ABSTRACTS OF ORIGINAL ARTICLES (IN JAPANESE LANGUAGE) IN THE OCHANOMIZU MEDICAL JOURNAL (OCHANOMIZU IGAKU ZASSHI) VOL. XII, 1964

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Abstracts of Original Articles

An Autopsy Case Report of Secondary Nephrocirrhosis Terminating in Acute Cardiac Decompensation

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An autopsy case of secondary nephrocirrhosis with acute cardiac decompensation seen in a 66-year-old, former professor of internal medicine is described. As the previous history, he had an attack of angina lacunalis, about 8 years prior to death, which was followed by acute nephritis. Since that time, he had been suffering from chronic nephritis which was noticeable clinically as the symptoms of occasional edema, palpitation, arrhythmia and albuminuria, however, as he unliked to have open medical consultations, the record was rather obscure. After his retirement in March, 1962, he apparently was feeling well and more active than ever. On Jan. 27, 1963, he took dinner at around 18:30 with ca. 300 cc of sake, as usual, and went to bed at about 19:00, where he was found dead by a house-keeper at 23:15.

At autopsy which was performed about 18 hours after death, (1) moderately advanced, secondary nephrocirrhosis, (2) generalized arterio-arteriolar sclerosis, (3) unusually severe dilatatoric hypertrophy of the heart (770 g), (4) chronic and acute congestion and hydrops showing generalized circulatory disturbances, (5) obesity of high grade, (6) cholelithiasis of the gall bladder, and (7) moderate emphysema of the lungs, etc. were revealed. From those autopsy findings, it was suggested that sudden cardiac arrest, which should be the immediate cause of death, occurred within an hour after he had taken his supper. The kidneys showed extensive subcapsular devastation and hypertrophy of the remaining glomeruli, however, there was apparently no high grade renal insufficiency. Marked

hypertrophy of the heart with dilatation had to be due to the nephrocirrhosis and subsequent hypertension although the latter of which was not rightly evaluated in his life time. Marked involvement of the conductive system of the heart suggested failure in cardiac action. There was no acute myodegeneration identified. It should be also noted that autopsy revealed no gastroduodenal ulceration which was supposed to be existing, clinically.

2. Two Cases of Porcine Embryonal Nephromas

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Embryonal nephroma has been known as one of the most common neoplasm in swine. But, as there was only one Japanese report by Katae (1933), it has been considered that the incidence of this tumour might be uncommon in Japan. In this report, embryonal nephromas in two pigs, which are one-year-old female Yorkshire hogs, are examined by the histopathological method.

Two cases were found from about 900,000 cases inspected at Tokyo Metropolitan Meat Inspector's Office during the years 1961 to 1962 inclusive.

The tumours were located in the left kidney and were firm, ovoid in both cases.

The sizes of the tumours were about $5\times6\times6$ 6 cm in case 1 and $4\times5.5\times4$ cm in case 2.

Grossly, they were surrounded by the well-formed capsule and on cross section they were separated into lobules by numerous connective tissue septa.

Microscopically, they consisted of a combi-

nation of neoplastic grandular and connective tissue although the epithelial element predominated, especially in the second case.

Generally both cases were similar in gross and microscopic structure and it was thought that they were typical porcine embryonal nephromas.

3. Studies of Rheumatoid Arthritis

(2) Fundamental Experiments in Relation to the Joint Ache and Histamine. (Change of the Histamine-like-substances in the Rabbit's Blood Followed by Intra-articular Histamine Injection.)

Hiroaki SAKAIDA (Dept. Orthopedics - I. Aoike)

In my preliminary report*, the following items were emphasized; (1) There is no histamine-like-substances (HTLS) in the normal synovial fluid of the human knee joint, but could be found in a few type of pathological synovial fluid. (2) The higher HTLS level of synovial fluid was proved in rheumatoid arthritis, and osteoarthritis deformans, simple arthritis and others showed lower HTLS level. (3) There are significant relationships between severity of the joint ache and the HTLS level in synovial fluid, but no significant connection was found between the HTLS level in serum and the HTLS level in synovial fluid.

