Radiation myelopathy

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SUMMARY Five cases of radiation myelopathy were found in a total of 10,000 cases given radiotherapy from 1968 to 1977. The clinical presentation and treatment details including the total dose, treatment volume, number of fractionations, overall time, and the RET value at the spinal cord were calculated and compared with other reports on this subject. The total number of fractionations ranged from 20 to 26 with an overall time of 32 days to 37 days. The dose received by four patients ranged from 1030 to 1900 RET, a little higher than the tolerance level of the spinal cord as compared to reported values. Two patients in this series had high blood pressure. The incidence of radiation myelopathy, already acceptably low, could possibly be reduced further by meticulous planning of radiation.

Approximately 80% of all cancer patients receive radiotherapy at some stage. With the availability of sophisticated equipment and development of radiotherapeutic techniques, more and more cancers are controlled. Some morbidity has to be accepted but the radiation dose to the critical organs in and around the target zone should be minimised. Since the first description of radiation myelopathy by Ahlbom in 1941, many reports have appeared on this subject (Boden, 1948; Maier et al., 1969; Jellinger and Sturm, 1971; Reinhold et al., 1976). During the last nine years (August 1968 to December 1977) more than 10,000 cancer patients have been registered at the Centre of Radiotherapy and Radiation Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Five patients have developed progressive radiation myelopathy during this period, and this presentation deals with these cases.

Patients and methods

Of the 185 patients with cancer of the oesophagus who received radiotherapy, four developed radiation myelopathy, a much lower incidence than the operative mortality (Sturdy, 1965; Collis, 1971). More than 30% of patients with cancers other than oesophageal received radiation to the spinal cord while being treated for head and neck tumours, lung cancers, testicular tumours, and lymphomas. Of these only one patient with carcinoma of the tonsil developed this complication. Case summaries of the five patients are given below.

Case summaries

CASE 1
A 50 year old woman (LNK, case 4908) was referred for radiotherapy on 22 January 1974. She complained of progressive dysphagia for two months. There was no chest pain, cough, or expectoration.

Examination of other systems showed no abnormality. There was no jaundice, anaemia or lymphadenopathy. Her blood pressure was 160/100 mmHg and pulse rate 140/minute. Liver and spleen were not palpable.

General blood picture was normal with a haemoglobin content of 12 g/dl. Total leucocyte count was 10,000/mm³, with polymorphonuclear leucocytes 80%, lymphocytes 19%, and eosinophils 1%. Gross biochemical and microscopic examination of urine revealed no abnormality. A barium swallow showed an irregular filling defect in the middle third of the oesophagus. Histology revealed an epidermoid carcinoma.

The patient received a course of ³²Co teletherapy from 22 January to 25 February 1974. A
tumour dose of 5000 rads was delivered in 26 treatments over 35 days by three fixed fields (one anterior and two posterior oblique fields) of 150 × 60 mm size.

She was free of her symptoms after treatment and was well till 20 September 1975 when she developed tingling sensation of the right lower limb and difficulty in walking. Examination showed impairment of sensory function with spastic paresis of the right lower extremity. A secondary deposit in the spine was considered. Radiological examination of the spine and contrast myelography failed to show any abnormality. A diagnosis of radiation myelopathy was made and she was put on symptomatic treatment, with physiotherapy. The last follow-up examination on 20 April 1978 showed no further deterioration in neurological status. Her bowel and bladder control was intact. For more than four years she has enjoyed good general health.

CASE 2
A 49 year old male teacher (PJP, case 6633) was referred to our centre on 21 July 1975 with a history of progressive dysphagia for solids for one month. He used to take betel with tobacco.

