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NEUROLOGIC COMPLICATIONS AFTER IRRADIATION OF THE CERVICAL SPINAL CORD FOR MALIGNANT TUMOUR OF THE HEAD AND NECK

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Serious, irreversible transverse lesions of the cervical spinal cord after irradiation of tumours in the head and neck have been reported (AHLBOM 1941, BODEN 1948, JACOBSSON 1951, VAETH 1965, VAN DEN BRENK et coll. 1968). Neurologic deficits developed as a result of radiation myelitis in 103 out of 4 365 patients from 15 treatment series who had received irradiation of the cervical, thoracic or lumbar spinal cord (survey by PALMER 1972). In addition to transverse spinal lesions milder transient neurologic symptoms such as parasthesias and weakness of the extremities were also reported. Taken together, the total incidence for mild and severe complications was 2.4 per cent.

The total dose to the spinal cord, the treatment time, and the area of the field are some of the physical factors of significance in the development of radiation myelitis. There is, however, no agreement regarding the significance of the dose–time relation (BODEN, VAETH) or of the treatment volume (PALLIS et coll. 1961, JONES 1964). A review of the available reports reveals that in the majority of cases radiation myelitis occurs in patients treated with very high doses, with large doses over a short period, with large fields, or with an irradiation technique that produces a 'hot spot' in the spinal cord.

In view of these observations special consideration to the dose to the spinal cord

Submitted for publication 5 July 1974.

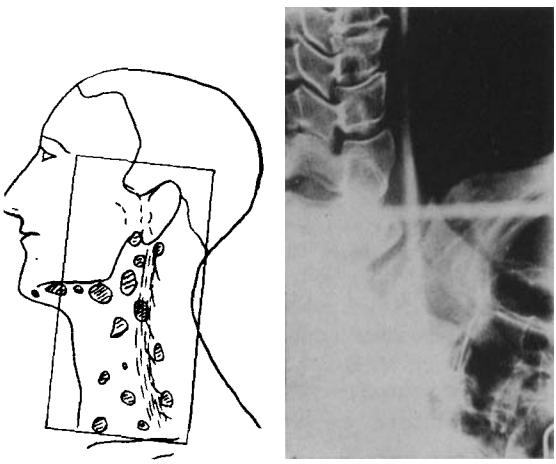

Fig. 1. Drawing and control film of arrangements for irradiation to the neck with 2 opposing lateral fields.

has not been paid at the Radium Centre since 1965, in the treatment of malignant tumours in the head and neck. During the period February 1965 to December 1971, 165 patients with such tumours received irradiation which included the cervical spinal cord. The records for these patients have been evaluated with reference to neurologic complications.

Material. The material consisted of 55 women and 110 men ranging in age from 6 weeks to 88 years, with the average age at 52 years. The lesions in 62 cases were solid tumours in the head and neck and in 103 malignant lymphomas.

All the patients were given high energy irradiation; the entire cervical cord was included in all cases, and the thoracic segment as well in 93 cases. The observation time was in all cases at least $1\frac{1}{2}$ years after completion of irradiation, except for those who died of their illness before the end of this time.

Technique of irradiation

Simple treatment arrangements with 2 opposing fields, 'standard fields', were mostly used. The patients were irradiated with photons from ^{60}Co (6 000 Ci) or a 6 MeV linear accelerator. The treatment distance varied between 80 and 130 cm.

In order to achieve homogeneous dose distribution in irradiated areas with differing tissue thicknesses, individually prepared compensation filters of aluminium blocks have been used since 1966. In most cases, the irradiation was given daily to both fields, 5 days a week. The general aim was to give a weekly tumour dose of 1 000 rad. During irradiation, the patients were immobilized in a plaster or plastic cast. The field adjustments were performed under fluoroscopy, and control films of the field arrangements were obtained.

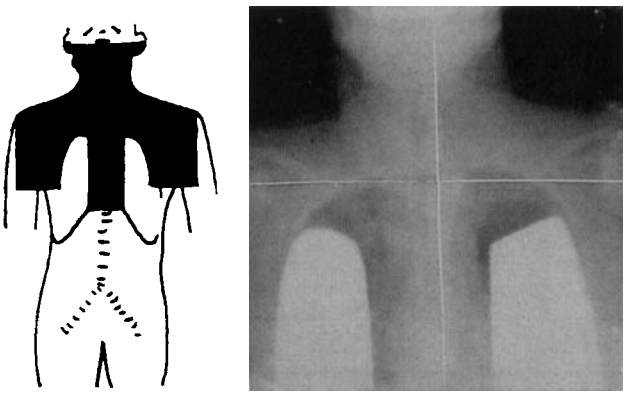

Fig. 2. Drawing and control film of field arrangement for irradiation with a mantle field.

