

CLINICAL AND RADIOTHERAPEUTIC ASPECTS OF RETICULUM CELL SARCOMA

by

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The results of radiotherapy of malignant lymphomas appear to have gradually improved during recent years, which may be partly attributable to the increased use of megavoltage therapy. The possibilities of improving the therapeutic results by means of prophylactic irradiation have also been discussed (EASSON 1967, JACOBS 1968). This means that the lymph gland regions involved as well as surrounding areas are included in the treatment programme. The significance of prophylactic irradiation in the treatment of Hodgkin's disease is generally recognized but there is little common agreement as regards such treatment in cases of lymphosarcoma or reticulum cell sarcoma.

Attention in the present studies was mainly directed towards establishment of the possible sites of secondaries and the chronologic sequence of the primary neoplasms treated locally. An attempt was also made to note the sites of predilection, if any, with a view to possible prophylactic irradiation.

Material and Methods. The material consists of 154 reticulum cell sarcoma cases, registered during the period 1951—1962. The diagnosis was based on microscopic examination in every instance. Histologic verification was not always

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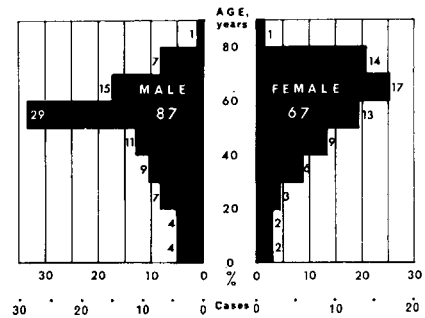


Fig. 1. Sex and age distribution in the series of 154 cases of reticulum cell sarcoma.

made in connection with the assessment of a recurrence or of a growth at a new site, the diagnosis then being based on the clinical signs. Lymphography was not yet in use at that time. In considering the mode of dissemination, data from the case histories were taken into account if consistent with the clinical signs.

The primary localization was considered to be the site at which the local disease was first diagnosed. Any new manifestation in an area already treated was considered to constitute a recurrence. Secondary occurrences were understood to be new areas of malignancy including those in the same region as the primary tumour but separate from the one treated. The secondary occurrences are presented according to a grouping by phases that indicate the chronologic order in which such occurrences were noted in each individual.

The age and sex distribution of the material are presented in Fig. 1. There were 87 men and 67 women, the male:female ratio thus being 1.3:1. The peak frequency occurs in the 50—60 year age group of men and in the 60—70 year age group of women. The higher incidence of the disease in the younger age groups of men is evident from the figures.

The primary localizations in the present material are recorded in Fig. 2, five patients, in whom the disease was in the generalized stage on admission for treatment, being excluded. The disease commenced in the region of the head and neck in 88 cases (57%) and in 85 of them (55% of the material) the primary tumour arose in the lymphatic tissue in the cervical region.

The degree of spread of the disease was classified in three groups according to PETERS (1963):

Stage I — Single lymph node region, or single site in extranodal tissue;

Stage II — Multiple lymph node regions, or single extranodal site with involvement of adjacent lymphatic region;

Stage III — Evidence of systemic disease, or involvement of the liver, spleen or bone marrow, or a single extranodal site with involvement of remote lymphatic region.