In this report, intra-articular histamine injection were performed into the rabbit knee in order to investigate the relationship between HTLS level in blood and that of synovial fluid. Change of HTLS in the blood of rabbit then measured with "Magnus Apparatus". At the same time effects of intraarticular injection with 6% HCl solution and physiological saline solution were studied with comparison of influences resulted by blocking of knee nerves of rabbit.

(1) 1.0 c.c. of 10⁻⁵ mol. histamine being injected into the joint cavity of rabbit knee, the values of HTLS in blood suddenly decreased in the first 1-2 minutes and then gradually increased. The former phenomenon

will be described as "Initial decreasing" in following.

- (2) 0.5 c.c. of 10⁻⁵ mol. histamine injected into the knee joint of rabbit, did not show "Initial decreasing", and simple gradual increasing was noted.
- (3) 0.5 c.c. of 10⁻³ mol. histamine injection showed "Initial decreasing", i.e. increasing of histamine dosage produced "Initial decreasing" phenomenon.
- (4) Intra-musclar injection of 1.0 c.c. of 10⁻⁵ mol. histamine did not make the phenomenon of "Initial decreasing", and increasing of HTLS in blood was noted.
- (5) 0.5 c.c. of 6% HCl intra-articular injection produced the initial and even secondary decreasing of HTLS level in blood, and this is equivalent to the result of 1.0 c.c. of 10-5 mol. histamine injection.
- (6) In the cases of intra-articular injection of physiological saline solution, with 4.0 c.c. of this solution produced gradual increasing of blood HTLS, with 6.0 c.c. made gradual decreasing and injection with 7.0 c.c. produced "Initial decreasing". The result of the last injection was similar to that of 1.0 c.c. of 10-5 mol. histamine injection or injection of 6% HCl solution.
- (7) The injection of Anti-histamic agents into rabbit knee joint did not produce "Initial decreasing", and tend to decrease of it's level until pre-injection state.
- (8) With the partial excision or procaine blocking of the sciatic nerve and the femoral nerve which were considered as pain receptor of rabbit's knee joint, 1.0 c.c. of 10-4 mol. histamine injection did not produce so-called "Initial decreasing".

The results of these experiments suggest that the initial decreasing of HTLS in rabbit blood was not specific phenomenon due to intra-articular histamine injection, but it seems to be the results of reflection from joint ache which was produced by intraarticular injection of any kind.

(3) Clinical Experiments in Relation to the Joint Ache and Histamine. (On the Clinical Effects of Intra-articular Injection of Antihistamic Agent for Relief of Rheumatic Arthralgia.)

^{*}July 1960. J. Japan. Orthopedic Association.

The clinical application of the results in preliminary reports with regard of the relationship between joint ache and histamine were studied. In 53 cases, the effect of intraarticular injection of anti-histamic was investigated for relief of joint pains in a few type of knee joint disease. The following results were obtained.

- (1) The intra-articular anti-hitsamine injection was effective to 50% of this series, including rheumatoid arthritis and few other type of arthritis, especially to the arthritis that accompanied with higher values of HTLS in the synovial fluid or severe articular pain.
- (2) The values of HTLS in the synovial fluid are decreased in all the cases due to intra-articular application of anti-histamine.
- (3) It was the most effective to the osteoarthritis deformans compared with any other type of arthritis.
- (4) For the rheumatoid arthritis, it is less effective, and almost no effect was proved for the arthritis simplex.
- (5) The effects of this injection could last for five to six days and usually giving of more than three injections made less effect, therefore a few injection is advisable.
- (6) Complication was noted in 50% of these cases, most of them were drowsiness and none of them were severely affected.

4. Observations on the Chick Embryo Frontal Bone Cells in Cell Culture

 $Masao\ MATSUMOTO$ (Dept. Orthopedics — I. Aoike)

The trypsin-dispersed cell suspension prepared from the developing frontal bone of the 12-day-old chick embryos was cultivated in test tubes as stationary culture. For the substrates the coverslips treated with three various methods were used. The culture media was renewed every 48 hours. The observations were made in the living state by means of phase contrast microscope and after fixation with 10% formalin or absolute alcohol various staining methods were used.

The author obtained the following results:

1) The differences of the results, including

cell attachment, cell morphology and intercellular relation might be dependent on the nature of the substrate surface.

