Paraplegia Caused by Spinal Metastasis from Thyroid Cancer*

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Paraplegia caused by metastases in the spine is a common and unfortunate incident in the natural history of many types of cancer. Even when the site of the primary tumour is known, treatment is too often symptomatic only, and when the primary is not known it is sometimes thought that energetic pursuit of the diagnosis is academic, and that the patient is better left to "die in peace." However, valuable time can also be wasted on extensive and sometimes fruitless searches for the primary tumour only to find that by this time the paraplegia is irreversible.

The striking complete success of treatment of a recent case of thyroid cancer, undiagnosed until eight months after the onset of spinal cord compression and two months after complete paraplegia, has prompted a review of nine cases seen at the Christie Hospital, Manchester, collected from about 700 new cases seen between 1945 and 1965.

Clinical Material

All but one (Case 9) of the patients had a history of thyroid disease, and in three (Cases 1, 4, and 5) thyroidectomy had been performed between three and nine years before in the belief that the lesion was benign (Table I). In these three cases, at least, it would seem that either dissemination or growth of metastases must have been very slow.

The presenting symptoms in four cases were related to the thyroid gland or neck and in the remainder to the spine. In only three cases was there a definite interval between the diagnosis of the primary tumour and the first signs of cord compression, this being three months and three and six years. However, in retrospect, if it is assumed that the apparently benign lesion had been malignant at the time of thyroidectomy, then the intervals between the appearance of the primary and the development of the spinal cord signs extend to three, six, and thirteen years.

In the seven cases for which full details are available paraplegia followed the first signs of compression in an average time of nine months and in all but one the paraplegia was complete (Table II). In the four cases showing recovery (Cases 1, 6, 8, and 9) the duration of the paraplegia was two months, two months, one month, and three weeks.

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Full recovery was thought to have occurred when the patient had regained full bladder and bowel control and could walk without any external support.

Treatment of the paraplegia was by decompression in five cases (Nos. 1, 4, 6, 8, and 9), and in two of these the biopsy obtained was diagnostic (Cases 1 and 9). In three (Cases 2, 3, and 7) paraplegia was a terminal event and no attempt was made to decompress the cord. In the remaining case (No. 5)

TABLE I

Case No.	Age and Sex	Previous Thyroid History	First Signs of Malignancy	Time of Development of Spinal Signs from Diagnosis of Malignancy
1	51 M	Thyroidectomy 3 years before for "benign goitre"	Weakness of legs	0
2	70 F	Lifelong goitre. No treatment	Cervical lymph node metastases	3 months
3	55 M	Malignant goitre with cervical node metastases	Swelling in thyroid with cervical node metastases	Not known
4	54 M	"Benign" thyroidectomy 9 years before	Recurrent swelling of thyroid and metastasis ileum	6 years
5	47 M	"Benign" thyroidectomy 6 years before	Pain and weakness in arm from spinal metastases	0
6	47 F	Swelling thyroid for 10 years	Weakness of legs, pain in neck, and paraesthesiae in arms	0
7	64 F	Goitre for 25 years, increased swelling for 5 years	Swelling in neck	Probably 4 years
8	54 M	Neck swelling for 2 years	Backache	0
9	66 F	None	Backache and sciatica	0

the biopsy was diagnostic, and, though some improvement followed treatment, death occurred six months later. Post-mortem examination showed evidence of transverse myelitis at the level of the lesion which may have been due to irradiation.

Abstracts of two cases are given.

Case 1

A 51-year-old man presented in January 1964 with a two-months history of weakness and numbness of the legs and urgency and increased frequency of micturition. A thyroidectomy had been performed in 1961 for a retrosternal goitre suggested histologically to be benign.