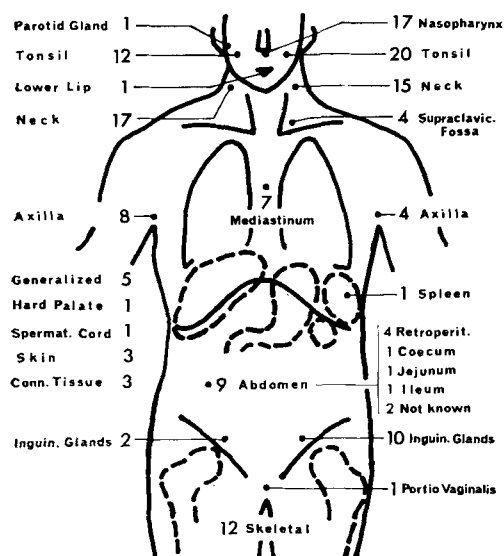


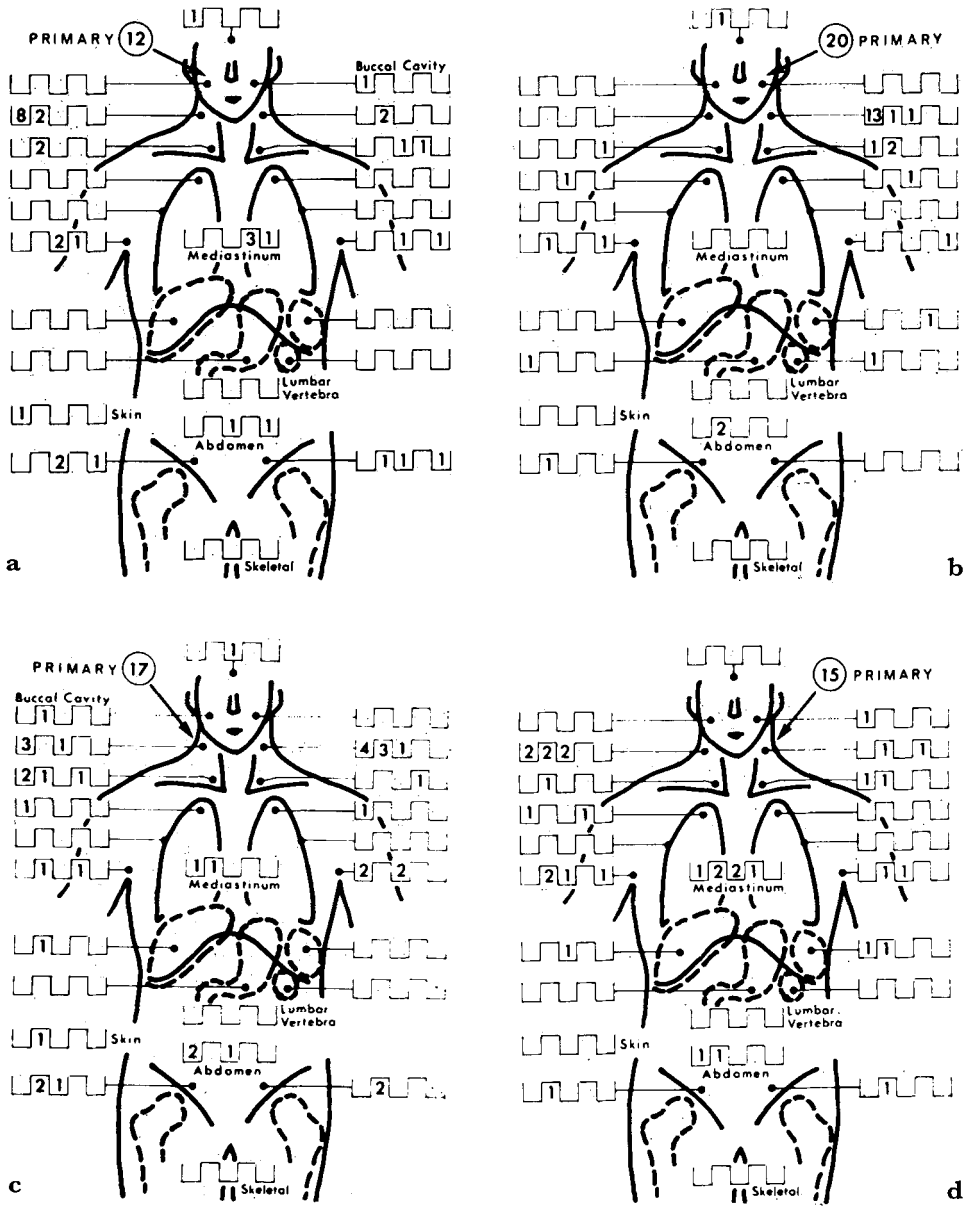
Fig. 2. Distribution of the series by the primary site of the tumour.

The distribution within this classification in the present material was stage I for 94 cases, stage II for 44 cases, and stage III for 16 cases.

Therapy. Most of the patients were treated with orthovoltage roentgen rays but twenty-one patients received teleradium treatment and seven telecobalt radiation.

