

LUNG CANCER METASTASES - MANAGEMENT

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ABSTRACT

Distant metastases from lung cancer is a common occurrence in a common malignancy. Almost every organ may be involved but the extra-thoracic sites posing common clinical problems are brain metastases, cord compression, painful bone metastases or pathological fractures, nodal spread and liver involvement. A review of the records of 225 lung cancer patients referred to the Therapeutic Radiology Department, Singapore General Hospital, during the calendar year 1985 showed a metastatic rate of 13.8% at referral. On subsequent follow up, an additional 49 patients (21.7%) developed metastases clinically. The organs involved were bone (21 patients), spinal cord (21 patients), brain (18 patients), liver (13 patients), other lung (7 patients) and other sites (17 patients). The management of metastases to the brain, bone and liver, and spinal cord compression will be discussed.

Key Words: Lung Cancer, Metastases

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INTRODUCTION

Lung cancer is the leading cause of cancer death in Singapore, accounting for 24% of cancer deaths and about 5.2% of deaths from all causes(1). Despite advances in detection and treatment, the overall survival at 5 years is still less than 10%(2).

At the time of presentation, the disease would have spread to regional nodes or distant sites in 70% of patients(2), making the prospect of cure unrealistic. In the group that underwent curative resection, about half may be expected to die from recurrence or metastasis within 2 years(3). In most cases, the presence of advanced local disease or metastasis causes much distress. The treatment of these distressing symptoms forms a significant proportion of the work in the management of lung cancer.

This retrospective study aims to provide the background to the lung cancer metastases problem in Singapore. The management of the common metastases will be reviewed.

METHODS AND MATERIALS

The records of 225 patients with lung cancer referred to the Therapeutic Radiology Department, Singapore General Hospital during the calendar year 1985 were retrospectively reviewed for this study.

The diagnosis of metastasis was made on clinical grounds and confirmed with the appropriate investigations in the majority of cases. No special routine "screening" was done, eg. radio-isotope bone scanning or C T scanning.

RESULTS

The distribution of patients by age and sex is given in Table 1. The sex ratio was 3.2 : 1 (M:F). This distribution is in

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agreement with the Cancer Registry data(4). The majority of cases for both sexes are in the age range of 40 to 79 years, with a peak at age 60 to 69 for each sex.

Table 1
DISTRIBUTION OF PATIENTS BY AGE AND SEX

AGE	MALE		FEMALE		TOTAL	
	N =	N ^m =	N =	N ^m =	N =	N ^m =
< 30	1	—	—	—	1	—
30-39	2	2	2	1	4	3
40-49	14	5	2	1	16	6
50-59	47	16	11	6	58	22
60-69	63	23	18	8	81	31
70-79	43	14	14	2	57	16
> 80	2	—	6	2	8	2
TOTAL	172	60 (34.9%)	53	20 (37.7%)	225	80 (35.6%)

N = All patients
N^m = Patients with metastases

Male:Female = 3.2:1

The major histologic types are fairly well represented in the study cohort, with the squamous cell cancers forming about 33% of cases, followed by the adenocarcinomas (15%) and the small cell cancers (5%). (Table 2)

Table 2
DISTRIBUTION OF METASTASES BY HISTOLOGY

HISTOLOGY	N =	N ^m =	%	1N ^m =	%	2N ^m + 3N ^m =	%	AUTOPSY*
Small Cell	11	1	(9.0)	3	(27.3)	4	(36.4)	74% - 96%
Squamous Cell	74	7	(9.5)	11	(14.9)	18	(24.3)	25% - 54%
Adenocarcinoma	34	7	(20.6)	17	(50.0)	24	(70.6)	50% - 82%
Large Cell	14	3	(21.4)	1	(7.1)	4	(28.6)	48% - 86%
Others	24	4	(16.7)	2	(8.3)	6	(25.0)	—
Unknown	68	9	(13.2)	15	(22.1)	24	(35.3)	—
TOTAL	225	31	(13.8)	49	(21.8)	80	(35.6)	

1N^m = Patients presenting with metastases

2N^m = Patients with subsequent metastases
* based on figures on autopsy studies (4)

The metastatic rate at referral was 13.8%. On subsequent follow up an additional 49 patients (21.8%) developed secondaries clinically (Table 2). These rates are lower than those obtained from autopsy studies. This is to be expected as occult secondaries would be asymptomatic and not be diagnosed clinically.

Table 3 shows the breakdown of metastases by site. The main organs that were involved include the bones (27 patients), the brain (18 patients) and the liver (13 patients). Thirteen patients developed extradural cord compression from secondaries to the vertebrae and seven had metastasis to the other lung. A total of 15 patients had multiple organs affected.

Table 3
DISTRIBUTION OF METASTASES BY ORGAN SITE

SITE	PRESENTING %	SUBSEQUENT %	TOTAL %
Brain	7 (3.1)	11 (4.9)	18 (8.0)
Bone	14 (6.2)	13 (5.8)	27 (12.0)
Sp Cord	9 (4.0)	4 (1.8)	13 (5.8)
Liver	1 (0.4)	12 (5.3)	13 (5.8)
Lung	—	7 (3.1)	7 (3.1)
Other	1 (0.4)	16 (7.1)	17 (7.5)
ALL	31* (13.8)	49* (28.4)	80* (35.6)

* 4 patients had multiple sites of metastases at presentation.
11 had multiple sites of metastases subsequently.