General systemic examination failed to show any abnormality. The blood picture, haemoglobin level, total and differential white cell counts were within the normal range. Urine and blood sugar were within normal limits. Barium examination showed a filling defect involving the upper third of the oesophagus. Chest radiography was normal. Endoscopy and biopsy were carried out, and histology revealed a moderately differentiated epidermoid carcinoma. He was treated by 60Co teletherapy from 21 July to 27 August 1975 (field size 150 × 60 mm). A tumour dose of 5500 rads was delivered in 24 treatments over 38 days. Initially a tumour dose of 3000 rads was delivered by parallel opposed fields and the further 2500 rads by a three fields technique, to minimise lung fibrosis. He responded well to treatment and was completely relieved of dysphagia. On 14 September 1977, more than two years after treatment, he developed a tingling sensation down the left lower limb and a dragging sensation in the right lower limb. Neurological examination revealed almost complete sensory loss for temperature, pain, and touch from T3 dermatomal level and below, and diminution of posterior column sensation. A motor power of grade 4 was noted in the right lower limb. Radiography of spine and myelography showed no abnormality. We diagnosed radiation myelopathy, and he was put on steroids and other supportive treatment, with physiotherapy. At the last follow-up examination on 3 May 1978, neurological deficit showed further deterioration, but bowel and bladder functions were still intact.

CASE 3
A 50 year old woman (SB, case 5974) attended our centre on 19 December 1974 with a six month history of dysphagia for solid food and loss of weight. She used to take betel with tobacco: she had no history of haemoptysis or haematemesis.

Examination showed pallor and anaemia. There was no jaundice or lymphadenopathy. Her liver was enlarged two fingers breadth below the costal margin, with nodular surface. Haemogram, urine, and radiograph of chest were normal. A barium swallow showed a filling defect at the junction of upper and middle thirds of the oesophagus. The histological diagnosis was epidermoid carcinoma.

She received 60Co teletherapy from 23 December 1974 to 24 January 1975. A tumour dose of 5000 rads was given in 23 treatments over 33 days by parallel and opposed fields of 150 × 70 mm size. Her symptoms disappeared after radiotherapy and she was well till 12 April 1976 when she experienced tightness and compression round the chest and weakness of both lower limbs. Lumbar puncture and the cytology of the CSF were normal. Myelography revealed no obstruction. A diagnosis of radiation myelitis was entertained and she was put on steroids and supportive measures. She is still living at the time of reporting with flaccid paralysis of lower limbs and normal bowel and bladder function.

CASE 4
A 70 year old woman (MD, case 6692) came to the centre on 29 July 1975 with a history of dysphagia for solids for three months. She had no other complaints. She also used to take betel with tobacco.

She was in fair general health. There was no jaundice, anaemia, or lymphadenopathy. Liver and spleen were not palpable.

Haemogram, urine analysis, and radiograph of chest were all within normal limits. A barium swallow showed irregular narrowing of the lower third of the oesophagus. Histology revealed epidermoid carcinoma. In view of her age, a palliative course of radiotherapy was given on a telecobalt machine from 31 July to 4 September 1975 by parallel and opposed fields of 180 × 70 mm. A tumour dose of 4500 rads was given in 20 treatments over 37 days overall.

Symptomatic improvement occurred after radiotherapy but follow-up barium swallow examination
showed persistence of irregularity at the original site of the lesion. She developed weakness in both lower limbs in February 1976. Radiography of the spine did not reveal any abnormality. Myelography was reported as normal. She is still living but without any neurological improvement.

CASE 5
A 50 year old man (UPS, case 1286) attended our centre on 21 March 1970 because of a sensation of a foreign body in the throat and difficulty in swallowing.

Examination showed a proliferative growth involving the right tonsil and extending to the anterior faucial pillar and lateral pharyngeal wall. There were two 20 mm mobile nodes in the right upper cervical chain. Systemic examination showed no abnormality.

Chest radiograph was normal. Haemogram was within normal limits and urine examination showed no abnormality. Biopsy from the tonsillar growth showed epidermoid carcinoma. He was treated by telecobalt therapy from 24 March to 24 April 1970. A midline dose of 6000 rads was delivered by parallel and opposed fields of 100×100 mm in 24 treatments in 32 days.

He responded well to radiotherapy and was symptom-free till 20 September 1975 when he experienced weakness on the right side of the body. Radiography of the cervical spine and myelography did not show any abnormalities. At the last follow-up examination on 5 April 1978 there was no change in his neurological status. Otherwise, the patient was able to walk and was maintaining normal life.