He was paraparetic with a sensory level at the sixth dorsal spinal segment. Radiographs showed a destructive lesion involving the

TABLE II

Case No.	Presenting Sign of Spinal Cord Compression	Time from First Sign of Cord Compression to Paraplegia	Duration of Paraplegia	Site of Lesion	Histology	Extent of Paraplegia	Treatment
1	Weakness of legs	8 months	2 months	D 6	Follicular	Complete	Thoracotomy. ¹³¹ I. X-ray treatment. Thyroxine
2	Not known	Not known. Terminal	Terminal	C 2	Not known	"	None
3	"	2 weeks. Terminal	2 weeks. Terminal	Lumbar spine	Hürthle cell	"	X-ray treatment to neck only
4	Backache	9 months	1 month	L 2. Later D 3-4	Not known	"	X-ray treatment. Laminectomy
5	Pain in the arm	6 months	7 months	D 1-2	Follicular	"	¹³¹ I
6	Weakness of legs	12 months	2 months	C 7. T 1	"	"	Laminectomy. X-ray treatment. ¹³¹ I. Thyroxine
7	Backache	14 months	Terminal	D 6-8. C 5-6. D 11-12	Anaplastic	"	X-ray treatment
8	"	6 months	1 month	D 7	Follicular	Incomplete	Thoracotomy. X-ray treatment. ¹³¹ I. Thyroxine
9	Backache and pain in legs	12 months	3 weeks	D 12. L 1. Later C 7	"	Complete	Laminectomy. X-ray treatment. ¹³¹ I. Thyroxine

sixth dorsal vertebra. No swelling was palpable in the neck and investigations failed to reveal a primary tumour.

He was admitted to hospital in August 1964, having been totally paraplegic for two months and unmanageable at home. Radiographs showed little change in the spine but a further metastasis in the ilium.

On 7 August a transthoracic anterior decompression of the spine was performed and the biopsy obtained showed a well-differentiated thyroid metastatic carcinoma. Radioiodine studies showed a 40% uptake in the neck and 9% in the region of the spinal metastasis. On 17 August 150 mCi of iodine-131 was given. By 30 August some movement had returned to the legs; he was walking between bars on 9 September and by 5 October with the aid of tripods only.

On 14 October tracer studies showed 2% uptake in the neck, 10% in the ilium, and 6% in the spine. A further dose of 200 mCi iodine-131 was given together with 4MV x-ray treatment of 1,500 rads skin dose each to the spine and the ilium. He was given 0.3 mg. sodium L-thyroxine daily by mouth from this time.

Rapid improvement continued so that by January 1965 he was able to walk a quarter of a mile (400 metres), ride a bicycle, and was laying concrete slabs in his garden. Bladder and bowel control was normal. Full motor power had returned to the legs. In February 1965 (after temporary cessation of thyroxine) 200 mCi iodine-131 was given, and in May radiographs showed regression and sclerosis of the spinal lesion.

He returned to work in August, and when last reviewed in May 1966 was completely well continuing the maintenance dose of thyroxine.

Case 6

A 47-year-old woman was admitted in July 1962 with a spastic paraplegia, having complained of weakness of the legs for 12 months and of a small goitre for 10 years.

At laminectomy a tumour was found in the seventh cervical and first thoracic vertebrae; histologically it was a poorly differentiated follicular thyroid cancer. During August four MV x-ray therapy of 3,000 rads skin dosage was given to the lesion over three weeks. By September there had been considerable return of power to the legs, and by January 1965 this was complete, together with normal bladder and bowel function.

In March 1965 the thyroid was ablated by 150 mCi iodine-131, followed two months later by a further 150 mCi. Maintenance therapy of 0.3 mg. sodium L-thyroxine daily was started.

In January 1966 the patient was completely well with normal gait and bladder and bowel function.

Cases Collected from the Literature

A search of the literature has produced histories of only four cases of paraplegia due to thyroid spinal metastases. Bradley Coley (1949) reported a case developing paraplegia 23 years after thyroidectomy for a "benign lesion" and 11 years after metastases had appeared. Full return of function followed decompression and x-ray treatment and the patient remained well for eight years. Outerbridge (1947) reported two cases. In one the paraplegia developed slowly over two years and recovery was only partial after decompression and x-ray therapy. In the other the onset was rapid, but the paraplegia was incomplete and complete recovery followed laminectomy and x-ray treatment. Barron, Hirano, Araki, and Terry (1959) reported a case of paraplegia of rapid onset showing complete recovery after decompression. Death occurred nine months later from widespread metastases.

