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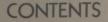
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September 1943

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Malignant Hypertension: Report of a Case 53 Otterbein Dressler and Victor R. Fisher

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TOTAL CYSTECTOMY WITH IMPLANTATION OF URETERS FOR CARCINOMA OF THE BLADDER IN A MALE, AGE 29

H. WILLARD STERRETT Professor of Urology

Mr. A. B., age 29, American, a bus driver by occupation, was first seen June 21, 1940. His chief complaint was continuous bleeding from the bladder. This had appeared first about two years previously, but at that time it had been particularly noted at end of urination. Medical attention was sought, but no cystoscopic study or x-rays were done. These attacks of bleeding occurred about every two or three weeks, were painless, spontaneous, and subsided "after taking the medicine." Three weeks prior to our consultation he had been bleeding continuously with no interruption. At this time his urine was so bloody as to appear to be almost entirely pure blood. He was advised to have hospitalization for study of "his stomach so as to find out what medicine should be administered." A local osteopathic physician was then consulted and the patient referred to the writer.

The family history was entirely negative. His father was 58, and his mother 48, both living and well. He had two brothers and one sister, all living and well. There was no history of carcinoma, diabetes, tuberculosis, or heart disease in his family.

His general health had been good, although he occasionally had some attacks of constipation, and on occasion some diarrhea. There had been no bleeding from the rectum or other parts of the body. Childhood diseases were few, and a negative venereal history was obtained. His weight had been practically constant for some time. His urinary history, other than the bleeding, was not striking. Occasionally he arose at night, and had a frequency during the day of four to six times. There had been no trouble starting or stopping the flow.

Physical examination showed a fairly well nourished male who weighed 152 lbs. No râles or other adventitious sounds were noted. Blood pressure was 110 systolic and 72 diastolic. Rectal examination showed the prostate to be normal in size and consistency. No inguinal adenopathy was noted.

Attempts to secure satisfactory local analgesia to carry out cystoscopy having met with failure, he was given nitrous oxide and cystoscopy was performed. This revealed a large papillary mass immediately within the internal sphincter, almost completely surrounding the same. Biopsy was performed, and a report of papillary transitional carcinoma was made.

A few days later he was readmitted to the hospital for surgery. The urinalysis at this time showed a specific gravity of 1.021, pH of 7.5, a one plus albumin, an occasional pus cell, a few phosphates, and blood cells too numerous to count. His blood picture at this time showed 4,710,000 erythrocytes and 24 per cent lymphocytes, suggesting an old, long standing process.

On July 29, 1940, a suprapubic incision was made, under spinal analgesia, at which time the mass on the right lateral wall and in the trigonal area was excised with cutting current, and 30 Radon seeds were implanted. These were gold, and contained one and one-half milicuries each.

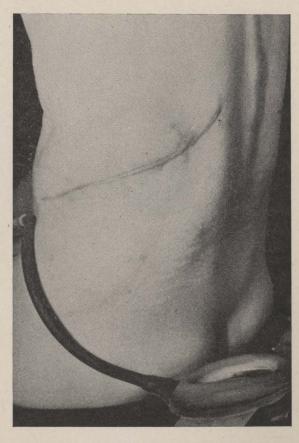


Fig. 1 The left ureterotomy opening with bag removed. A similar opening is on the right side.

The patient made an uneventful recovery, the wound healing by first intention, and he was discharged from the hospital on August 15. He was reexamined on October 4, 1940, at which time he looked well, and was symptom free, although cystoscopy showed some redness and induration immediately within the sphincter on the right side.

He was next seen on November 29, 1940, at which time he stated that he had been feeling very badly, and that he had been vomiting for the past few days. Cystoscopy revealed a marked recurrence of the lesion, and he was told to go home and arrangements were made for his read-



Fig. 2 Harness in place with leg urinal.

mission to the hospital. Incidentally, one week later the patient did not remember anything of the two or three days prior to this visit.

The following day he was admitted to the hospital in convulsions and deep coma. A marked odor of uremia was present. Chloroform was administered to permit the intravenous administration of saline and glucose. Restraint was necessary throughout the night, although he quieted toward morning. Hourly osteopathic treatments were administered to his renal splanchnics. By noon of the following day he was rational and was able to state that he was unable to see anything except light and darkness.

His urinalysis at this time was but little different from his first admission, being alkaline with many triple phosphates, and 2 plus albumin. Wassermann and Kahn were both negative. Erythrocytes had dropped to 3,360,000. Blood sedimentation was 33 mm. in 60 minutes, an almost perpendicular drop, reaching maximum in 15 minutes. Blood urea nitrogen was 195.