Discussion
Radiotherapeutic treatment of malignant diseases involves direction of a high energy beam of x-rays or gamma rays to the tumour tissue. The principle of radical radiotherapy is to deliver a cancercidal dose of radiation to the tumour bearing area with little or minimal dose to the surrounding normal tissues or to adjacent critical organs. However, this cannot always be achieved. In treatment of lesions of the oesophagus, vulnerable structures such as the spinal cord come in the way of treatment fields. To avoid this, oesophageal cancers are treated by three fields at 120°, one anterior and two posterior oblique fields (Figure). This brings the radiation dose reaching the spinal cord to a minimum level but not always below the risk level, so compromise is necessary. The higher dose received by the spinal cord sometimes produces unwanted sequelae, such as radiation myelitis, which has to be accepted by the radiotherapist in the interests of the patient.

The radiation dose concept is quite different from the dose system used in other branches of medicine. It is mainly concerned with the concentration or absorption of energy per gram of tissue (integral dose). This concept is well described by Brewin (1977). The radiation dose is usually defined in units such as the Roentgen or Rad. To compare the biological effectiveness of various treatment schedules Ellis (1968, 1969, 1971) has given a new concept to the dose which is given in RET.

The incidence of radiation myelitis has been reported to range from 0.6% (Boden, 1948) to 12.5% (Locksmith and Powers, 1968). Delayed
radiation lesions constituted 1% of all cases of myelopathy observed at the Mayo Clinic (Reagan et al., 1968). Since the first description of radiation myelopathy by Ahlbom in 1941 several reports have appeared dealing with the clinicopathological aspects of this disorder (Boden, 1948; Pallis et al., 1961; Atkins and Tretter, 1966; Locksmith and Powers, 1968; Van den Brenk et al., 1968; Phillips and Buschke, 1969; Combes et al., 1975; Reinhold et al., 1976).

Phillips and Buschke (1969) put forward three criteria for radiation myelitis. The cord should have been included in the radiation treatment field, the main neurological symptoms should correspond to the spinal segment, and myelography and other investigations should rule out cord compression or metastatic deposits.

Reagan et al. (1968) described four categories of radiation myelopathy depending on the type of clinical symptoms and course of the disease. Group 1 is characterised by a transient form of myelopathy causing purely subjective and often mild sensory symptoms. L'hermitte's sign has been described in this syndrome, a sensation of electrical discharge down the spine and limbs on flexing the neck. This form of myelopathy undergoes spontaneous recovery.

In the second group, symptoms of paraplegia or quadriplegia develop acutely as a result of infarction of the cord by involvement of blood vessels supplying the segment of the spinal cord.

The third group, which is the most common, is characterised by chronic and progressive myelopathy. Initial symptoms are often sensory with loss of pain, and temperature sensations and perception in the extremities: a Brown-Séquard syndrome is the usual manifestation. The condition progresses to spastic quadriplegia or paraplegia with gross sensory loss with or without bladder and bowel dysfunction.

In group 4, the symptoms manifest as lower motor neurone disease in the lower extremities. There is atrophy of the muscle groups corresponding to the involved spinal segments together with loss of deep reflexes.

The clinical presentation in four of our patients can be placed in the third group with one case in the last group of lower motor neurone type. One patient (case 2) had a Brown-Séquard syndrome. Table 1 contains a summary of the details of these five cases with the latent periods of development of symptoms. The shortest duration was six months and the longest interval after radiotherapy was 64 months.

Warren (1943) commented that neurological sequelae after irradiation result more commonly from secondary vascular changes than from direct neuronal damage. Pennybacker and Russell (1948) described the histological findings in a series of cases and concluded that brain necrosis was the result of vascular damage. Kristensson et al. (1967), Castaigne et al. (1970) and Jellinger and Sturm (1971) observed various histological changes in the irradiated spinal cord.

We do not have any histological confirmation of radiation myelitis in our cases but the clinical course and the findings of relevant investigations including plain radiographs and contrast myelography of spine strongly favour this diagnosis.

