- 34) Nukada, S., T. Kimura, K. Ohba, C. Ryu, etc.: *Ibid.*, 34:106, 1944.
- 35) Nukada, S., C. Ryu and T. Yoshii: *Kekkaku* (Jap.), 15:999, 1937.
- 36) Nukada, S., C. Ryu and T. Yoshii: *Laboratory and Clinic* (Jap.), 1:17, 1947.
- 37) Nukada, S. and M. Okutani: *Medicine and Biology* (Jap.), 9:32, 1946.

STUDIES ON CLINICAL AND PATHOLOGICAL ASPECTS OF RETICULOSARCOMATOSIS, ESPECIALLY ON THE DIFFERENCE IN RADIOSENSITIVITY AND PROGNOSIS OF VARIOUS HISTOPATHOLOGICAL TYPES*

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Among the malignant tumors arising from lymphatic tissue and showing the clinical picture of Kundrat's lymphosarcomatosis, we can discern two kinds. Lymphosarcoma, in a narrow sense, being derived from lymphatic cells which are parenchyme cells of lymphatic organs, can be discriminated theoretically from the cells or reticulo-endothelial system; which consist of reticulum cells, and which can be regarded as supporting tissue of lymphatic organs. Reticulosarcoma which appertains to the latter forms the subject of the present discussion.

Rössle and Roulet named it retothelsarcoma, and Ahlström called it reticulum-cell sarcoma. However, according to the classification of the tumors of hematopoietic tissues advocated by Ogata, it may conveniently be called lymphatic reticulosarcoma. There are quite similar tumors in myeloic tissue too, and the tumor named "Sarcoma of Ewing" is the typical myeloic reticulosarcoma. Reticulosarcoma which spreads systematically throughout the whole body is then called reticulosarcomatosis. According to the above definition, almost all my cases are lymphatic reticulosarcoma. However, there are also some cases which are impossible to deny their myeloic nature.

During about 10 years since this Hospital was established in 1934 up to year 1944, 348 patients of all kinds of sarcoma visited us in the Radiological Division of the Hospital. Among them were 110 cases of reticulosarcoma, which were carefully examined histopathologically, amounting to 31.6% of all the sarcoma cases. (See Table 1.) This is a noteworthy fact especially, since these cases have heretofore been believe to be rare. For all these 110 cases, diagnosis had been determined by biopsy, and 18 of them also

* The gist of this paper was presented already at the first Scientific Conference of the Japanese Foundation for Cancer Research in November, 1942, and at the meeting of Radiological Committee of the National Research Council in June, 1944.

Table I

Primary Site Histology	Lymphosarcoma	Reticulosarcoma	Round cell sarcoma	Polymorphocell S.	Leucaemiosarcoma	Giant cell sarcoma	Fibrosarcoma	Spindel cell S.	Chondrosarcoma	Osteosarcoma	Melanosarcoma	Angiosarcoma	Myxosarcoma	Lymphoepithelioma	Sarcoma	Whthout Specimen	Total
Tonsil	2	37	1												7	3	50
Epipharynx	1	20													8	2	31
Pharynx	2	7	1				1								4	5	20
Palate		2					1										3
Oral Cavity		3									1				3		7
Head	1				1		1			3					1		7
Nasal Cavity											1				2		3
Maxilla	1	7	1	3			4	2							5		23
Jaw	1			1			1	2									5
Other Part of Face								1			1	1			1	2	6
Parotid	1	3													2	3	9
Submaxillary Region	3	8	2		1									1	3	2	20
Neck	5	12		2	1	1	1	1						1	7	4	35
Thyroid		1				1	1										3
Axilla	1	1										2			1	2	7
Mediastinum	1	2													1	5	9
Trunk		2		1		2	4	3	3	11		1	1		3	1	32
Abdomen	4														2	6	12
Inguinal Region	1	1													2		4
Extremity		3	1	1		1	6	1	1	19	1	1			5	10	50
Kidney			1													2	3
Bladder													1				
Testicle			1												2	2	5
Rectum											1						1
Larynx		1															1
Total	24	110	8	8	3	5	20	10	4	33	5	5	2	2	59	50	348

by autopsy. I hereby express especially my gratitude to Dr. T. Ban of Pathological Division in our Foundation for Cancer Research for his cooperation in histological examination.

In the light of pathology, I had classified these 110 cases of reticulosarcoma into several types, making observations on various clinical aspects and especially on radio-sensitivity and prognosis with regard to each type; I have been led to very interesting conclusion that had not been known much among workers.

Even though reticulosarcoma had already been classified into several types by pathologists, according to the grades of development of cells composing the tumors, I have classified them into the following 4 types with advantage in dealing with the aspects of radiosensitivity in view.

1. The immature, or undifferentiated type.
2. The mature, or fibrogenic type.
3. The polymorphocellular type.
4. The mixed reticulo-lympho type.

