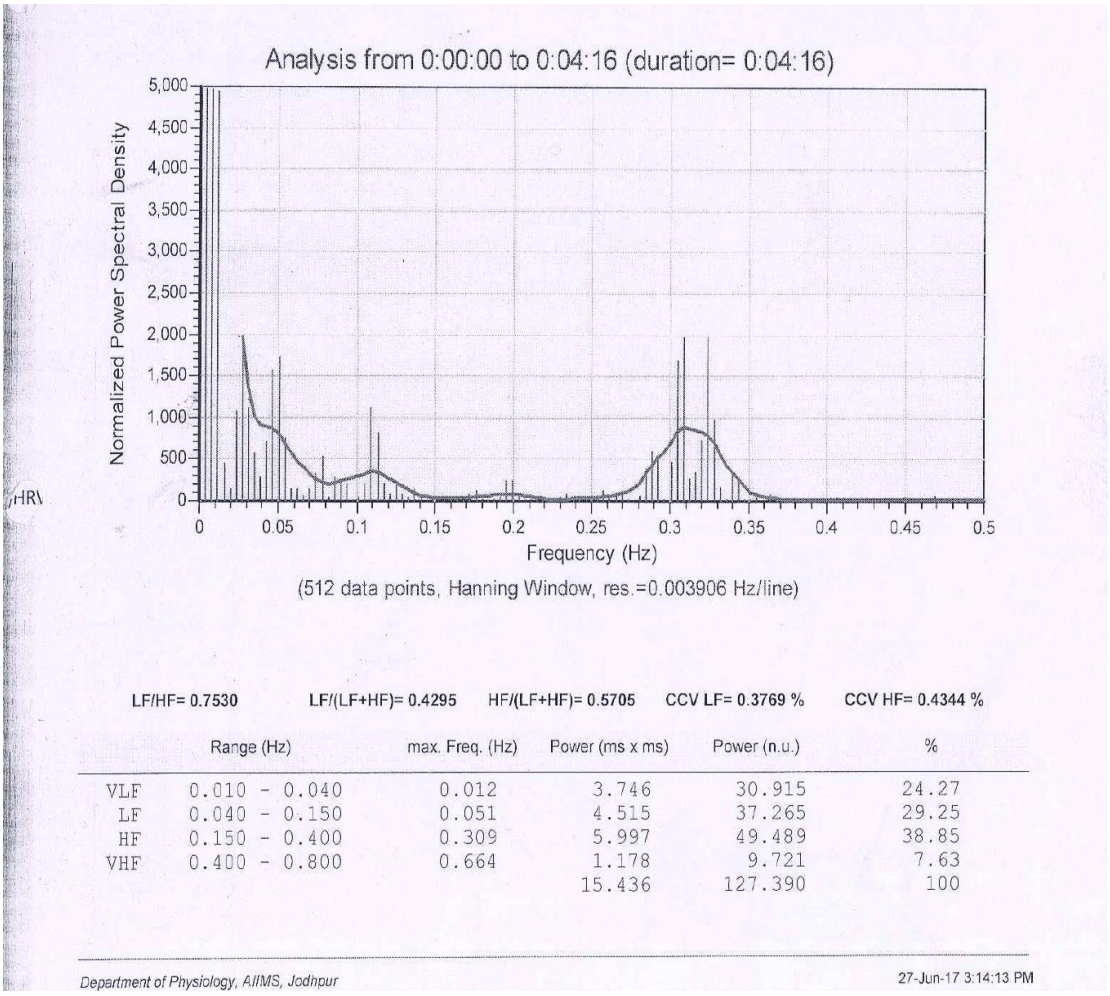


SD1 abs.	2.3096 ms	dRRt abs.	14.1421 ms	Centroid	563.7566 ms
SD2 abs.	6.2448 ms	dRRr abs.	34.6482 ms	Ellipse Area	45.3122 ms^2
SD1 norm.	0.4097 n.u	dRRt norm.	2.5086 n.u	R^2	0.5969
SD2 norm.	1.1077 n.u	dRRr norm.	6.1460 n.u	SEE	2.9589
SD1/SD2	0.3698	dRRt/dRRr	0.4082		
CSI	2.7038				
CVI	2.3632				



LF/HF= 0.7530 LF/(LF+HF)= 0.4295 HF/(LF+HF)= 0.5705 CCV LF= 0.3769 % CCV HF= 0.4344 %

	Range (Hz)	max. Freq. (Hz)	Power (ms x ms)	Power (n.u.)	%
VLF	0.010 - 0.040	0.012	3.746	30.915	24.27
LF	0.040 - 0.150	0.051	4.515	37.265	29.25
HF	0.150 - 0.400	0.309	5.997	49.489	38.85
VHF	0.400 - 0.800	0.664	1.178	9.721	7.63
			15.436	127.390	100

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Reactivity Testing

Basic Autonomic Function Test				
	Test	Normal Range	Results	
1	Deep Breathing Test			
a.	Change in Heart Rate	≥ 15 bpm	8	
b.	E:I Ratio	≥ 1.21	1.07	
2	Valsalva maneuver			
	Valsalva Ratio	≥ 1.21	1.17	
3	Isometric Exercise Test (Hand- Grip)			
	Rise in Diastolic	≥ 16 mmHg	38	
4	Cold Pressure Test			
	Rise in Diastolic Blood Pressure	≥ 10 mmHg	16	
5	Postural Challenge (Lying to Standing)			
a.	Change in Systolic Blood Pressure	Fall of ≤ 10 mmHg	24	
b.	30:15 Ratio	≥ 1.04	1.00	

CONCLUSION

Further evaluation of this patient might be needed to explain the paradoxical findings on sympathetic reactivity testing. In addition, this case highlights the close relationship of thyroid hormone with the cardiovascular system, especially the neural components responsible for maintaining homeostasis in response to physiological stimuli.

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