- 2) The cells got to the round shapes at the beginning of the culture, but soon they became spindle, triangular or flat polygonal shapes. In general, they had included the eccentrically placed nucleus with one to two conspicuous nucleoli in the cytoplasm and fine dark granules were recognized in the peripheral cytoplasm.
- 3) The migrating cells on the coverslip surface showed the tendency to gather centripetally to each other.
- 4) In the silver impregnated samples migrating cells formed irregularly arranged collagen fibrils around them. It might be suggested that they secreted the ground substance materials of the osseous tissue.

5. The Study of U Vector Loop or Arc. (1) Normal Subjects

Syozi TAKIGAWA

(Inst. Cardiovascular Diseases - T. Sano)

The U vector loop was studied on 30 subjects with normal heart. Vectorcardiograms were taken by the lead system of Frank and the U vector loop or the T-U loop was dissected electrically by the method of differential vectorcardiography.

The U loop of normal subjects resembled a small, slightly curved club and was inscribed almost in the direction of continuation of the terminal limb of the T loop.

The T-U junction vector, namely, the vector from the null point to the junction between the T loop and the U loop, was directed to the left, inferiorly, and mostly anterior.

Studies on Insulin Antibody. (I) Insulin Antibody and Histological Research of Insulin by the Fluorescent Antibody Technique

Takao WAKABAYASHI (1st Dept. Internal Medicine)

Insulin antibodies were produced in adult guinea pigs by repeated injections of an

insulin-Freunds complete adjuvant mixture. Crystalline pork or beef insulin, or pork regular insulin (Novo) were used. Injections were performed 2 times a week for 4 weeks. The sera of immune guinea pigs showed the insulin-neutralizing activities in the tests by mouse-convulsion assay procedure, changes in blood-sugar levels of mice and diabetes induced in mice. The titres of hemagglutination of insulin-conjugated erythrocytes with bis-diazo-benzidine were 1/64 to 1/2048. Precipitin of the immune sera with insulin were detected by the agar diffusion technique of Oakley or Ouchterlony. On immunoelectrophoresis the immune sera gave precipitation line with insulin corresponding to the β - or γ -globulin position.

The γ -globulin fraction of immune sera, fractionated by half-saturated ammonium sulfate method, was conjugated with fluorescein isothiocyanate. Using the fluorescent antibody technique, the states of insulin in mouse-tissues at several conditions of mice were observed. The specific yellow-green fluorescence was observed in the islet β -cells of Langerhans at normal mouse. The specific fluorescence was presented in the tubules of kidney and sometimes in the blood of livervessels. This evidence may be suggested the role of liver and kidney at the change of blood insulin-types. No specific fluorescence was presented in the section of pancreas of the mouse in which diabetes was induced by repeated injections of an anti-insulin guinea pig serum, and so in other tissues (liver, spleen, kidney and muscles). This state proved the absolute insulin deficiency. Yellow-green fluorescence was increased in all tissue-sections of the mouse in which hyperglycemia was induced by a single injection of glucose. This state proved the increasing of insulin in blood and the utilization of insulin on tissues.

Studies on Insulin Antibody. (II)
 ^{I131}-insulin Binding Antibody and
 the Binding to Serum Protein
 with I¹³¹-insulin

Takao WAKABAYASHI (1st Dept. Internal Medicine)

On paperelectrophoresis with I¹⁸¹-insulin the anti-insulin sera of immune guinea pigs showed peaks of radioactivity in the β - to γ -globulin region and at the origin. The peak of radioactivity at the origin was a precipitating I¹⁸¹-insulin-antibody complex. On the other hand, the sera of normal guinea pigs showed a peak of radioactivity at the α -globulin region.

On immunoelectrophoresis with I¹⁸¹-insulin the binding to the β - and γ -globulin fraction of immune guinea pig serum occurred, while the binding to the α -globulin fraction of normal guinea pig serum can be noted.

The binding to the β - and γ -globulin fraction (antibody) with I^{181} -insulin was so strong that the binding to the α -globulin fraction (normal insulin-carrying protein) with I^{181} -insulin was inhibited. By the addition of non-radioactive insulin to the system the binding to the β - and γ -globulin fraction with I^{181} -insulin decreased, while the binding to the α -globulin fraction with I^{181} -insulin occurred and increased in proportion to the more concentration of non-radioactive insulin.