A diagnosis was made of uremia due to occlusion of the ureters by the lesion in the bladder. He was then studied radiographically, and no evidence of osteolytic or osteographic changes were discovered. His chest was also pronounced free from metastases.

He was then administered 500 cc. of whole blood, and on December 7 he was admitted to surgery. Under spinal analgesia, occasionally supplemented with cyclopropane, a right sided cutaneous ureterotomy was done. The ureter was very much dilated, being approximately 4 cm. in diameter. The kidney was greatly swollen and engorged, and urine gushed out of the ureteric opening under great pressure. Following surgery, there was an immediate response for the better. The ureterotomy permitted 1850 cc. of urine the first day, while that recovered from the bladder measured but 350 cc. The following day there was 2830 cc. from the ureterotomy and but 125 from bladder. Undoubtedly there had been almost complete occlusion of both ureteric ora. Uneventful recovery followed, the wound healing by first intention, and he was allowed out of bed on the ninth day following surgery.

On December 20 he was readmitted to surgery. Again under spinal analgesia, the left ureter was brought to the skin and placed in a location similar to that of the opposite side.

His blood urea nitrogen showed an interesting response. On admission it was 195, immediately before his first surgery it was 112, one week later it dropped to 74.2, and on December 26, following his second ureterotomy, it dropped to 21.7.

Both ureteric catheters drained well, and temporary bags were fastened to them, the patient being wet on occasion. He was now allowed to be up and about. By early January he stated that he felt fine, his vision had returned, and he was very optimistic and cooperative.

On January 15, 1941, he was once more admitted to surgery. Under spinal analgesia, supplemented with cyclopropane, a total cystectomy was done. The prostate was removed as it was felt that some invasion had taken place into this organ. He stood the ordeal fairly well, although there was considerable shock. It was felt that due to his condition it would be unwise to prolong the surgery, and no perineal drain was inserted, dependence being placed on a large suprapubic drain located deep in the pelvis. Drainage was profuse for several days, and irrigations were used. Some sutures were placed in the lower angle of the wound under local analgesia on February 3. Uneventful recovery followed, he became ambulatory on February 18, and was discharged from the hospital on March 1. The suprapubic wound was still slightly moist.

Following his discharge from the hospital, he was allowed to follow

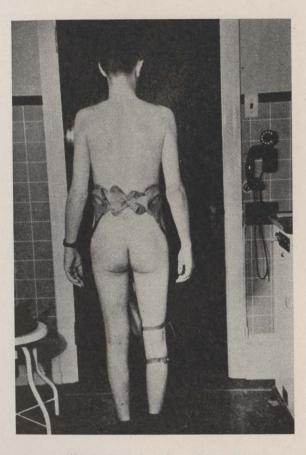


Fig. 3 Posterior view of harness.

his own inclination; and two suprapubic cystotomy bags were adapted to fit the ureteric fistulae. In about two months after his discharge he returned to work and has been well since, apparently suffering very little inconvenience from his urinary fistula. It is interesting to note that despite all this surgery, the patient is living a normal married life, stating that sexual desire or coitus have been little, if at all interfered with. The patient was seen in July, 1943, at which time he appeared to be well, with no evidence of recurrence of disease, and he was working at his usual occupation.



Fig. 4 Appearance of patient with apparatus in place and functioning.

Discussion

This case illustrates two important features: First, the serious result of neglecting diagnosis. Most all bladder tumors originate as benign lesions, and fulguration is the indicated treatment. This is usually simply done; and while the lesions tend to recur, becoming more malignant with each recurrence, one treatment is frequently satisfactory for the cure. Second, a cardinal rule that should be observed and one which is, I am sorry to say, more frequently broken than kept: It is, "never stop bleeding until you know where it is coming from." Cystoscopy and an intravenous urogram would have provided all the clinical evidence to establish the diagnosis in this patient. Neglect of the lesion with its subsequent extension, which involved both ureteric ora, produced sufficient urinary back pressure to result in uremia. Had the condition of stenosis been recognized earlier, even though the case would have progressed to radical surgery, it would have been possible to implant both ureters into the bowel thereby enabling him to live a much more normal life. As it was, the extreme dilation of his ureters as well as the severity of his illness obviously precluded any such ideal surgery, and we were forced to implant the ureters into the skin. This, of course, produced a problem in the control of his urinary leakage, and a particularly fortunate result followed experimentation with various urinary containing apparatuses.

