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A COMPARATIVE STUDY OF THE EFFECTS OF VARIOUS TREATMENTS ON THE CALCIUM AND PHOSPHORUS METABOLISM IN TETANY

II. CHRONIC ADULT IDIOPATHIC TETANY

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Chronic tetany in adults is usually one of two types. In the first type it is associated with loss of parathyroid glands during operations of thyroid. In the second, it occurs in individuals with lesions in the gastro-intestinal tract leading to alkalosis. Cases of chronic tetany in elderly individuals unassociated with either of the above-mentioned conditions are extremely rare in the literature. The following case is recorded on this account as well as in view of metabolic data obtained that may throw some light on the pathogenesis of this type of tetany.

REPORT OF CASE

L. H. C., Hospital No. 15810, a Chinese man of 46, unmarried, gardener by occupation, was admitted to the Peking Union Medical College Hospital on January 14, 1927, and discharged slightly improved on June 20, 1927.

Present illness. The patient remained in excellent health until three years and a half before admission when he first noticed spasmodic stiffness of hands and arms, and at times of feet and legs. The spastic attacks started from the finger tips, spreading upward to the arms and shoulders, usually preceded by numbness and a prickling sensation. With severer attacks, there were slurring of speech, feeling of obstruction in the larynx and difficulty in deglutition. Each attack lasted from a few minutes to many hours, occurring with a frequency varying from several times a day to once in several days. At times the spasms were more or less continuous. Both the severity and frequency of the attacks bore no relation to season. Shortly after the onset of the spastic attacks, he began to have diarrhea, 10 to 15 stools daily, watery, with mucus, but no blood. Abdominal cramps and tenesmus were present. Since the acute attack of diarrhea, which lasted for about a month, his stools continued to be loose, once or twice daily. A year ago, he had the first attack of unconsciousness with clonic convulsions of all extremities, cyanosis, stertorous breathing and foaming in mouth. He regained consciousness

in about ten minutes. Since then, similar epileptiform fits have occurred irregularly once every few days to once in several months. The last attack, which prompted his visit to the hospital, took place two days prior to admission.

Past history. He had no past illnesses that he could recollect. No operation had been performed on his neck. There was no history of tetany in early childhood, and no other members of the family were similarly affected. His diet was not essentially different from that of the laboring class to which he belongs. There was no nausea, vomiting or other gastro-intestinal disturbance in the past that would possibly suggest gastric tetany.

Physical examination. This revealed a middle-aged man, well-developed and fairly well-nourished. Weight 56.9 kgm. Height 164 cm. His hands and feet were held in typical carpopedal spasm. A strongly positive Chvostek's sign was obtained. Raising the arms vertically over the head caused pain in the upper extremities (Pool's phenomenon). Besides the signs of hyperirritability of the neuro-muscular system, other neurological examinations were negative. The hair was normal, and there were no dental changes. The thyroid gland was palpable, but not enlarged. The heart and lungs were normal. Blood pressure 98/72. The abdomen was slightly distended with gas. The liver, spleen and kidneys were not palpable.

Laboratory findings. Urinalysis showed no albumin, and no sugar. Indican reaction was slightly positive. Stools were semi-fluid containing ascaris and hookworm ova in small numbers. Blood examination: White blood cells 7200 with 66 per cent of polymorphonuclear neutrophiles, 12 per cent of lymphocytes, 9 per cent of large mononuclears, 12 per cent of eosinophiles, and 1 per cent of basophiles. Blood Wassermann reaction and Kahn test were negative. Total serum calcium was 6.0 mgm. per 100 cc. with 2.4 mgm. diffusible, and 3.2 mgm. non-diffusible. Serum inorganic phosphorus was 7.21. mgm., plasma sodium chloride 550 mgm., and carbon-dioxide combining power 67.2 volumes per cent. Basal metabolism with Tissot's spirometer was +0.2 per cent. Gastric analysis showed no free acid either in the fasting content or in the specimen one hour after the Ewald's test meal. Gastro-intestinal roentgen ray examination revealed some retention of barium meal in ascending, transverse, and descending colon in 48 hours. Otherwise it was normal. Roentgenogram of pelvis showed no changes in the bones.