In the above classification, type 1 is equivalent to groups I & II of Guilherme de Oliveira, type 2 is equivalent to groups III & IV of the same author and types 3 & 4 are equivalent to groups V & VI respectively. There were more difficult and more complicated types in addition to the above four. However, the explanation about them have been left out and they are summarized together as the "other types" in this paper.

Of the 110 cases which came under my observation 73 cases were males and 37 cases females, that is to say, male is twice the number of female, and greatest majority of the cases were 51 and 70 years of age. (See Table II.)

Table II

Age \ Sex	Male	Female	Total
1 — 10	0 (18)	1 (7)	1 (25)
11 — 20	4 (25)	0 (13)	4 (38)
21 — 30	6 (16)	1 (15)	7 (31)
31 — 40	10 (24)	5 (11)	15 (35)
41 — 50	15 (34)	7 (15)	22 (49)
51 — 60	16 (25)	8 (7)	24 (32)
61 — 70	16 (10)	8 (10)	24 (20)
71 — 80	5 (10)	7 (2)	12 (8)
81 — 90	1 (0)	0 (0)	1 (0)
Total	73 (158) 231	37 (80) 117	110 (238) 348

The number in () are other kinds of Sarcoma

Table III

Type \ Sites	Immature Type	Mature Type	Polymorpho-cellular Type	Mixed Reticulo-Lympho Type	Other Type	Total
Tonsil	8	23	3	2		37
Epipharynx	6	12	1	1		20
Pharynx	4	2		1		7
Palate	1	1				2
Maxilla		6			1	7
Parotid	1	2				3
Submaxillary Region	2	5	1			8
Neck	2	8	1		1	12
Mediastinum		2				2
Trunk		1			1	2
Extremity	1	1	1			3
Others	1	2	1	1	1	7
Total	26	65	8	5	4	110

As to the primary site of the tumor, there are 37 cases in tonsil which is the greatest number of the cases, 20 cases in epipharynx, 12 cases in cervical region, 8 cases in submaxillar region, 7 cases in pharynx, 7 cases in maxillar cavity, etc. (See Table III.)

As to the relation of duration of life, that is the period between the date of the beginning of illness and the date of death, to the pathological types, it may be said that in immature type and in mixed reticulolympho type, the greatest majority takes the acute form and tumor generalizes rapidly throughout whole body, i. e., forms the sarcomatosis in a short period of time. On the contrary there are considerable numbers of mature type, in which the growth remains localized in the original site for a comparatively long time and metastasizes slowly. That is to say, 16 cases, 73%, out of 22 cases of the immature type died within one year and no case was cured. However, among 54 cases of the mature type, 23 cases, 42.5%, died within one year, but 12 cases, 22.2%, were cured, which have been free of symptom more than two years and have not recurred up to the present. (See Table IV.)

Table IV

Histological Type Duration of Life	Immature Type	Mature Type	Polymorpho-Cellular Type	Mixed Reticulo-Lympho Type	Total
Within $\frac{1}{2}$ year	4	6			10
" 1 "	12	17	3	2	34
" 1 $\frac{1}{2}$ years		11	2		13
" 2 "	3	4			7
" 3 "	2	5 (2)			7 (2)
" 4 "	1	2 (2)			3 (2)
" 5 "		5 (4)	1 (1)		6 (5)
" 6 "		1 (1)			1 (1)
" 7 "		1 (1)	1		2 (1)
More than 7 years		2 (2)			2 (2)
Total	22	54 (12)	7 (1)	2	85 (13)

The figures in () are the cases which survived more than 2 years after irradiation without recurrence.

From these results it appears that the mature type has high radiosensitivity, and better chance of cure, while the immature and mixed reticulo-lympho type have poor radiosensitivity, and therefore hard to be cured. However, on the examination of radiosensitivity of local tumors of each type, I obtained the opposit results.

In regard to the radiosensitivity of the local tumors in these cases I tried to separate them into 4 groups, from the 1st grade to the 4th, according to their radiosensitivity. I will now observe the radiosensitivity of tumor through the dosage of X-ray or radium necessary for the disappearance or reduction in size of the tumor in certain sites. My 1st grade is the exceedingly radiosensitive group in which a large tumor can be made to disappear rapidly by irradiation of less than 2000 r. of X-ray or radium. The 2nd grade has also a rather high radiosensitivity, requiring for the same results irradiation of 2000 to 4000 r.

tion of 4000 r. but the effect is not so rapid as in the 1st grade. The 3rd grade is of poor radiosensitivity; the tumor can be reduced in size gradually by irradiation of from 4000 r. to 6000 r. 4th grade show no reactions, even though irradiated with more than the above dosage.