Summary

A case of highly malignant carcinoma of the bladder in a young man of 29 is presented.

Total cystectomy was followed by recovery and an apparently normal life.

Upon the establishment of urinary drainage, the extremely high blood urea nitrogen rapidly returned to normal.

Occlusion of the ureteric ora produced partial amnesia.

POSTMORTEM BLOOD CHEMISTRY: AN ILLUSTRATIVE CASE*

OTTERBEIN DRESSLER

Professor of Pathology in the College and Special Deputy Coroner, City of Philadelphia

During life, clinical evidence of diabetes mellitus can be supported by chemical analysis of the blood and urine. The fallacies of urinalysis for this purpose have been well elucidated. Blood sugar, glucose, is a very labile substance. In a flask or test tube it is subject to great quantitative change on standing. How much greater, and more rapid change might take place in the dead body, in a warm room has been theorized upon. In spite of the probability of not getting useful information we decided to do postmortem blood sugar determinations.

Autopsy No. 43-1915 Died: July 11, 1943—8:15 p.m. Autopsy: July 12, 1943—2 p.m.

At the City Morgue

Clinical Data

An adult, negro, widowed female, said to be 56 years old, was taken from the highway by the police to a Philadelphia Hospital. She was admitted at 8:12 p.m. and died at 8:15 p.m. of the same day, July 11, 1943. The deceased was a known diabetic treated at the above hospital for three months.

External Examination

The body was that of an adult female negro of medium size and build, said to be 56 years old. There were no evidence of trauma nor of caustic poison to be found anywhere on the body. A somewhat fungating keloid was noted involving the areola and surrounding tissues of the skin of the left breast. A keloid was found on the lobe of the right ear. Keloids were found on the dorsum of the left hand and in an abdominal cicatrix, which extended from the umbilicus to the pubes. Saber shins of syphilis could be demonstrated but there were no other stigmata of syphilis to be demonstrated. The body was not grossly edematous. Hallux valgus was noted involving both feet.

Internal Examination

Approximately 25 cc. of clear amber fluid was found in the pericardial sac. A milkspot was noted over the tip of the left ventricle. The

^{*} Case reported through the courtesy of Dr. Herbert M. Goddard, Coroner, and Dr. Benjamin Gooley, Chief Coroner's Physician, City of Philadelphia.

heart measured 13 cm. in greatest diameter; the thorax 23 cm. at the level of the dome of the diaphragm. The cardio-thoracic ratio 13/23. There were no valvular lesions of the heart and no suggestions of syphilis about the aortic valves.

The coronary system showed advanced atherosclerosis involving chiefly the left coronary, anterior descending limb and circumflex branch. The latter was completely obstructed about its mid-portion. There were evidences of older coronary occlusive disease, as shown by scar formations in the left ventricular wall. The myocardium was 2 cm. in thickness in the left ventricle except for the tip which was somewhat thinner. The left ventricle was dilated.

Atherosclerosis was demonstrated throughout the aorta and was marked in the superior mesenteric artery and in the cerebral vessels.

One hundred fifty cc. of amber fluid was found in the right thorax, 125 cc. in the left thorax. The lungs were edematous with the dependent portions of increased density suggesting the possibility of early broncho-(lobular) pneumonia. There were no foreign bodies in the pulmonary arteries.

The esophagus presented no noteworthy lesions. The stomach and duodenum were negative for pathology.

The small and large bowel presented extensive adhesions attached to the abdominal incision cicatrix, noted above, extending from the umbilicus to the pubes.

The liver did not show the nutmeg change of passive hyperemia.

The gallbladder contained four cholesterol stones.

The pancreas presented no noteworthy changes.

The spleen measured $9 \ge 6 \ge 3$ cm. and presented the general characteristics of this organ in the colored race.

The uterus, tubes and ovaries were absent and a small cervical stump was identified, suggesting previous supra-vaginal hysterectomy.

The bladder contained no urine, so that urinalysis for sugar could not be carried out. The ureters were not distended. The kidneys measured respectively, left and right, $11 \ge 5 \ge 3$ cm. and $11 \ge 6 \ge 3$ cm. Their capsules stripped with difficulty. The cortex was irregular on both sides and the kidneys were congested. The waxy cut surface of cloudy swelling was suggested.

There were no noteworthy lesions of the suprarenal glands.

The mammary glands contained no neoplasm other than the keloid referred to above.