RESULTS

This patient was put on the same régime and studied in the same manner as the two cases reported in the first paper of this series (1). His diet was kept constant throughout the experimental period with an intake of calcium of approximately 0.35 gram daily. The results of the study are summarized in table 1 and chart 1.

The first line of treatment was parathyroid extract given subcu-

TABLE 1

Period	Date	Treatment	Intake			Output			Balance		Retention		Blood serum			Plasma					
			Ca	P	CO ₂	Urine	Stool	Total	Ca	P	Ca	P	Total	Diffusible	Non-diffusible	Ca	P				
			grams	grams	vol.-%	grams	grams	grams	grams	grams	per cent	per cent	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.				
1927																					
1	January 19-22		1.3960	5.3590	0.2037	3.0540	1.2440	1.3600	1.4477	4.4140	-0.0517	0.9450	-3.7	17.6	6.0	2.4	3.2	7.21	550	67.2	
2	January 23-26	Parathyroid extract 60 units daily	1.4190	5.3138	0.1223	3.4610	1.1970	1.5820	1.3193	5.0430	0.0997	0.2708	7.0	5.1	6.5	3.2	3.1	7.10	594	61.4	
3	January 27-30	Parathyroid extract 25 units daily	1.4540	5.0178	0.1136	3.1460	0.9100	1.0100	1.0236	4.1560	0.4304	0.8618	29.6	17.2	9.0	6.5	3.6	6.25	575	65.5	
4	January 31-February 3		1.3367	5.1024	0.3283	1.9648	0.3250	0.5750	0.6533	2.5398	0.6834	2.5626	51.1	50.2	6.2	2.9	3.7	6.25	588	60.7	
5	February 12-15	HCl 10 per cent 12 cc. daily	1.4296	4.6574	0.3114	2.4184	0.4987	0.6246	0.8101	3.0430	0.6195	1.6144	43.3	35.7							
6	February 16-19	HCl 10 per cent 14 cc. daily	1.4440	4.3242	0.3382	2.2654	0.8867	1.1993	1.2249	3.4647	0.2191	0.8595	15.2	19.9	5.8	3.3	2.5	7.14	597	55.7	
7	February 20-23	HCl 10 per cent 28 cc. daily	1.4410	3.8596	0.3121	2.4496	0.9860	0.9657	1.2981	3.4153	0.1429	0.4443	9.9	11.5	5.2	3.1	2.5	6.67	582	65.2	
8	February 28-March 3	CaCl ₂ 2 grams daily	4.3260	3.5564	0.2737	1.8165	1.4203	0.5406	1.6940	2.3571	2.6320	1.1993	60.8	33.4							
9	March 4-7	CaCl ₂ 2 grams daily	4.2975	3.4874	0.2523	2.0230	2.5345	1.1211	2.7868	3.1441	1.5107	0.3433	37.5	9.8	6.5	3.2	3.3	7.70	569	65.5	
10	March 8-11	CaCl ₂ 2 grams daily	4.2770	3.3934	0.2673	1.9053	1.9629	0.8964	2.2302	2.8017	2.0468	0.5917	47.9	17.7	6.5	2.6	3.9	8.33	569	65.3	