Thirty-one patients had secondaries at presentation. In the 49 patients who developed metastases at follow up, the interval from diagnosis to metastases was less than 6 months in 63.3% of patients. On the other hand, the study also yielded 4 patients who developed metastases at or more than 18 months after diagnosis (Table 4).

Table 4
INTERVAL TO METASTASES

INTERVAL (months)	No of Patients %
0 — 2	31 + 16 * (32.7)
3 — 5	15 (30.6)
6 — 8	10 (20.4)
9 — 11	2 (4.1)
12 — 17	2 (4.1)
18 — 23	1 (2.0)
> 24	3 (6.1)
ALL INTERVALS	31 + 49 (100.0)

* 31 patients presented with metastases.

Radiotherapy was the treatment modality most frequently used in the management of metastases, as shown in Table 5. Surgery was performed in 2 cases with extradural spinal cord compression. Nine patients received chemotherapy and 6 were treated by a combination of modalities.

The outlook for these patients is generally dismal with

Table 5
TREATMENT MODALITY FOR METASTASES

SITE	TREATMENT MODALITY				
	RT	SURG	CHEMO	NIL	COMBIN
Bone (27)	24	—	3	2	2
Cord (13)	10	2	1	2	2
Brain (18)	14	—	1	4	1
Liver (13)	—	—	1	12	—
Lung (7)	2	—	—	5	—
Others (17)	9	—	3	6	1

median life expectancy of 1 to 2 months and few surviving over 6 months (Table 6).

REVIEW OF MANAGEMENT

Autopsy studies have shown that lung cancer can metastasise to virtually any organ in the body(5). The presence of disease in these organs can give rise to severe and distressing symptoms for the patients and the majority will require some form of treatment to palliate the condition. This will be discussed under the principal metastatic sites.

Table 6
SURVIVAL (in months) BY SITE

SITE	RANGE	MEDIAN	MEAN
Brain	0-13	1	3
Bone	0-9	2	3
Cord	0-9	1	3
Liver	0-8	1	2
Lung	0-13	2	5
Others	0-13	2	4
ALL SITES	0-13	1	3

BRAIN METASTASIS

Carcinoma of the lung has a strong tendency to spread to the brain. In a recent series by the Radiation Therapy Oncology Group (RTOG), 60% of patients with metastatic brain disease had primaries in the lung(6). Although the patient with brain secondaries is not expected to survive more than 18 weeks(6), the morbidity associated (neurological deficits, headaches, fits etc) demands maximum effort at palliation. The early administration of high dose steroids followed subsequently with cranial irradiation (eg 3000cGy in 10 fractions) is expected to produce satisfactory response in about 70% of patients(6).

BONE METASTASIS

"To many people, incurable cancer means a painful progressive illness ending in an agonising death"(7). A commonly seen example of this dreaded end is shown by the patient with bone metastasis. Treatment strategy involves the use of the appropriate analgesics and radiotherapy for bone pain. Surgery is used to prevent or to fix pathological fractures involving long bones.

While simple analgesics such as panadol, aspirin or the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) may suffice for mild pain, most patients with bone pain would probably require some form of opiate analgesia. The drugs should be given regularly to prevent pain, not just to suppress it. Morphine mixture is commonly used. It has a plasma half life of 2-3 hours(8) and is administered at 4 hourly intervals, at an initial dose of 5-10mg increasing by 5mg each dose until pain relief is achieved. Morphine is also available in the form of suppositories. Laxatives (eg senokot) should be prescribed together with morphine if constipation is to be avoided and anti-emetics may be required when nausea becomes a problem.

Radiotherapy (3000cGy in 2 weeks) is highly effective in treating areas of localised pain. For patients with widespread bony metastasis, large field or hemibody irradiation may be used. This technique has been found to achieve subjective pain relief in 78% of our patients with minimal side effects and inconvenience(9).

SPINAL CORD COMPRESSION

Lung cancer accounts for about 15% of all causes of extradural spinal cord compression(10). In this study, 13 patients (5.8%) developed cord problems. The main clinical problem associated is paraplegia with loss of sphincteric control.

Treatment is controversial. While most agree with the early administration of steroids, subsequent management by surgery and post operative radiotherapy vs radiation treatment alone has not shown any difference in results(11). The prognosis for ambulation is highly dependent upon the duration of symptoms and the neurological deficit before therapy(10). A patient who is paraplegic at diagnosis is very unlikely to ambulate after treatment.

LIVER METASTASIS

Hepatic involvement may be accompanied by pain, gastrointestinal symptoms as well as symptoms attributable to liver failure - such as ascites and jaundice. Radiotherapy

has been known to provide pain relief in about half the patients treated(12). Unfortunately, the majority at that stage are quite ill and may not be able to withstand irradiation. Low dose steroids and analgesics may be a more suitable alternative.

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