Abundant cerebral atherosclerosis was demonstrated, as noted above, and the brain presented an old organized hematoma 1 cm. under the cortex in the left frontal lobe.

Blood was secured from the heart and quantitative blood sugar measured 539 mgms. per 100 cc. in spite of the fact that the body had been dead 18 hours before the blood was secured.

Anatomic Diagnosis

Coronary occlusive disease Generalized atherosclerosis Pulmonary edema Hydrothorax Cholelithiasis Organized cerebral hematoma Multiple keloids Diabetes mellitus

Cause of Death

Immediate—coronary occlusive disease with myocardial insufficiency. Predisposing—diabetes mellitus.

To the section of students assembled in the autopsy room, and we might hasten to add their instructors as well, this case presented many facets of interest for study. Indeed, the body illustrated most eloquently Krumbhaar's expression "the constellation of diseases." The "saber shins" of syphilis, though we were unable to demonstrate other stigmata of syphilis; the multiple keloids, one resulting from the trivial injury of pricking the ear for earrings; the apparently silent hematoma in the frontal lobe; the association of disturbed cholesterol metabolism as evidenced by cholelithiasis; advanced atherosclerosis with coronary occlusive disease; might well have arrested attention for hours of interesting discussion. However, we were struck by the helplessness of the pathologist at the autopsy table to demonstrate tangible evidence of diabetes mellitus.

In this case the finding of 539 mgms. of sugar per 100 cc. is noted. Without definite tables of decline, postmortem, we are inclined to believe that the blood sugar in this case antemortem probably was well over 1000 mgms. per 100 cc. Thus, in this case we believe we have been able to demonstrate tangible, postmortem evidence of diabetes mellitus though it is our impression that the diabetes mellitus was only a contributory factor in the sudden death of the individual.

This finding of a high postmortem blood sugar has raised many questions that we are trying to answer by experimentation and postmortem observation. We recognize that all the materials in the blood reacting like sugar were probably not sugar. Attempts are being made to fractionate these materials and arrive at a figure for sugar. It is to be remembered that in the usual clinical practice, a blood sugar report does not indicate sugar alone but other reducing substances as well. The method of quantitative analysis was the same in this case as that employed in the usual clinical examinations.

If we find that there is a decline in blood sugar postmortem, we will try to establish a rate of decline. This latter we have undertaken from

POSTMORTEM BLOOD CHEMISTRY

many angles which will be reported when sufficient data are collected. In the meantime, this case has served to stimulate interest in postmortem blood chemistry.

Summary

An autopsy protocol on a known case of diabetes mellitus is presented. In spite of the fact that the body had been dead 18 hours, the blood sugar at autopsy was found to be 539 mgms. per 100 cc.

Possible sources or error are suggested and further investigations now being pursued to make this information more useful are mentioned.

THE EFFECTS ON THE BLOOD PRESSURE AND PULSE RATE OF SOFT TISSUE MANIPULATION COMBINED WITH SUDDEN SPINAL JOINT MOBILIZATION IN THE UPPER THORACIC REGION IN A GROUP OF "NORMAL" COLLEGE STUDENTS

FREDERICK A. LONG Director of Research

and

GUY S. DEMING

Associate in Research

Previous reports from this laboratory on the effects of manipulation on blood pressure and pulse rate have published results of sudden spinal joint mobilization alone of the cervical and upper thoracic regions, of the lower thoracic and lumbar regions, and of the entire spine; of soft tissue manipulation alone in the sub-occipital region, in the upper thoracic region, and in the cervical region; and of soft tissue manipulation combined with sudden spinal joint mobilization in the cervical area.^{1,2,3,4,5,6,7} The purpose of the experiment presently reported was to observe the effects of soft tissue manipulation combined with sudden spinal joint mobilization in the upper thoracic region upon systolic and diastolic blood pressure, and upon pulse rate in a group of "normal" college students. The work was completed in July, 1943.

Sixty male students of the Philadelphia College of Osteopathy were taken at random from the freshman and sophomore classes and divided into one group of thirty subjects for manipulation, and an equal group who served as controls. The average age of the subjects was 23.2 years with a range from 19 to 31 years. The average age of the controls was 22.8 years with a range from 19 to 32 years. All participants were informed of the nature of the experiment.