11	March 12-15	Cod liver oil 30 cc. daily	1.4337	3.5132	0.2399	1.7144	1.1266	0.9268	1.3665	2.6412	0.0672	0.8720	4.7	24.8	6.5	2.6	3.9	9.09	562	69.1	
12	March 16-19	Cod liver oil 30 cc. daily	1.4018	3.3302	0.2299	1.213	1.4159	0.7945	0.6451	2.9158	-0.2433	0.4144	-17.3	12.4							
13	March 20-23	Cod liver oil 30 cc. daily	1.4298	3.9524	0.3041	2.2687	0.8120	0.8232	1.1161	3.0919	0.3137	0.8605	21.9	21.8	6.5	3.3	3.2	7.14	559	69.1	
14	March 24-27		1.4227	3.4914	0.2962	1.9995	0.8767	0.7816	1.1729	2.7811	0.2498	0.7103	17.5	20.3							
15	March 28-31	Kaolin 30 grams daily	1.4223	3.4244	0.3665	1.9016	1.0150	1.7863	1.3815	3.6869	0.0407	-0.2625	2.8	7.7	6.5	3.2	3.4	3.84	575	64.3	
16	April 1-4	Kaolin 30 grams daily	1.3747	3.3464	0.3383	2.0017	0.3559	0.6923	0.6942	2.6940	0.6805	0.6524	49.5	19.3	6.4	3.2	3.3	6.66	583	65.3	
17	April 5-8		1.3610	3.2772	0.3091	1.9909	0.8043	0.8791	1.1134	2.8700	0.2476	0.4072	18.2	12.4							
18	April 9-12		1.4145	3.5576	0.2684	2.1919	0.8715	0.8850	1.1399	3.0769	0.2746	0.4807	19.4	13.5	6.5	3.6	3.1	6.25	600	65.5	
19	April 13-16	Parathyroid extract 72 units daily; CaCl ₂ 2 grams daily	4.2548	3.1728	0.5026	3.4809	1.5360	0.5448	2.0386	4.0257	2.2162	-0.8529	52.1	-26.9	9.6	6.8	3.1	5.00	575	66.4	
20	April 17-20	Parathyroid extract 60 units daily; CaCl ₂ 2 grams daily	4.2783	3.2358	1.4409	2.9045	1.9310	0.9362	3.3719	3.9407	0.9064	-0.6049	21.2	-18.7	11.1	6.6	4.6	4.35	587	70.2	
21	April 29-May 2	Ultraviolet radiation (3 days only)	1.4076	3.9454	0.4136	2.1926	0.8720	0.7644	1.2856	2.9570	0.1220	0.9884	8.7	25.1	6.8	3.4	3.4	5.20	562	72.1	
22	May 3-6	Ultraviolet radiation	1.4440	4.1694	0.2961	2.1852	1.1285	0.8991	1.4246	3.0843	0.0194	1.0851	1.3	26.0	6.6	3.2	3.5	5.88	569	71.1	
23	May 7-10	Ultraviolet radiation (3 days only)	1.3376	3.5444	0.3976	1.8096	0.7152	0.6329	1.1131	2.4425	0.2245	1.1019	16.8	31.1	6.6	3.5	3.1	6.66	578	64.3	
24	May 11-14	Ultraviolet radiation (3 days only)	1.3377	3.8252	0.2858	2.0766	0.9586	0.6233	1.1444	2.6999	0.1933	1.1253	14.5	29.4	6.6	3.5	3.1	8.33	575	71.1	