Discussion and Review of Literature

Cancer of the thyroid is a rare disease, approximately 12 cases occurring per million population per year and accounting for 0.1% of all deaths from malignancy.

Metastatic spread from an apparently benign lesion of the thyroid was first described in 1876 by Cohnheim as "benign metastasizing goitre." Malignant change may not be apparent clinically and may not be recognized on histological examination. This occurred in three of our patients (Cases 1, 4, and 5) and in one of these the failure to recognize the possibility of malignant change resulted in an extensive and fruitless search for a primary tumour. The incidence of malignant change in non-toxic nodular goitre in three large series of cases was 7.6% (Hinton and Lord, 1945), 7.8% (Surridge and Kroger, 1961), and 8.5% (Fowler, Majarakis, and Cole, 1961).

Though spread to bone, in particular the vertebrae, is common in thyroid cancer (Halnan, 1965), the primary tumour itself is so uncommon that spinal metastases from the thyroid are rare in comparison with those from the bronchus, breast, and gastrointestinal tract. Reviewing metastases to the spine, Arseni, Simionescu, and Horwath (1959) found only two from the thyroid among 231 cases; Barron *et al.* (1959) found three among 127; Toumey (1943) two among 95; Alexander, Davis, and Field (1956) one among 15; Mullan and Evans (1957) one among 50; and Brice and McKissock (1965) none among 160. Collectively these series give an incidence of thyroid metastases causing paraplegia of about 1%.

Botterell and FitzGerald (1959) commented on the remarkably constant presentation of spinal metastases with local back pain sometimes together with nerve-root pain. This has been confirmed by Brice and McKissock (1965) in 90% of their cases, by Barron *et al.* (1959) in 82%, and by Arseni *et al.* (1959) in 86%. Back pain alone occurred in three of our cases, with leg pain in one, but in two others weakness of the legs alone was present.

The progress from the first signs of cord compression to paraplegia varies according to the source of the metastasis. Kennady and Stern (1962) found that in bronchogenic metastases the average time from local compression to paraplegia was four weeks, while in those from the breast it was 14 weeks. Prognosis is related to the rate of progress; the more rapid the rate the worse the prognosis. In our cases the progress was very slow, in two cases extending over a year and in two further cases between six months and one year.

Difficulty in diagnosis may occur when no evidence of bony destruction is seen on the radiographs, as occurred in 12% of the cases of Barron *et al.* (1959) and 10% of those of Brice and McKissock (1965). However, in thyroid cancer in all our cases and in those collected from the literature radiological bone changes were seen, and this may be related to the slow rate of growth. In thyroid metastases uptake of radioiodine is diagnostic but its absence is by no means exclusive. In 18% of cases extensive searches may fail to demonstrate a primary tumour (Arseni *et al.*, 1959).

Treatment should be by immediate decompression of the spinal cord, and if the primary tumour is unknown a biopsy will provide the diagnosis. Decompression is most commonly by laminectomy, but an anterior approach may often be better and leave the spine more stable.

The results of decompression of the spine in general are disappointing. Of 21 cases operated on by Mullen and Evans (1957) there were only two good results and one of these was from the thyroid. Arseni *et al.* (1959) noted improvement in 29% and complete recovery in 7.8% of cases; this series did not include any from the thyroid. Kennady and Stern (1962) noted worth-while improvement in sphincter control in 19 out of 59 cases. Brice and McKissock (1965) reported improvement in 30%.

In our series three cases were terminal, but of the remaining six complete recovery of the spinal cord lesion occurred in four (Cases 1, 6, 8, and 9) (Table III). In two cases recovery occurred in spite of the presence of paraplegia for two months. Full recovery has been maintained in two cases (Nos. 1 and 6) for 22 months and three and a half years after decompression.

In Case 8 the improvement has so far continued for six months after decompression. In Case 9 the paraplegia recurred four years later but there are now multiple metastases.