In the treatment of nodes in the neck and in axilla or groin the factors were 180 to 190 kV, 0.5 mm Cu filter and 40 cm focus-skin distance, and in the treatment of mediastinal, abdominal and bone tumours 230 to 250 kV, 1 mm Cu filter and 60 cm FSD. The most common field sizes were 6 cm × 8 cm and 8 cm × 10 cm. The daily field dose on the skin was 250 to 350 rad; most often two converging fields were used. The tumour dose in the entire material varied between 2 000 and 6 000 rad, and the total treatment period from 14 to 28 days. When teleradium (5 g cannon) was applied, the daily dose usually amounted to 732 rad to each field of 28.26 cm² at 6 cm distance; 3 to 4 fields were employed. Teleradium was mainly used for treating the nasopharynx and tonsils. Telecobalt treatment with a daily skin dose mostly of 300 rad and a focus-skin distance of 60 to 80 cm was given 6 times weekly. The treatment area was confined to the tumour and to its immediate environment. No prophylactic irradiation was applied. The treatment was administered to forty-one cases postoperatively after excision of the primary tumour. Chemotherapy was included in three instances.

The survival rate was calculated from the start of treatment.



KEY: 1st 2nd 3rd 4th 5th etc.

SECONDARY OCCURRENCES

Fig. 4. Secondaries at different sites. *Upper left*: in eleven out of twelve cases of primary tumour of the right tonsil. *Upper right*: in sixteen out of twenty cases of primary tumour of the left tonsil. *Lower left*: in sixteen out of seventeen cases of right primary cervical tumour. *Lower right*: in eight out of fifteen cases of left primary cervical tumour.

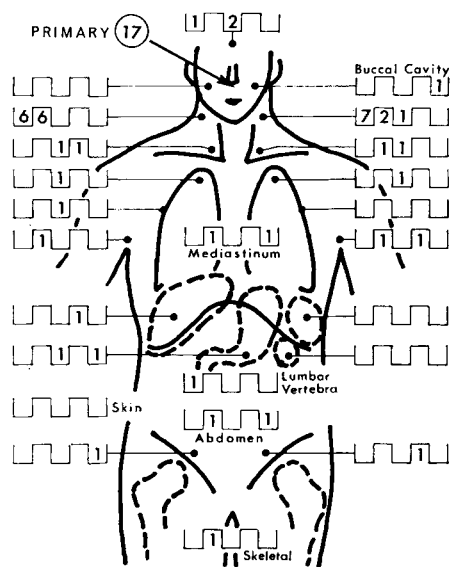


Fig. 5. Secondaries in fifteen out of seventeen cases of primary nasopharyngeal tumour. (See key in fig. 4.)

the level of the clavicles in a lumbar vertebra, whereas fourteen were located above this level. In the second phase, too, there were still nine supraclavicular and only five infraclavicular sites. The latter increased in relative number at the subsequent phases. No preferential locations were noted among those below the level of the clavicles, three of which occurred in the axilla, two each in the mediastinum, groin, abdomen and lungs, and one each in the pleura, bones and liver.

Of the thirty-two cases with primary site of tumour in the neck, twenty-four developed further growths (Fig. 4, c and d). Six of these consisted of local recurrences while new locations numbered sixty-six. Of the secondary growths, forty-one (57%) lay below the level of the clavicles and half of this number in the adjacent lymph gland areas, namely, twelve in the axillae and eight in the mediastinum. The site of the secondaries was supraclavicular and infraclavicular in thirteen and eleven cases, respectively, in the first phase, and in ten and seventeen cases in the second phase.

The primary growth was situated in the skeleton in twelve cases, in nine of which the disease recurred. Five of the secondaries (56%) appeared in the bones. In contrast, only fourteen secondaries were associated with 118 non-skeletal primary tumours (12%).

As regards the relation in time of the secondaries to the primary tumours in the preceding groups it was observed that regional secondaries appeared within 2 to 6 months in a considerable number of cases. No distinct relationship

seemed to exist between the time preceding the appearance of secondaries and the prognosis. On the other hand, secondaries at a more remote site usually preceded rapid deterioration, even when such an occurrence did not follow for some time.

