

METASTATIC CANCER TO BONE

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Metastatic cancer to bone can arise in any bone and from almost any primary cancer. While once a terminal event, it must now be considered as an incident in the over-all care of the cancer patient. As we have grown more efficient in the support of the subject of disseminated cancer, so the incidence of pathological fractures has increased. A statistical analysis gives only limited and somewhat misleading information regarding results of modern therapy. Because we are treating a multiplicity of disease presenting in various ways, often at different phases of the disease, each case poses a separate problem and must be assessed on its own merits.

We have collected 1,550 cases of cancer metastatic to bone, and it is on these that most of this work is based. An accurate histological diagnosis was obtained in 1,421 instances; in 129 cases the diagnosis was established, but the primary lesion was undetected and the histological picture of the secondary tumour was insufficiently clear for classification. The statistics are expressed in Table I and are self-explanatory:

TABLE I. METASTATIC CANCER TO BONE*

Ossophile 1,092 (70%)		Gastro-intestinal tract 104 (6%)	
Breast	446	Colon	56
Lung	196	Stomach	17
Kidney	160	Oesophagus	10
Thyroid gland	65	Pancreas	11
Prostate	57	Liver	8
Hodgkin's	57	Gallbladder	2
Leukaemia	57	Gynaecological cancer 66 (4%)	
Neuroblastoma	54	Cervix	29
Ossophobe 458 (29.5%)		Corpus	19
Gastro-intestinal tract	104	Ovary	14
Head and neck	76	Vulva	4
Gynaecological	66	Genito-urinary 33 (2%)	
Genito-urinary	33	Bladder	18
Miscellaneous	50	Testicle	11
Unknown primary	129	Adrenal	2
Head and neck cancer 76 (5%)		Penis	1
Larynx	19	Urethra	1
Nasopharynx	17	Miscellaneous 50	
Parotid	10	Melanoma	30
Tongue	8	Lymphosarcoma	4
Mouth	8	Rhabdomyosarcoma	5
Salivary gland	4	Basal-cell carcinoma	3
Tonsil	4	Thymus	3
Parathyroid	2	Haemangiopericytoma	2
Palate	2	Kaposi's	1
Antrum	2	Fibrosarcoma	2
Total cases	1,550		
Diagnosis histologically confirmed	1,421		
Unknown primary	129		

*The series of cases listed in Table I were collected by Dr. Norman H. Higinbotham of Memorial Hospital for Cancer and Allied Diseases, New York, who has kindly permitted me to publish them—W.D.G.

When undertaking the care of such cases it is essential that a histological diagnosis of the bony lesion be obtained; a sufficient number of cases have been encountered with a double cancer pathology to make one extremely wary of a presumptive diagnosis. For example, in 8% of lymphosarcoma cases there developed a second different primary cancer.

Certain tumours have a predilection for metastasizing to bone, while others rarely do so. These cases have been divided into the ossophile and the ossophobe lesions respectively.

It is uncommon in routine postmortem examinations to examine the skeleton carefully. It has been my experience that in many patients dying of cancer, particularly if the cancer has been present for a considerable period, minute

metastatic bony lesions will be seen which were undetectable clinically or radiologically before death.

Which cancers produce osteoblast lesions and which produce osteolytic lesions? Osteoblastic lesions are seen with breast, lung and prostate cancer. An occasional case of gastro-intestinal tract and bladder cancer will produce osteoblastic lesions. Sometimes mixed lesions are seen and this is particularly common in prostate and breast cancer. Metastases which were originally lytic, particularly breast metastases, may be converted to blastic lesions under hormonal therapy. This is usually a sign of a favourable result of hormone treatment.

As has been stated, the presence of radiologically apparent and symptomatic bony metastasis was considered a terminal event until recent years. That this is not true has been firmly established. I have encountered many cases, particularly of cancer of the breast, when metastases to bone have been present and have been treated successfully, usually by radiotherapy, for many years.

What has been gleaned from recent study is that several tumours have a distinctly sinister history if they metastasize to bone. This is certainly true of melanoma, cancer of the gastro-intestinal tract, head and neck cancer, cancer of the lung, and particularly, cancer of the pancreas.