The experiments were performed on one subject and one control at a time in a well-ventilated room kept at even temperature. Twentysix of the experiments were conducted between the hours of 1:00 p.m. and 4:00 p.m., the remainder between the hours of 10:00 a.m. and noon. A uniform amount of clothing was worn by subjects and controls, and all constricting bands were loosened before the experiment was begun. Conversation between subject and control was interdicted, and conversation between the two operators was rarely necessary. The cuff of a mercury type sphygmomanometer was applied to the left arm, the auscultatory method of determining blood pressure employed, and the pulse rate was determined by counting the radial pulse at the left wrist for one-half minute.

Procedure

In all the procedures employed, the control assumed concurrently with the subject all the positions described for the subject, but received neither soft tissue manipulation nor sudden spinal joint mobilization.

Subject and control rested in the supine position on straight type osteopathic treatment tables for ten minutes. At the end of this period, systolic and diastolic blood pressures and pulse rates were determined. Immediately thereafter, the following procedure was carried out with the subject: The subject turned on his left side, the operator stood facing the subject, passed his left hand and forearm under the subject's right arm, and his right hand posterior to the subject's scapula in such a way as to bring the operator's finger tips over the paravertebral muscle mass close to the spinous processes on the subject's right (upper) side. Soft tissue manipulation consisted in repeated stretching of the paravertebral muscles by force applied by the operator's fingers, starting just lateral to the spinous processes and exerted at right angles to the spinal column in the region extending from the first to approximately the fifth thoracic vertebra. This manipulation was continued for two and onehalf minutes, and then the opposite side was manipulated in a similar manner for two and one-half minutes. The subject then sat up with his feet hanging over the side of the table. The operator, standing directly behind the subject, passed his hands and forearms through the subject's axillary spaces, in front of the subject's shoulders, and clasped his own hands on the base of the subject's cervical column. The subject then clasped his hands loosely on top of the operator's hands. The subject was instructed to let his head, arms, and body drop in a relaxed position. The operator held the subject's upper thoracic region against the operator's chest, brought the subject's upper thoracic spine into extension tension and then by a sudden upward movement in line with the extended spine, produced sudden mobilization of the subject's upper thoracic vertebrae. The subject then resumed the supine position on the table. Systolic and diastolic blood pressures and pulse rates were determined in subject and control immediately, and again after they had rested in the supine position an additional five minutes. This concluded the experiment.

Results

Table 1 records the blood pressures and pulse rates following the initial ten minute rest period before manipulation.

Figure 1 shows the changes which occurred in the average systolic blood pressure immediately following manipulation and five minutes after manipulation. Both subjects and controls showed an immediate rise and later drop in average pressure which is without statistical significance.

Figure 2 shows the changes which occurred in the average diastolic

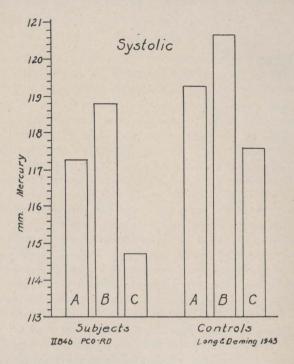


Fig. 1—Average systolic blood pressures before soft tissue manipulation combined with sudden spinal joint mobilization in the upper thoracic region (A), immediately after manipulation (B), and five minutes after manipulation (C). Based on findings in 30 subjects and 30 controls.

TABLE 1

Original systolic and diastolic blood pressures, and pulse rates in 30 subjects and 30 controls used in study of the effects of the combination of soft tissue manipulation and sudden spinal joint mobilization in the upper thoracic region.

	Sub	jects	Controls		
	average	range	average	range	
Systolic	117.3	98-158	119.3	96-152	
Diastolic	74.5	- 52- 98	70.4	52-108	
Pulse	75.3	58-102	71.7	54- 92	

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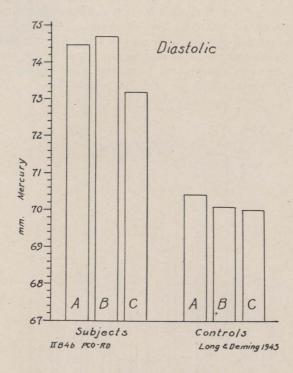


Fig. 2—Average diastolic blood pressures before soft tissue manipulation combined with sudden spinal joint mobilization in the upper thoracic region (A), immediately after manipulation (B), and five minutes after manipulation (C). Based on findings in 30 subjects and 30 controls.

blood pressure at corresponding periods. The graphs for subjects show an immediate rise and later drop. Those for the controls show a progressive drop. The changes have no statistical significance.