Results

The survival rate in the total series is presented in Fig. 6. Those surviving for one year or longer after demonstration of the primary tumour form 50 % of the series. The survival rates after 2, 5 and 10 years were 27 %, 17 % and 9 % of all patients, respectively. The corresponding figures can also be read from the graphs presented for the groups in different clinical phases of the disease. The stage on admission for treatment had a distinct influence on the survival. The same is true in respect to the age of patients on admission (Fig. 7); the prognosis deteriorated with increasing age. Patients under 40 years constitute an exception to this, in that their survival rate graph was nearly identical to that of those aged 60 to 70 years (5-year survival less than 15 %). This poor prognosis of patients under 40 is even more marked in the female age groups where the graph of those aged 60 to 70 on admission roughly approximates that for the patients who were 40 to 50 and 50 to 60 years old when treatment was undertaken for the primary growth.

Fig. 8 gives the survival rates in the groups with different primary tumour sites. The most favourable 5-year results were in the groups of tonsillar, mediastinal and abdominal primary tumours (20 % or better). The survival rate was poorest in the group with primary skeletal growths; 25 % after 2 and zero after 5 years.

The results of treatment in relation to the amount of radiation employed are seen in Fig. 9, which indicates that the tumour dose of 3 000 rad over 3 weeks constitutes a limit; below this the survival rates are obviously lower than the rates obtained when higher dose levels were the rule, whereas virtually no differences were recorded between the groups of patients who received 3 000 to 5 000 rad and more than 5 000 rad, respectively.

Of the 14 patients who survived for 10 years or longer, the site of the primary tumour was tonsillar in four, nasopharynx in one, neck in four, axillar in two, retroperitoneal glands in two and inguinal gland in one. In seven of these, no secondaries were noted, while the other seven were later treated for neoplasms. As an example of the last-mentioned, a male patient aged 55 years with a primary tumour of the neck, was treated with irradiation up to 5 500 rad. Secondaries subsequently necessitated treatment of the left axilla ad 4 000 rad, the left

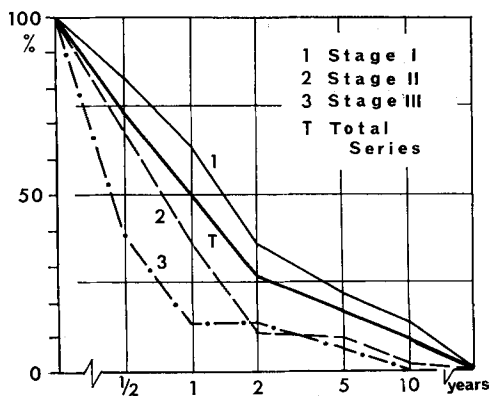


Fig. 6. Survival rates in the total series.

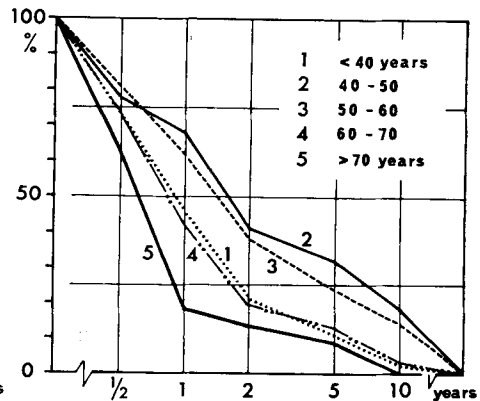


Fig. 7. Survival rates in the different age groups of the series.

pulmonary hilum ad 5 000 rad, both inguinal folds ad 5 000 rad, a recurrence in the left axilla ad 4 000 rad and the left parotid area ad 4 000 rad. The patient was then symptom-free for 8 years.

Discussion

Reticulum cell sarcoma is a disease of late middle age, with peak incidence in male patients aged 50 to 60 and in female patients aged 60 to 70 years. A higher frequency of onset of the disease in the younger age groups occurs in men. The male:female ratio was 1.3:1, which is consistent with other reports (e.g. BERGSTEINOVÁ et coll. 1967).

Of the primary growths 57 % arose in the region of the head and neck. This agrees approximately with other reports (GYENES 1967 with 50 % per cent; SCHEER 1963 with 62 %). BONADONNA et coll. (1967) found 53% of the primary tumours within Waldeyer's ring, whereas in the present series the contribution of the tonsils and nasopharynx amounted to 31 %.