In my immature type, 19 cases, 82.6%, out of 23 cases, and in the mixed reticulo-lympho type, all the cases, showed the reaction of the 1st grade. On the contrary, in the mature type, only 16 cases, 30.7%, out of 52 cases belonged to 1st grade, while 30 cases, 57.7%, to the 2nd grade and this is the majority. Furthermore, only in the mature type there were the less sensitive groups, i. e., the 3rd and 4th grades. (See Table V.)

Table V

Histological Type Radiosensi- tivity	Immature Type	Mature Type	Polymorpho -Cellular 'Type	Mixed Reticulo- -Lympho Type	Type
I (1st Grade)	19	16 (6)	3	5	43 (6)
II (2nd Grade)	4	30 (5)	3 (1)		37 (6)
III (3rd Grade)		4			4
IV (4th Grade)		2			2
Total	23	52(11)	6(1)	5	86(12)

The figures in () are the cases which were free from symptom more than 2 years after irradiation

The above facts show the paradoxical results that the immature type and the mixed reticulo-lympho type, which have the highest radiosensitivity, have the worst prognosis. In other words, as to healing of reticulosarcoma, it is thought that there must be some important factor outside of the radiosensitivity of tumor in determining the prognosis; otherwise these facts cannot be explained.

I believe that the essential nature of the disease is at the base of this factor, and the theory of the multicentric genesis of the disease may be the true explanation. If it is understood that the tumors are multicentric in genesis, the healing of a local tumor by X-ray or radium, may be accomplished easily on account of its high radiosensitivity, without being able to cure the entire illness. Therefore, it is no wonder that the illness has not been cured by this method of treatment.

From these points of view I support the multicentric genesis of the tumor, and explain the reasons why the types with high radiosensitivity may be difficult to cure.

REFERENCES

- 1) Ahlström, C.: Acta path. Scandi. (Kobenh.), Bd. 10, S. 241, 1933.
- 2) Akazaki, K. & Kuroiwa, K.: Gann, Jap. J. of Cancer Research, Vol. 36, No. 4, P. 134, 1942.
- 3) Baumann-Schenker: Strahlentherap., Bd. 51, S. 201, 1934.

- 4) Döring, G.: Beitr. z. path. Anat., Bd. 101, S. 348, 1938.
- 5) Edling, L.: Radiology, Vol. 30, P. 19, 1938.
- 6) Ewing, J.: Amer. J. of Path., Vol. 25, P. 97, 1929.
- 7) Gohn, A. u. Roman, B.: Frankf. Z. Path., Bd. 19, S. 1, 1916.
- 8) Itōw, M. & Makino, L.: Gann, Jap. J. of Cancer Research, Vol. 34, No. 6, P. 329, 1940.
- 9) Ogata, T.: Gann, Jap. J. of Cancer Research, Vol. 33, No. 6, P. 455, 1939.
- 10) Oberling, C.: Bull. l'Assoc. Franc. l'Étud. Canc., T. 17, P. 259, 1928.
- 11) Oliveira, G.: Virchow's Arch., Bd. 292, 1934.
Oliveira, G.: Virchow's Arch., Bd. 298, S. 464, 1936.
- 12) Roulet, F.: Virchow's Arch., Bd. 277, S. 15, 1930.
Roulet, F.: Virchow's Arch., Bd. 286, S. 702, 1932.
- 13) Rössle, R.: Virchow's Arch., Bd. 295, S. 1, 1930.
- 14) Verhagen, A.: Zeitschr. f. Krebsforsch., Bd. 50, S. 163, 1940.

LENS EXERCISE AS A TREATMENT OF MYOPIA

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Formerly it was believed that most myopia was of an axial nature, i.e., a result of lengthening of the antero-posterior diameter of the eyeball, so that parallel rays focussed in front of the retina. While axial lengthening of the eyeball is undoubtedly the cause of myopia of high degree (the so-called progressive or malignant myopia), yet development of myopia of slight degree (the so-called school myopia or benign) can be explained better on another basis.

School myopia must be a lens myopia. In the case of prolonged eye strain, such as produced by continuous attention on minute objects, the ciliary muscle is maintained in a state of contraction; finally a spasmodic condition makes its appearance, which then causes the lens to be in a state of increased convexity. This "spasmodic convexity" was found to be the primary or acute condition producing school myopia. With increasing age the lens gradually loses its inherent elasticity, and the lens becomes less capable of correcting its convexity even if the ciliary muscle were released from its spasmodic condition. This "inelastic convexity" is the secondary or chronic condition for the production of school myopia. It is for this reason that the acute spastic convexity can be relaxed easily by atropine, but the secondary inelastic convexity can not.

There is much evidence to support this theory. Statistically, the distribution of the refraction of the new born shows a "normal variability curve" or "probability curve", with a slightly hyperopic point as the mode. This curve changes its form noticeably in the school age period, in which the slopes of the curve are much steeper, with the apex at the emmetropic point. This phenomenon is called emmetropization or centralization of the refraction. The problem arises as to how this emmetropization is brought about. The refraction curve of patients after cataract extraction provides the answer.