taneously 60 units a day for two periods of four days each. This was followed by complete disappearance of tetany with cessation of diarrhea and epigastric discomfort. His serum calcium was raised from 6.0 to 9.0 mgm., the rise being mainly in the diffusible fraction. The calcium balance, being negative during the fore-period, became positive, and increasingly so with the further administration of the extract. The blood calcium decreased to 6.2 mgm. at the end of the period during which parathyroid extract was discontinued.

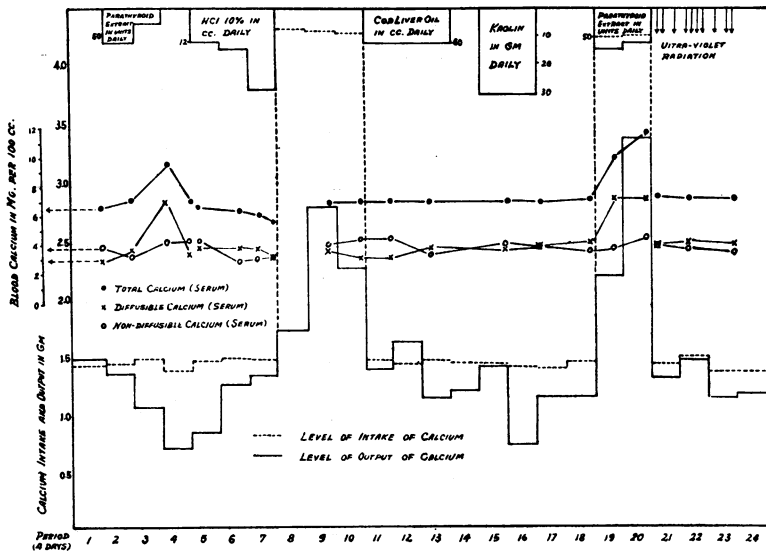


CHART 1. SHOWING THE EFFECT OF VARIOUS TREATMENTS ON THE CALCIUM BALANCE, AND THE TOTAL, DIFFUSIBLE AND NON-DIFFUSIBLE SERUM CALCIUM

Then three periods were devoted to hydrochloric acid treatment during which he experienced moderate relief of symptoms, but Chvostek's and Trousseau's signs remained marked. The blood calcium, instead of being increased, decreased from 6.5 to 5.2 mgm., the further reduction here being in the non-diffusible portion. The calcium retention was lowered from 43.3 per cent during the first period to 9.9 per cent during the third period of the acid administration, the increased excretion occurring chiefly in the stools.

During the next three periods, calcium chloride, 2 grams daily, was given, thus increasing the intake three-fold. This caused no improvement in the patient. The blood calcium remained at 6.5 mgm., in spite of the strongly positive calcium balance, 37 to 60 per cent of the intake being retained.

Cod liver oil given in 30 cc. daily doses for the next three periods again made no change in the patient's condition. His blood calcium stayed at about the same level, and the retention of calcium was not increased. In fact, during the second period of cod liver oil administration, the balance was negative.

In view of the possibility of this case being associated with intestinal intoxication, two periods were used for the oral administration of kaolin in 20 per cent suspension which might adsorb any toxins from the intestines, as suggested by the work of Braafladt (2). This was not followed, however, by any beneficial effect. The blood calcium again failed to rise. During the first period of kaolin treatment, the calcium intake and output approximately balanced each other, while the output of phosphorus was remarkably increased giving rise to a negative balance. During the second period, however, both calcium and phosphorus were fairly well retained.

After two rest periods, parathyroid extract and calcium chloride were given together for two periods, during which all signs of tetany disappeared and the blood calcium rose from 6.5 to 11.1 mgm., a level higher than normal. Here the rise of blood calcium was again more in the diffusible than in the non-diffusible fraction. During the first period of combined treatment when the blood calcium was approaching the normal level (9.6 mgm.), the calcium retention was about the same in extent as during the periods in which calcium chloride alone was given. But in the second period of combined treatment when the blood calcium (11.1 mgm.) was elevated above the normal level, markedly increased excretion of calcium occurred in the urine, giving rise to a decreased calcium retention as compared with the periods of calcium chloride alone.

Ultraviolet radiation was given a trial for the next three periods. Each exposure was made at 40 cm. distance for 5 to 15 minutes on the chest, abdomen, legs or back. There were ten exposures in twelve days of the experimental periods. There was no subjective improve-

ment noticed. Neither the blood calcium, nor the retention of calcium was increased by the treatment.