Figure 3 shows the average pulse rate changes. The graphs for subjects show a progressive drop while those for controls show an initial drop and partial recovery. These changes are likewise without statistical significance.

Tables 2, 3, and 4 show individual variations in systolic pressure, diastolic pressure, and pulse rate immediately after and five minutes after manipulation.

Table 2 shows that the systolic pressure was altered in a slightly greater proportion of subjects than of controls immediately following manipulation but that this ratio was exactly reversed five minutes later.

Table 3 shows that the diastolic pressure was altered in a slightly greater proportion of subjects than of controls immediately following manipulation, and that this disparity was doubled five minutes later.

Table 4 shows that the pulse rate was increased in 16.7 per cent more subjects than controls immediately following manipulation, and that this disparity was reduced to 13.3 per cent five minutes later.

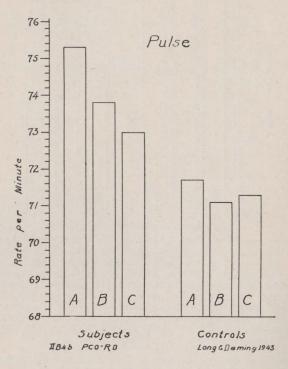


Fig. 3—Average pulse rates before soft tissue manipulation combined with sudden spinal joint mobilization in the upper thoracic region (A), immediately after manipulation (B), and five minutes after manipulation (C). Based on findings in 30 subjects and 30 controls.

Summary

Thirty male students of the Philadelphia College of Osteopathy were studied to observe the effects of a combination of soft tissue manipulation and sudden spinal joint mobilization in the upper thoracic region on systolic and diastolic blood pressures, and on pulse rate. Thirty male students were used as controls.

TABLE 2

Average and maximum changes in systolic blood pressure in 30 subjects receiving a combination of soft tissue manipulation and sudden spinal joint mobilization in the upper thoracic region and corresponding data in 30 controls. Figures based upon comparison with original values before manipulation was carried out.

		Immediately After Manipulation			5 Minutes After Manipulation			
		по.	per cent	mm. mercury	no.	per cent		ım. rcury
	Increase	16	53.3	av. max. 5.0 10.0	3	10.0	av. 4.0	max 10.0
Subjects	Decrease	9	30.0	4.0 8.0	21	70.0	4.4	12.0
	No change	5	16.7		6	20.0	-	-
Controls	Increase	14	46.7	6.0 10.0	7	23.3	3.4	8.0
	Decrease	10	33.3	4.0 10.0	18	60.0	4.1	16.0
	No change	6	20.0		5	16.7	-	-

TABLE 3

Average and maximum changes in diastolic blood pressure in 30 subjects receiving a combination of soft tissue manipulation and sudden spinal joint mobilization in the upper thoracic region and corresponding data in 30 controls. Figures based upon comparison with original values before manipulation was carried out.

		Immediately After Manipulation			5 Minutes After Manipulation			
		no.	per cent	mm. mercury	no.	per cent	mm. mercury	
	Increase	12	40.0	av. max. 3.6 16.0	7	23.4	av. max. 3.3 8.0	
Subjects	Decrease	13	43.3	3.6 6.0	17	56.6	3.7 12.0	
No	No change	5	16.7		6	20.0		
Controls	Increase	12	40.0	2.7 6.0	9	30.0	3.8 8.0	
	Decrease	11	36.7	3.6 6.0	11	36.7	4.2 10.0	
	No change	7	23.3		10	33.3		

TABLE 4

Average and maximum changes in pulse rate in 30 subjects receiving a combination of soft tissue manipulation and sudden spinal joint mobilization in the upper thoracic region and corresponding data in 30 controls. Figures based upon comparison with original values before manipulation was carried out.

		Immediately After Manipulation			5 Minutes After Manipulation			
		no.	per cent	mm. mercury	no.	per cent ·	mm. mercury	
	Increase	9	30.0	av. max. 3.6 8.0	6	20.0	av. max. 4.0 6.0	
Subjects	Decrease	15	50.0	5.2 10.0	19	63.3	5.0 16.0	
	No change	6	20.0		5	16.7		
	Increase	8	26.6	3.2 6.0	10	33.3	3.8 8.0	
Controls	Decrease	11	36.7	3.8 12.0	11	36.7	4.4 10.0	
	No change	11	36.7		9	30.0		

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No statistically significant changes in either blood pressure or pulse rate were observed following this manipulation.