Standard treatment of carcinoma. The volume of tumour tissue consisting of the primary tumour and the regional lymph nodes on the sides of the neck was treated as a rule through 2 opposing lateral fields with a safety margin of 2 to 3 cm (Fig. 1). The area of the field varied as a rule within a range of 10 cm × 16 cm. A dose of 5 700 rad in 6 weeks was used as the standard dose, and for postoperative irradiation the dose was reduced to 5 300 to 5 500 rad because of the risk of fibrosis.

Standard treatment of malignant lymphomas. Of 103 patients with malignant lymphomas 93 were irradiated via a mantle field. All supradiaphragmatic lymph node groups were irradiated through opposing anteroposterior fields from the base of the cranium to Th 10 (Fig. 2). A dose of 3 700 to 4 300 rad was given in the course of 28 to 30 days. In 83 patients, the field was undivided, and the treatment distance 130 to 140 cm; in the 10 earliest cases, anteroposterior fields bordering on one another were used, which involved a possibility of over- and underdosage corresponding to the borderline. No neurologic complications developed in these patients however.

In 10 patients with localized lymphomas on the sides of the neck, opposing lateral fields were irradiated as in carcinoma, with a dose of 4 000 to 4 500 rad in 28 to 32 days.

Neurologic symptoms and signs

The material was estimated from the aspect of the occurrence of all neurologic symptoms or signs arising after irradiation, including mild complications such as parasthesias in the fingers and toes.

The observation time after completion of radiation appears in Table 1. As the more severe neurologic complications described in the literature occurred mainly in the period from 1 to 1½ years following treatment, the patients with an observation time of less than one year were evaluated separately. The material was also

Table 1

Observation time after radiation therapy in 165 patients

Observation time (years)	0–1	1–2	2–3	3–4	4–5	5–6	Total
No. of patients	52	27	25	36	11	14	165

Table 2

Distribution of tumour dose and neurologic symptoms in 52 patients under observation for less than 1 year

	Dose (rad)					Total
	< 3 000	3 000–3 999	4 000–4 999	5 000–5 999	6 000–6 200	
No. of patients	3	11	17	17	4	52
Neurologic complications	1	1	1	1	0	4

divided up according to the size of the dose to the spinal cord and whether cytostatic agents had been used during the observation period. The cytostatic treatment included in all cases vincristine (oncovin), which is known to be neurotoxic (WHITELAW et coll. 1963).

Observation time of less than 1 year. Fifty-two patients died within 1 year after completion of treatment. The neurologic complications in relation to the size of the dose to the spinal cord and the use of cytostatic agents are given in Tables 2 and 3.

Mild, transitory paresthesias in the fingers and toes occurred in 3 of the 14 patients who received cytostatic therapy after the primary irradiation. These symptoms arose immediately after the treatment with cytostatic agents and they were attributed to those agents. The dose varied in these patients between 3 000 and 4 000 rad in 3 to 4 weeks.

Table 3

Occurrence of neurologic symptoms in relation to cytostatic treatment in 52 patients under observation for less than 1 year

	Cytostatic agents		Total
	Given	Not given	
Without complications	37	11	48
With complications	1	3	4
Total	38	14	52

Table 4

Distribution of tumour dose and neurologic symptoms in 113 patients under observation for more than 1 year

	Dose (rad)					Total
	<3 000	3 000–3 999	4 000–4 999	5 000–5 999	6 000–6 200	
No. of patients	4	56	30	21	2	113
Neurologic complications	0	13	6	0	0	19

In one patient who had not received cytostatic treatment, slight weakness in both legs developed three months after irradiation. The patient was a man of 43 with carcinoma of the epiglottis, T3 N2 M0, who was irradiated through 2 opposing lateral fields with a tumour dose of 5 700 rad in 42 days. The symptoms disappeared within one month. Three months later, he died of his original disease without any neurologic deficits.