DISCUSSION

This is a case of chronic tetany in a man of 45, accompanied by diarrhea and epileptic fits. It is not associated with operative removal of the parathyroids. The absence of gastro-intestinal lesion that would lead to alkalosis, and the repeated findings of a normal bicarbonate and chloride content in the blood would exclude gastric tetany. A very few possibly similar cases in women are reported in the literature, but none in men. Moffitt (3) in 1911 described two cases of chronic tetany in women, aged 41 and 45 respectively, in whom neither an operation had been performed on the neck, nor a lesion in gastro-intestinal tract found. Findlay and Sharpe (4) reported another case of chronic tetany in a woman of 52 with diarrhea as a pronounced feature, as in the present case. Underhill, Tileston and Bogert (5) studied a similar case of tetany in a woman of 35, associated with intestinal putrefaction and foul diarrhea. They found that calcium absorption proceeded normally, but the blood calcium was not raised by even a large intake of calcium. Pregnancy did not enter as a factor in any of these cases.

The association of epileptic attacks in this type of tetany is not known. Gibson (6) reported a case of juvenile idiopathic tetany in a boy of thirteen with epileptic fits, and quoted Redlich as reporting 72 cases in which epileptic seizures accompanied or followed tetany. Of them, 21 were in tetany following loss of the parathyroids, 17 in chronic juvenile cases, 5 in obstetrical cases, and the remainder in gastric and infantile tetany. No mention was made of chronic adult idiopathic tetany such as existed in our case.

Concerning the metabolic data obtained, the most striking feature is that none of the treatments instituted had any marked beneficial effect except the parathyroid extract, given either alone or combined with calcium chloride. Cod liver oil, the effective remedy for infantile tetany and the type of tetany in adolescent girls reported in the first paper (1), failed entirely in this case. There was no alleviation of symptoms, nor was there any increase in blood calcium or retention of calcium. Likewise ultraviolet radiation proved inadequate.

Kaolin was also ineffective. There was an increased retention of calcium when the calcium intake was raised, but no relief of symptoms nor rise of blood calcium. Hydrochloric acid induced only slight improvement in the spastic attacks, but the resultant lowering of the blood calcium and decrease of calcium balance indicate that the administration of hydrochloric acid is not a desirable treatment.

The effect of parathyroid extract in this case is unique in that it completely relieved the symptoms and signs of tetany as well as the intestinal disturbance coincidently with the prompt and marked rise of blood calcium, especially of the diffusible calcium. When the blood calcium was raised nearly to normal, there was a slight increase in calcium retention, but when it rose above normal, the excretion of calcium in the urine was increased. The variation in calcium excretion correlated with the blood calcium level probably accounts for some of the discrepancies in the reports by various authors regarding the effect of the parathyroid extract on the excretion of calcium.

The failure to obtain results with other treatments than parathyroid extract in this case suggests the existence of a primary parathyroid deficiency with resulting disorder of calcium metabolism, hyperirritability of the neuro-muscular system and intestinal disturbances. Such a deficiency can only be remedied by supplying the normal hormone of the parathyroid glands which is supposedly contained in the extract. Swingle and Rhinhold (7) in the treatment of ten parathyroidectomized dogs with ultraviolet radiation found that this did not prevent tetany nor the fall of blood calcium. Similarly Jones (8) failed in his treatment of parathyroidectomized dogs with cod liver oil. The lack of response to either cod liver oil or ultraviolet radiation in the case presented, as in these dogs with actual loss of the parathyroids, would also lend support to the hypothesis that this case represents one of parathyroid deficiency.

SUMMARY AND CONCLUSIONS

An unusual case of chronic tetany in a Chinese male of 46, unassociated with alkalosis or removal of the parathyroids is reported. Epileptic fits and intestinal disturbances were accompanying features. Of all the treatments instituted only parathyroid extract gave relief of symptoms and elevation of blood calcium. When the blood calcium

approached normal, there was an increased retention of calcium, but when it rose above normal a decreased retention occurred. Cod liver oil, ultraviolet radiation, kaolin, calcium chloride, and hydrochloric acid were all ineffective. The lack of response to all other treatments except the parathyroid extract is taken to indicate a probable primary parathyroid deficiency as the cause of tetany in this case.

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