Acknowledgment

We wish to acknowledge the assistance rendered in these experiments by Viola C. Kruener, Joseph V. Horn Fellow in Osteopathic Research.

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MALIGNANT HYPERTENSION: REPORT OF A CASE

OTTERBEIN DRESSLER Professor of Pathology

and

VICTOR R. FISHER Assistant in Clinical Osteopathy

Clinic No. 43-345 Hospital No. 13,595

An adult, married, negress, 31 years of age was admitted to the general clinic April 28, 1943, complaining of "weakness and nervousness," which she said had existed for a period of two and one-half years. She further stated that she was easily excited. The patient had been admitted to the Women's Homeopathic Hospital in 1940 for a period of one week for observation. In 1941, she was a patient in the hospital of the University of Pennsylvania for 19 days and was told that she had hypertension. She stated that the doctor did not know the cause. On March 24, 1943, she was admitted to the Douglas Hospital which discharged her on April 20, 1943.

The father and mother were living at the time of admission to our clinic. The mother, said to be 54 years of age, has hypertension and one sister has rheumatic heart disease.

Nothing significant could be found in the past history of the patient, but in the six months before admission she had lost 20 to 25 pounds in weight. Her obstetrical history noted two pregnancies, both males. The first died at 19 months of bronchopneumonia, the second is now living and well. Both were spontaneous deliveries.

On admission to the clinic, the patient's temperature was 100.2° F., her systolic blood pressure was well over 260, and the diastolic 166. The pulse was 108 and the respirations 22. Fine tremors were noted in some of the skeletal muscles. The eyes were markedly exophthalmic. There was a suspicion of a mass in the right lumbar area. The thyroid gland was palpable but not enlarged.

Her blood counts averaged 4,200,000 erythrocytes per cu.mm. with hemoglobin on several occasions ranging between 12.5 and 13.5 grams. The color index was persistently slightly above one. No significant data could be elicited from the white count, nor from the stained smears. Her urinary output averaged 1500 cc. per 24 hours with the night quantity half the day quantity. The Mosenthal test showed a range in specific gravity of 18 points. On May 13, 1943, her urea nitrogen was 17 milligrams per 100 cc., the blood cholesterol 228, and the standard urea clearance 24.6. The basal metabolism rate was plus 33 per cent. By compliment fixation and precipitation she was sero-negative for syphilis. Antero-posterior abdominal survey films demonstrated some prominence of the dependent margin of the liver, though the findings did not permit an opinion of frank liver enlargement. The renal shadows were bilaterally quite well delineated and occupied an average normal anatomic position. Some gas was seen distributed within the stomach, small bowel, and colon, with abdomino-pelvic soft parts otherwise negative for significant changes. Multiple small calcifications situated to the dependent pelvis were in all probability representative of phleboliths. The lumbo-pelvic structures as visualized were negative for gross bone or joint pathology, and the included diaphragmatic leaflets possessed an average normal contour and relief.

On June 4, 1943, the patient was admitted ambulatory to the hospital for further study. On admission, her weight was 113 pounds and her height 62 inches. The blood pressure was upwards of 300 systolic and 170 diastolic. The pulse was 120. Except for the complaint of headache, there were no significant changes. The erythrocytes had dropped to 3,300,000, and the hemoglobin to less than 7.5 grams. Her N.P.N. had risen to 77.8, and the urea nitrogen to 52. The chlorides were 553.5 and the blood plasma protein 7.5 per cent. The basal metabolic rate had increased to plus 42 per cent. The electrocardiogram showed the T wave changes characteristic of hypertensive disease.

On June 8, 1943, radiographic examination of the heart revealed the following: Cardiac enlargement with left heart preponderance, and 20 per cent transverse cardiac enlargement. Left ventricular myocardial insufficiency which may have been existent upon the basis of left ventricular enlargement or dilatation. Bilateral prominence of bronchial vascular relief attributed to a congestive state was present.

On June 12, 1943, the patient developed marked dyspnea, slight cyanosis, moist râles over both bases posteriorly, and a pulse rate of 150. Treatment for congestive heart failure was instituted consisting of digitalis 0.1 gram every three hours, high protein and salt-free diet, and osteopathic manipulative therapy directed to the upper dorsal and cervical areas. Considerable clinical improvement was noted. Within 48 hours the dyspnea and cyanosis completely disappeared, and all congestive signs were absent. The pulse rate dropped to 120 where it remained. The total dosage of digitalis was 0.8 gram following which signs of digitalis intoxication occurred, and the drug was discontinued for a period of 36 hours. A maintenance dose of 0.1 gram was then administered once daily for three doses, at the end of which time the nausea and vomiting recurred so severely that the drug had to be discontinued permanently. The patient appeared to be doing fairly well; her blood pressure had dropped to 240 systolic and 140 diastolic, and she offered no complaints.