Regarding other locations, i.e. sites below the level of the clavicles, remarkably uniform distribution of the primary growths, without any indication of predilections, was noted. The same observation applies to other series reported (SCHEER 1963, GYENES 1967).

Of the secondaries following a primary growth of the tonsils, nasopharynx or cervical region, 59 % in all arose above the level of the clavicles. Of the tonsillar, nasopharyngeal and cervical tumours, 89 %, 93 % and 54 % respectively, produced first-phase secondaries at supraclavicular site (50 % in SCHEER's series

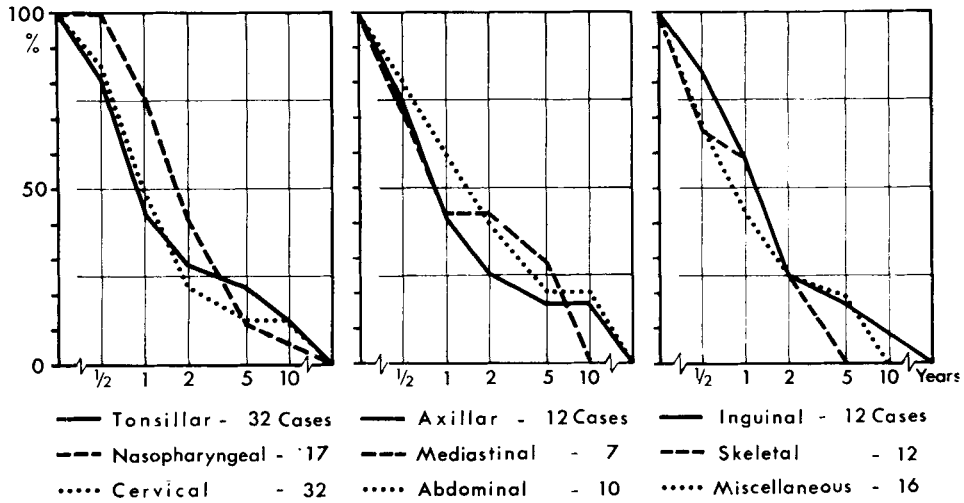


Fig. 8. Survival rates in reticulum cell sarcoma at different primary sites.

of primary tumours in the cervical region). Late secondaries below the level of the clavicles are widely dispersed, with a predilection however for the axillae and mediastinum.

Primary reticulum cell sarcomas of bone also display a distinct tendency to produce secondaries at skeletal sites (in 56 % of cases) as against only 12 % when the primary is in any other location.

A comparison of the results of treatment against other series reported on the basis of the 5-year survival rates is presented below:

BERGSTEINOVÁ et coll. (1967)	49 cases	34.6 per cent
MOLANDER & PACK (1965)		21.3
COOK et coll. (1960)	94	21.2
GYENES (1967)	40	20
PETERS (1963)	73	16
ROSENBERG et coll. (1961)	554	13.9
JACOBS & MARASSO (1964)	26	7.7
Present series (1969)	154	17

It would appear that the 5-year results in the present series are in the same order of magnitude as in many of the other series reported. The 50 % mortality noted during the first year also confirmed previous observations (PETERS, BERGSTEINOVÁ et coll., COOK et coll.).

The tumour dose of 3 000 rad over 3 weeks, established as a significant limit from the results, is in keeping with other series as well. According to GYENES

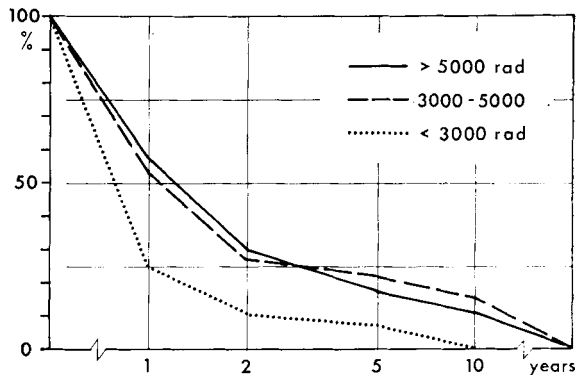


Fig. 9. Survival rates in groups of the series treated at different radiotherapeutic dose levels.