Observation time of 1 to 6 years. A total of 113 patients were observed for 1 to 6 years after completion of irradiation; 46 were observed for more than 2 years and 61 for more than 3 years (Table 1). The neurologic complications in relation to the size of the dose to the spinal cord and the use of cytostatic compounds are given in Tables 4 and 5.

Mild, transitory neurologic deficits, in the form of hypoesthesias or paresthesias in the peripheral parts of the extremities, were observed in 19 patients, all of whom had been irradiated via mantle fields and with a dose varying from 3 000 rad to 4 400 rad in 3 to 4½ weeks. In 12 of these patients, the symptoms arose in connection with cytostatic therapy and disappeared within a few months after this was discontinued; one of them also had temporary weakness in the right arm, which arose after an exploratory laparotomy and was probably caused by an incorrect position

Table 5

Occurrence of neurologic symptoms in relation to cytostatic treatment in 113 patients observed for more than 1 year

	Cytostatic agents		Total
	Given	Not given	
Without complications	73	21	94
With complications	7	12	19
Total	80	33	113

of the arm during narcosis. In 7 patients, the neurologic complications could be attributed to the irradiation. A common characteristic for these 7 patients was that they were all cases of Hodgkin's disease, and were irradiated with a mantle field, in two instances supplemented with an inverted Y field; the dose was in all instances 3 500 to 3 700 rad in 28 to 29 days.

Discussion

The clinical symptoms and signs in radiation myelitis can be divided into 2 main types, reversible and irreversible (PALMER). The milder, transient cases, with paresthesias in the extremities, usually arise three to six months after completion of irradiation (DYNES & SMEDAL 1960). If the symptoms are aggravated by flexion or extension of the cervical portion of the vertebral column the designation L'Hermitte's sign is often used. These symptoms disappear as a rule within a few months. The irreversible type manifests itself as symptoms and signs of varying severity, up to total para- or tetraplegia with paralysis of the sphincter. The latent period before the appearance of these complications varies, in different reports, but the average time stated is 1 to $1\frac{1}{2}$ years. The present material differs from other series in which radiation myelitis was mentioned through the fact that many of the patients received cytostatic treatment, including vincristine (oncovin), in addition to irradiation. As this drug often gives rise to neurologic complications that may be confused with radiation myelitis the patients given vincristine were evaluated separately. Neurologic deficits occurred in 15 (30 per cent) of 47 who received the drug, whereas only 8 (6.8 per cent) out of 118 not given vincristine developed such symptoms (Tables 2, 5). In the vincristine-treated patients, the nature of the deficits and their close time-relationship to the cytostatic therapy excludes the likelihood that they could reasonably be interpreted as being signs of radiation myelitis.

In 8 patients, the neurologic complications could be attributed to the radiation treatment; 7 were patients with Hodgkin's disease who had received mantle treatment. Both the cervical and thoracic parts of the spinal cord were included in the treatment field. This suggests that the risk of neurologic complications increases appreciably with increasing area of the field. The eighth patient was the one mentioned with an observation time less than one year.

A total of 69 patients were treated by a mantle field, and signs of radiation myelitis arose in 7 of them, corresponding to a frequency of 10 per cent; 63 of these patients had Hodgkin's disease. All the complications were mild and reversible, and were probably due to affection of the nerve roots. (No electromyography was carried out.)

Neurologic complications similar to those in the present material have been described in connection with the active form of Hodgkin's disease, but an accumulation of 7 active case of Hodgkin's disease in a total of 63 cases is hardly likely. Doses to the spinal cord of over 5 000 rad were given to 44 patients (Tables 2, 4); most of them received 5 700 rad in 6 weeks. Only 1 of these 44 patients developed mild transitory signs of radiation myelitis. The spinal cord tolerance limit has been

Table 6

Review of possible causes of some of the neurologic complications following irradiation of the cervical spinal cord reported in the literature