Of the case of insulin-treated diabetic patients, only one serum from a boy treated 100 units insulin daily had the I¹³¹-insulin binding antibody at the γ -globulin fraction and showed a loss of the binding to the α -globulin fraction. Others were not insulinresistant clinically, who were treated 30 to 42 units insulin daily. In these cases the specific activity of I¹³¹-insulin was weak (2 mc/mg) and the concentration of insulin was high.

8. A Clinical Research of Vitamin A Deficiency through Electrical Skin Resistance

Yoshiichi SUGA (1st Dept. Internal Medicine)

With purpose to indicate numerically the degree of xeroderma in A-avitaminosis, we tried to determine the electrical skin resistance with Katsuki's ohmmeter.

Five different portion, namely posterior and lateral aspects of left upper arm, flexor aspects of left forearm, and lateral and medial aspects of lower leg was examined three times under the same condition and the results was averaged.

Vitamin A in blood plasma was also determined on the same day with Kimura's Glycerol dichlorohydrin method.

The average fasting level of the total vitamin A in blood of 40 healthy persons was $156.8 \pm 7.7 \text{ I.U./dl.}$

The average value of the electrical resistance of their skin was $3.5\pm0.8\,\mathrm{M}\Omega$ on the posterior aspect of left upper arm, $3.5\pm0.8\,\mathrm{M}\Omega$ on the lateral aspect of left upper arm, $4.1\pm0.9\,\mathrm{M}\Omega$ on the flexor aspect of left forearm, $5.4\pm1.5\,\mathrm{M}\Omega$ on the medial aspect of left lower leg and $5.3\pm1.4\,\mathrm{M}\Omega$ on the lateral aspect of the left lower leg respectively.

In the 20 patients with marked dry skin the average level of vitamin A $(88.1\pm4.0$ I.U./dl) was lower than the control group.

The average value of the electrical resistance of skin of those patients was 20.7 ± 4.4 M Ω on the posterior aspects of left upper arm, 21.0 ± 4.7 M Ω on the lateral aspect of the left upper arm, 26.8 ± 7.5 M Ω on the flexor aspect of left forearm, 28.7 ± 5.1 M Ω on the medial aspect of left lower leg and 28.6 ± 4.6 M Ω on the lateral aspect of left lower leg respectively.

15 patients with slight dry skin had the normal level of vitamin A and higher value of electrical resistance of skin than the control group.

On administration of vitamin A, however, the electrical resistance of skin of those patients gradually approached to normal value. 6 patients with Grave's disease had lower value of vitamin A in blood and lower level of electrical resistance of skin than the control group.

This fact may be accounted mainly through the increased tendency of sweating in those patients.

From the above-mentioned results the determination of electrical skin resistance may be well utilized as the diagnostic aid of vitamin A deficiency.

9. Oscillometry, Venography and Plethysmography in Shouldergirdle Syndrome

 $\begin{tabular}{ll} \it Masao SEKINE \\ \it (Dept. Orthopedics-I. Aoike) \end{tabular}$

With the aim of investigating the role of neuro-vascular compression in the shoulder girdle as a cause of brachialgia, the author examined the peripheral circulation of upper extremities in both cases with and without cervicobranchialgia by means of oscillometry, venography and plethysmography.

1) Deep inhalation and breath holding, deep inhalation and breath holding with neck extension, neck extension, head rotation, head tilting, head rotation with neck extension, spine extension and pressure on the carotid sinus were carried out on 150 normal persons, while oscillometric pulse was being recorded.

With deep inhalation and breath holding, a distinct diminution of oscillometric index was observed for more than 10 seconds duration, bilaterally, in 57.3% of normal persons. By deep inhalation and breath holding with neck extension, a diminution of pulse amplitude was seen in 78.0%, and in 14% the pulse waves disappeared completely as long as the experiment was carried out. By head rotation, head tilting, and neck extension, a diminution of pulse amplitude was observed in about 25% of normal persons and there was positive correlation (r=0.28, F_0 =12.51> F_{150}^{1} (0.01)=6.81) between the pulse amplitude diminution of head rotation with neck extension and pressure on the carotid sinus.