(1967), the frequency of recurrence was clearly higher among those who received less than 3 000 rad; his doses varied between 3 000 and 4 000 rad. Similarly, JACOBS et coll. (1964) recommended doses of 3 000 rad and higher. PETERS (1963) suggested 5 000 rad over 4 weeks; she used between 4 000 and 6 500 rad. BERGSTEINOVÁ et coll. (1967) stated that they applied a method in which following disappearance of the tumour 50 % of the dose thus far administered was given. HOLME & KUNKLER (1961) gave 3 000 rad over 4 weeks and FULLER & FLETCHER (1962) 5 000 rad with a 750 rad weekly dosage with orthovoltage and 1 000 rad per week with supervoltage therapy. The various recommendations made in the literature may be summarized to the effect that most authors use a total dose of 4 000 to 5 000 rad. This is in agreement with the experience of the present writers.

Divergent opinions have been expressed concerning prophylactic irradiation. Most authors consider there is no advantage to be gained by prophylactic irradiation of unaffected lymph gland regions (PETERS 1963, BERGSTEINOVÁ et coll. 1967, SCHEER 1963). PARKER (1968) believed that as long as the dissemination of lymphomas is not completely understood, the primary regions and regional lymph regions should be treated. EASSON (1967) has also recommended prophylactic irradiation similar to that in Hodgkin's disease.

BONADONNA et coll. (1967) considered prophylactic irradiation to be indicated only in connection with primary tumours established within Waldeyer's ring. The present series suggests it wise to treat the entire cervical region prophylactically in reticulum cell sarcoma of the tonsils or nasopharynx. On the other hand, prophylactic treatment of the axillae and mediastinum does not appear suitable in primary tumours of the cervical region, as SCHEER (1963) has pointed out. The same is also obviously true for other primary locations; particular attention at follow-up examinations should be paid to all lymph gland areas, and not only

to the probably affected areas. The possibility of secondaries in tissues other than the lymphatic system should be kept in mind.

Conclusions

1. The primary locations of reticulum cell sarcoma are above the level of the clavicles in more than half of cases.

2. Secondaries occurred in 83 % of the cases with tonsillar and nasopharyngeal primary growths; with only few exceptions, the first secondaries occurred (89 % and 93 % of cases, respectively) in the neck. These primary locations justify prophylactic irradiation of the entire cervical region; prophylactic radiotherapy does not appear suitable when the primary growth is elsewhere.

3. The tumour is locally curable with the comparatively large total dose of 4 000 to 5 000 rad over 4 to 5 weeks. The reaction of the tumour to irradiation should be followed and the total dose adjusted accordingly.

4. The course of the disease is remarkably malignant, half of the patients dying within the first year. The authors agree with the reports in the literature, however, that even good treatment results may be achieved in certain instances, an inducement to endeavours to find the optimum therapeutic technique. Megavoltage therapy would appear to offer considerable possibilities in this direction.

Acknowledgement

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SUMMARY

The treatment results and spread of the tumour in 154 cases of reticulum cell sarcoma treated during the period 1951—1962 have been analyzed. Particular attention was paid to the largest groups, i.e. those with nasopharyngeal, tonsillar and cervical primary location of the tumour. Prophylactic irradiation of the entire cervical region is discussed.

ZUSAMMENFASSUNG

Strahlenbehandlungsergebnisse und Ausbreitung der Tumoren wurden in 154 Fällen von Retikulumsarkom während der Periode 1951—1962 analysiert. Besonders wurden die grössten Gruppen beobachtet, d. h. in denen die Tumoren im Nasopharynx, in den Tonsillen und im Hals lokalisiert waren. Der Wert der prophylaktischen Bestrahlung der ganzen Halsregion wird diskutiert.

RÉSUMÉ

Les auteurs ont analysé les résultats du traitement et l'extension de la tumeur dans 154 cas de sarcome à cellules réticulaires traités pendant la période 1951—1962. Ils ont prêté une attention particulière aux groupes les plus nombreux, c'est-à-dire ceux des localisations primitives nasopharyngées, amygdaliennes et cervicales. Ils étudient la valeur de l'irradiation prophylactique de toute la région cervicale.

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