Berg and Lindgren (1958) studied brain and skin tolerance in rabbits after single or multiple dose irradiation such as might be encountered clinically. A similarity was noted in the slope of the time-dose relationship for delayed radiation lesions in the brain and skin. Lindgren (1958) analysed the literature and his own material and reported that the time-dose relationship for human brain tolerance was 0.26. Du Sault (1956) found the slope to be 0.27.

Boden (1948) established the tolerance level as 300 R in 17 days when the whole cervical spine was irradiated. A dose of 5000–5500 R in 17 days or 2000 R in a single day was the tolerance level for smaller fields. Pallis et al. (1961) recorded 20% tolerance level as compared to Boden's figures. Friedman (1954) concluded that 5000 R was a critical level beyond which the risk of radiation myelitis is 10% of all the treated cases.

Van den Brenk (1968) demonstrated that the spinal cord was not more sensitive in hyperbaric oxygen than in air. Asscher and Anson (1962) stressed that neurones might be more sensitive to radiation damage in hypertensive patients than in the normotensive.

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Site of lesion</th>
<th>Diagnosis</th>
<th>Latent period (months)</th>
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<td>30</td>
<td>F</td>
<td>Middle third of oesophagus</td>
<td>Epidermoid carcinoma</td>
<td>19</td>
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<td>M</td>
<td>Upper third of oesophagus</td>
<td>Epidermoid carcinoma</td>
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<td>50</td>
<td>F</td>
<td>Middle third of oesophagus</td>
<td>Epidermoid carcinoma</td>
<td>14</td>
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<tr>
<td>6692</td>
<td>70</td>
<td>F</td>
<td>Lower third of oesophagus</td>
<td>Epidermoid carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>1286</td>
<td>50</td>
<td>M</td>
<td>Right tonsil</td>
<td>Epidermoid carcinoma</td>
<td>64</td>
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</table>
Two of our patients (cases 1 and 4) had hypertension but only one of them (case 4) developed symptoms relatively early with more severity than the rest of the cases even though she was given a palliative course of radiotherapy (4500 rads in 20 treatments).

Phillips and Buschke (1968) recommended the RET value for tolerance of the spinal cord. It was 1500 RET for cervical and thoracic spinal cord for shorter segments and 1300 RET for longer ones using cobalt therapy. A midline dose of 4000 rads in 20 treatments over 28 days approximates this value. Table 2 documents the RET values in our cases. This is higher than the suggested value of Phillips and Buschke (1968). Paterson (1963) suggested the use of a three fields technique at 120° to each other while treating this lesion. From the Figure, it can be seen that the doses received by the tumour and the spinal cord are not very different. We have tried to calculate the radiation dose to the spinal cord in individual cases from the available myelography. We have not corrected for bone density as suggested by Maier et al. (1969) in calculating the dose to spinal cord.

It is apparent that the field sizes for oesophageal cancer in these cases are quite big. Most of our patients come with advanced disease, and to include the lesions with adequate coverage of the normal segment we have to use longer fields.

The total fractionations and overall time in our cases were greater than those reported by others (Dynes and Smedal, 1960; Phillips and Buschke, 1969). The only explanation we can put forward for this is that the volume of tissue irradiated and personal radiation susceptibility may be the factors responsible for the development of myelopathy in these cases. In one case, hypertension and arteriosclerotic changes may have precipitated the complications.

Late complications of radiotherapy should not deter anyone from trying to achieve cure but modifications and refinements of techniques should be sought so that fewer patients develop this type of unwanted sequelae (Sewchand et al., 1978).

### References


Friedman, M. (1954). Calculated risk of radiation

### Table 2  RET values

<table>
<thead>
<tr>
<th>Case number</th>
<th>Field size (mm x mm)</th>
<th>Field arrangement</th>
<th>Dose (rads)</th>
<th>Number of treatments</th>
<th>Overall time (days)</th>
<th>RET value at spinal cord</th>
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<td>4908</td>
<td>150 x 60</td>
<td>Three fields</td>
<td>5000</td>
<td>26</td>
<td>35</td>
<td>1030–1340</td>
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<td>38</td>
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<td>23</td>
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<td>1575</td>
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<tr>
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<td>20</td>
<td>37</td>
<td>1475</td>
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<td>24</td>
<td>32</td>
<td>1900</td>
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