2) Deep inhalation and breath holding

interfere with the normal peripheral circulation, as described above, so that the original method of Adson test (1. take and hold a deep breath, 2. extend the neck fully, 3. turn the chin toward the side being examined with the arm at the side) must be substituted by only head rotation with neck extension.

- 3) The modified Adson test (head rotation with neck extension without taking and holding a deep breath) was tried on 250 normal persons and 2 (0.8%) were positive in the test. However, in 185 cases with cervico-branchial syndrome, 17 cases (8.9%) had a positive test, in which 6 cases were regarded as primary scalenus anticus syndrome, and 11 cases seemed to be secondary scalenus anticus spasm.
- 4) The exaggerated military posture, with the shoulder drawn backward and downward, was used to detect vascular compression on 100 normal persons, 7 were positive in the test. In 94 cases with cervico-branchial syndrome, 20 cases (21.3%) were positive. In 33 cases with the syndrome and without any pathological cervical x-ray finding, 16 cases (48.5%) were positive in the test.
- 5) Of 100 normal persons, 8% were positive in the hyperabduction test (the person is in the supine position and the arm is elevated in the lateral plane high above the head). In 103 cases with cervico-branchial syndrome, 5.8% had a positive hyperabduction test.
- 6) Axillary and subclavian vein venography was done on 12 patients (17 upper extremities), which had positive military posture test in oscillometry, and a typical form of venous obstruction at the site of costo-clavicular region was found in 15 upper extremities, while the remaining 2 upper extremities showed an atypical form of venous obstruction in the area of axilla, which seemed to be due to changes of obstructive phlebitis.
- 7) Digital plethysmography was done on 36 normal persons and 57 patients with cervico-brachial syndrome, including 17 cases with costoclavicular vascular compression recognized by oscillometry.

The mean pulse amplitude was 13.9 mm in normals and 9.1 mm in cases of cervico-

brachial syndrome, and the difference was recognized as significant. As for the difference between right and left pulse amplitude, the mean decreasing rate was 6.5% in normal persons and 18.6% in patients with cervical spondylosis and 9.8% in cases with costoclavicular compression syndrome. (18.6% was recognized as significant comparing with the normal, 6.5%) Mean crest time value was 14.3% in normals and 19.9% in cases with costoclavicular compression, and the difference was recognized as significant. The mean crest time value of cases with other branchialgia showed no difference comparing with the normal. Abnormal irregular forms of pulse waves which seemed to be due to an irritative state in the autonomous vascular nerve system, were observed in 42.2% of patients with costo-clavicular compression and in 31.0% of cases with cervical spondylosis, but in only 0.3% of normal persons.

The Study of U Vector Loop or Arc. (2) Left Ventricular Hypertrophy

 $Syozi \;\; TAKIGAWA$ (Inst. Cardiovascular Diseases — T. Sano)

The U vector loop was studied on 31 subjects with left ventricular hypertrophy by the method of differential vectocardiography.

Five of these subjects were excluded from the present study because they had the complication of myocardial infarction.

The U loop of left ventricular hypertrophy began with a marked bend at the T-U junction and extended in various directions, resembling a small curved club like the normal U loop, but sometimes much larger than it.

Occasionally, the U loop was inscribed in continuation of the terminal limb of the T loop like the normal U loop, but in such cases the T loop itself was abnormal.

All cases of left ventricular hypertrophy showed such an abnormal feature of the T-U loop in at least one planar projection, except for one case in which normal features were retained in all three planes.

Relatively slight left ventricular hyper-

trophy showed such an abnormal feature of the T-U loop in at least one planar projection, except for one case in which normal features were retained in all three planes.

Relatively slight left ventricular hypertrophy tended to be found in those cases which retained normal features in any one of the planes or those which showed abnormality in the U loop only, whereas relatively marked left ventricular hypertrophy tended to be found in those cases which

showed a distinct abnormality also in the T loop.

Such U-loop abnormalities were already evident in the early stage of left ventricular hypertrophy when there were no (or minute) evidences for such in ordinary electrocardiograms, including the U-wave changes. Thus, they are useful for diagnostic purposes in detecting slight left ventricular hypertrophy.