Reference	No. of patients treated	No. of cases with cervical myelitis	Dose	Ret	Possible cause			
					Over-dosage (1 700 ret)	Over-lapping of fields	No compli-cations	Other comments
AHLBOM (1941)	235	4/4						Dose not reported
BODEN (1948)	161	10/10	2 000 R/1 day –5 200 R/17 days	1 090–2 080	4			
BUSCHKE (1963)	125	6/6	7 000–8 000 rad/50 days	1 950–2 220	6			
DYNES & SMEDAL (1960)	800	3/10	4 350 R/18 days –6 750 R/69 days	1 740–2 300	1	5	3	1 rotation therapy
JACOBSSON (1951)	322	13/13	5 000 R/20 days –6 000 R/30 days	1 710–1 780	13			Dose not reported especially for patients who developed complications
PALMER (1972)	Not reported	4/12	3 920 rad/30 days –7 700 rad/59 days	1 500–1 925	1	2	4	
REAGAN et coll. (1968)	1 018	8/10	4 000 rad/10 days –6 900 rad/43 days	1 350–1 900	5	1	3	
VAETH (1965)	166	3/3	4 800 rad/27 days –6 000 rad/56 days	1 520–1 580				

estimated to 5 000 rad (FLETCHER et coll. 1962, RUBIN & CASARETT 1968). Our results suggest, however, that with fields of an area corresponding to about 10 cm × 16 cm a dose of up to 6 000 rad may be given to the spinal cord without serious complications, if the irradiation is extended over 6 weeks. It should be pointed out, however, that only 23 of the patients who received more than 5 000 rad to the cord have been under observation for longer than one year.

A tolerance level of 5 000 rad to the spinal cord presents a therapeutic dilemma in the majority of cancer forms, when irradiation is to be applied. An attempt to

avoid including the spinal cord in the irradiation involves a risk of underdosage of tumour-affected areas; this has to be weighed against the risk of producing radiation myelitis.

A review of the materials describing serious irreversible neurologic complications (Table 6) reveals without question in several cases the possibility of direct overdosage (defined here as a dose larger than 1 700 ret): overdosage to the cord as a result of irradiation via fields bordering on one another with the concomitant risk of a 'hot spot' at the border, or overdosage because a compensation filter was not used in connection with varying surface levels and different tissue thicknesses. These materials can thus only be used with reservation as an indication of the limit of tolerance of the spinal cord to irradiation. In the present material, in which a simple treatment technique, undivided fields, and the use of a compensation filter were applied, the dose homogeneity may be considered reasonable.

SUMMARY

A total of 165 patients with tumours of the head and neck were irradiated via fields including the entire cervical portion of the spinal cord. Eight patients (4.8 per cent) developed mild reversible signs of radiation myelitis. Only one of these cases was found among the 44 patients who received a dose to the spinal cord of over 5 000 rad via fields of less than 16 cm in length; 7 cases were patients with Hodgkin's disease who were given up to 3 700 rad via mantle fields. A survey of previous reports on transverse spinal lesions provoked by irradiation revealed a possibility of overdosage in several cases, and dose tolerance limits mentioned previously should accordingly be applied with caution.

ZUSAMMENFASSUNG

Insgesammt wurden 165 Patienten mit Tumoren des Kopfes und Nackens mit Feldern bestrahlt, die den gesamten cervikalen Teil des Rückenmarks umfassten. Acht Patienten (4,8%) entwickelten leichte reversible Zeichen einer Strahlenmyelitis. Es wurde unter den 44 Patienten, die eine Rückenmarks-Dosis von über 500 rad durch Felder von weniger als 16 cm in der Länge erhalten hatten, nur ein Fall gefunden; 7 Fällen waren Patienten mit Hodgkin'scher Ekrankung, denen bis zu 3 700 rad durch Mantelfelder gegeben worden war. Eine Übersicht älterer Berichte über Querschnittslähmungen, hervorgerufen durch Bestrahlung, liess die Möglichkeit der Überdosierung in verschiedenen Fällen erkennen, und früher genannte Dosis Toleranz-Grenzen sollten entsprechend mit Vorsicht verwendet werden.

RÉSUMÉ

Un total de 165 malades atteints de tumeurs de la tête et du cou ont été irradiés par des champs comprenant la totalité de la moelle cervicale. Huit malades (4,8%) ont présenté des signes de myélite radiothérapique peu sévère et réversible. Parmi les 44 malades qui avaient reçu une dose à la moelle de plus de 500 rad par des champs de moins de 16 cm de long, un seul a présenté des signes de myélite; les 7 autres cas étaient des malades atteints

de maladie de Hodgkin qui avaient reçu jusqu'à 3 700 rad par des champs en mantelet. Une revue des publications sur les lésions transverses de la moelle provoquées par les radiations a montré la possibilité d'un surdosage dans plusieurs cas, c'est pourquoi les limites tolérance de dose mentionnées auparavant devraient être appliquées avec précaution.

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