On June 21, 1943, the patient complained of headache and shortness of breath. The blood pressure had increased to over 300 systolic. She became comatose, and following several convulsive seizures expired on June 22, 1943.

Clinical Impression

- 1. Malignant hypertension
- 2. Hyperthyroidism
- 3. Uremia (terminal)

Clinical Comment

This patient presented the characteristic symptoms of Graves' disease, e.g., exophthalmos, tremor, and high metabolic rate. Absent, however, were thyroid enlargement and a low blood cholesterol. Of differentiating interest were the extreme hypertension and the possibility of the mass in the lumbar area being a suprarenal tumor.

The blood pressure in hyperthyroidism is frequently increased, but rarely to the extreme noted in this patient. In addition, in Graves' disease the hypertension is most common in the early stages of the disease before exhaustion occurs. Later, both the systolic and the pulse pressure fall because of the myocardial damage. In the patient the exact opposite occurred, e.g., with exhaustion and congestive heart failure the blood pressure increased.

Serious consideration was given to the possibility of a tumor of the adrenal medulla. Such a tumor in an individual 31 years of age would be of the pheochromocytomata variety. This type of tumor is rare, is usually discovered only at autopsy, and is characterized by mainly affecting adults and by a paroxysmal form of hypertension—the blood pressure changes with the increase and decrease in the output of adrenalin. The development of congestive heart failure followed by uremia prevented further studies of value such as pyeolograms and x-ray examination following subdiaphragmatic injection of air.

AUTOPSY

A-43-288 Died: 6-22-43, 12:05 a.m. Autopsy: 6-22-43, 9 a.m.

Autopsy Protocol

The body was that of a somewhat cachectic negro female, said to be 31 years old. There were no marks of surgical incision nor evidence of trauma.

Twenty-five cc. of amber fluid was found in the pericardial sac. The heart measured $14.5 \ge 10 \ge 9$ cm. This organ weighed 465 grams. Concentric hypertrophy of the left ventricle was demonstrated with some dilation. Atheromatous deposits were demonstrated in the mitral curtain. The left coronary artery presented two openings from the aorta instead of a single opening. Some atheromatous degeneration was noted throughout the vascular tree.

Fifty cc. of fluid was found in the right thorax and 50 cc. in the left

thorax. The lungs were edematous. There were no suggestions of tumor and no suggestions of active pulmonary tuberculosis.

The esophagus presented no noteworthy lesions. There were no pathological changes to be noted in the stomach, nor along the intestinal canal.

The liver was 18.8 cm. in height and weighed 1600 grams. It was reasonably firm and showed some nutmeg change. The gallbladder was dilated with somewhat inspissated bile, but there were no calculi noted. The pancreas presented no changes.

The spleen weighed 120 grams, and measured $11 \ge 8.5 \ge 4$ cm. It was comparatively firm to the touch.

The urinary bladder was empty. The ureters were not dilated. The kidneys measured left and right, respectively, $15 \ge 6 \ge 6.5$ cm. and $12 \ge 7 \ge 3$ cm. Their total weight was 430 grams. The capsules stripped easily, but the cortex presented the flea-bitten appearance of malignant hypertension. There was no contraction of the kidney and no irregularity, but a fine granularity of the cortex was evident. One branch of the left renal vein passed between two branches of the left renal artery. The pelvic viscera presented no noteworthy changes. The suprarenal glands, likewise, presented no pathological phenomena.

The thyroid gland presented no obvious enlargement. The gland could not be dissected out in its entirety, but those portions removed presented no gross lesions.

Sections of the kidneys present an extremely variable microscopic picture. Large numbers of casts composed of coagulated proteins can be demonstrated in the tubules. The blood vessels present an hyperplastic type of sclerosis with piling up of layers of cells on the intima. The glomerulae are quite variable in size, some are of huge proportions, but all stain poorly. Some glomerulae present the "necrotizing glomerulitis" described as characteristic in cases of this type. Many of the glomerulae present a pattern that does not conform to any of the previously reported descriptions.

Conclusions

Based on the clinical record, the rapid renal decompensation manner of death (uremic), and the autopsy findings we believe this to have been a case of malignant hypertension.