TABLE III

Case No.	Outcome	Length of Follow-up
1	Complete recovery	22 months
2	Death	
3	"	
4	Improvement following laminectomy for 2 years, when further metastases caused return of paraplegia, which was terminal	
5	Death probably due to radiation myelitis and not metastases. Temporary and partial improvement	3½ years
6	Complete recovery	
7	Death due to terminal quadriplegia	6 months
8	Complete recovery	
9	Complete recovery, but later on signs of further cervical cord compression were developing	4 years

The prognosis of thyroid cancer, particularly when well differentiated, may be surprisingly good, especially in the younger age groups (Halnan, 1966). Thus the presence of distant metastases may not be a terminal event even when paraplegia occurs, unless the latter itself is allowed to lead to death. Furthermore, bone metastases characteristically occur from follicular cancer with good uptake of radioiodine, as in all our cases that recovered. An optimistic and energetic approach seems justified in this type of case, quite different from the management of a patient with rapidly growing multiple metastases from undifferentiated carcinoma, whether originating in the thyroid or elsewhere.

Conclusions and Summary

Thyroid carcinoma is rare, but commonly metastasizes to bone, the well-differentiated variety sometimes spreading exclusively to bone.

Cases of paraplegia due to thyroid metastases are rare and few have been reported in the literature.

Metastasis to the spine causing cord compression should be treated as an emergency procedure and attempts to find the primary tumour should not delay this, particularly since in some cases no primary tumour may be found.

A thyroid tumour should always be considered as a possible origin of spinal metastases, and a history of thyroidectomy (even though apparently for benign disease) should add to rather than remove suspicion.

Though the results of surgical decompression for spinal metastases are often poor this should not rule out operation, since, even though life may not be prolonged, relief of the paraplegia is of considerable benefit. After thyroid metastases the extent and duration of recovery are significantly better than after most other tumours.

The duration of the paraplegia should not contraindicate operation. With thyroid metastases full recovery may occur even when two months have elapsed.

The first local treatment should be surgical, but this must be followed by treatment to both the primary and the secondary tumours; thyroidectomy is sometimes appropriate, but either or both radioiodine and x-ray therapy are almost always needed.

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Medical Memoranda

Need for Clarity in Infant Feeding Instructions

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The danger of hypernatraemia occurring as a result of accidental salt-poisoning or excessive administration of solute is well recognized in infancy (Finberg and Harrison, 1955). The present report describes two cases admitted to the Royal Hospital for Sick Children, Edinburgh, within the past year with hypernatraemic dehydration resulting from parental failure to interpret correctly the manufacturers' instructions for reconstituting dried-milk formulae.

CASE 1

A 4-week-old male infant was admitted to hospital in January 1966 with a two-day history of irritability, refusal of feeds, and a high-pitched cry. He had been born in hospital at full term. This was the mother's first pregnancy and was uncomplicated. His birth weight was 4 kg. (8.8 lb.). There were no immediate neonatal problems, but on discharge from hospital on the fifth day of life

his feeding was changed from half-cream milk to Ostermilk No. 2, reconstituted as follows: 6 measures dried-milk powder+3 tablespoonfuls water+1 teaspoonful of sugar, four-hourly. Despite the paste-like consistence of this mixture he had accepted feeds until two days before admission to hospital. When admitted he was dehydrated, with early peripheral circulatory failure. His cry was high-pitched and feeble. Neurologically he was generally hyper-tonic, with neck retraction, twitching of the eyelids, vertical nystagmus, and tremor of the limbs. His abdominal wall was doughy in consistency. Examination showed nothing else of note. Initial electrolyte values were—sodium 207 mEq/l., potassium 7.5 mEq/l., chloride 165 mEq/l., and calcium 7.2 mEq/l. His pH was 7.08, Pco₂ 71 mm. Hg, and standard bicarbonate 15.8 mEq/l. The blood urea nitrogen was 250 mg./100 ml.

He was treated as recommended by Harrison and Finberg (1964), being gradually rehydrated with a solution containing 20 mEq sodium per litre. Over the next three days he had repeated convulsive episodes, but gradually the serum electrolytes and blood urea nitrogen levels returned to normal. His subsequent progress has not been satisfactory and he is now severely handicapped mentally.

CASE 2

This 4-week-old female infant was admitted to hospital in October 1966, with symptoms and clinical features identical to those in