Certainly tumours, particularly those which respond well to hormone therapy, may have a favourable prognosis, and one must always be guarded in stating any specific time of survival. This is particularly true of cancer of the breast, the ovary, the prostate gland and an occasional case of thyroid cancer. Tumours of the testicle, particularly seminoma, may respond dramatically to chemotherapy, and the patient may be alive and well many years after the diagnosis was established.

When metastatic deposits develop in bone a pathological fracture may occur and usually there is little attempt at healing. However, as we have become more accomplished in our general treatment of malignant disease, so we have seen that certain pathological fractures will heal, depending on the effectiveness of the systemic therapy, the radiosensitivity of the tumour and the site of the lesion. It is perhaps easier to list those that rarely, if ever, heal, although occasional cases may be seen that do not behave in the usual way. Fractures due to melanoma, gastro-intestinal tract, kidney and liver have little power to heal and usually the disease overwhelms the patient rapidly. Fractures due to lymphosarcoma, leukaemia, cancer of the breast; cancer of the prostate, and cancer of the testicle and thyroid will very often heal promptly, provided the local disease is controlled and adequate orthopaedic therapy is instituted.

The progress of a metastatic lesion to bone may often afford a useful clue to the effectiveness of systemic treatment, as in the case of conversion of a lytic breast lesion to a blastic one.

The treatment of a pathological fracture must be predicted by many factors, such as the site of the lesion, the type of tumour, the general condition of the patient and

the necessity for employing short cuts, in order to rehabilitate the patient as rapidly as possible.

In general the aim must be to restore continuity of the bone and stability of the fracture and thus afford relief of pain. In the majority of cases this can be accomplished and the patient restored to a useful, often self-supporting, life in a relatively short period. In the case of most fractures, internal fixation by the use of an intramedullary apparatus with exhibition of radiotherapy to the lesion in the immediate postoperative period will result in the relief of pain and allow rapid return to ambulation. When the fracture occurs in the shaft of a long bone, such as in the femur or the humerus, a Kuntscher rod is probably the instrument of choice.

In fractures around the upper end of the femur, a nail and blade plate fixation has proved satisfactory. It is wise to use the McLaughlin type nail and plate so that any minor adjustments of position can be taken up on the metallic joint rather than on the patient. In cervical fractures healing is rarely, if ever, seen. The blood supply of the head of the femur is rendered precarious by the presence of the tumour, further compromised by the fracture and if insulted by nailing, will surely fail and the head will die. The final blow is usually the addition of 2,000 roentgen, just to make sure union will never take place. I have therefore abandoned nailing the subcapital or transcervical pathological fracture and treat these lesions by excision of the head and neck of the femur, followed by radiotherapy.

Occasionally it is necessary to re-operate in order to provide more adequate fixation when the disease has progressed or when initial surgery has proved insufficient.

Radiotherapy

Radiotherapy will almost always be used in conjunction with the operation of internal fixation. Even though many fractures will not heal, radiotherapy would appear to inhibit the tumour sufficiently to bring relief of pain. The average dose administered is approximately 2,000 r, given with a high-voltage machine through multiple ports, or the 250 KV machine may be used to administer some of the total dosage if there is any superficial or soft-part involvement. It is preferable to use the radiotherapy post-operatively rather than pre-operatively so as not to compromise wound healing. The presence of a metal within the substance of the bone causes an increased tumour dose by reflection, but will also cause shadowing and it is always necessary to utilize multiple ports. If the lesion has been irradiated before operation, the incision should be sited through as normal an area of skin as possible and the skin sutures left *in situ* for a much longer period than is usual.

Healing of the soft tissues is not generally a problem if the sutures are left in for long periods, and fungation has occurred in no case to my knowledge.

When tissues have been heavily irradiated, particularly when a dead space has been left such as after excision of the head and neck of the femur, accumulation of haematoma gives rise to a fine pabulum for the growth of organisms, thus infection has proved a difficulty on several occasions. In general, however, primary healing of the soft-tissue wound following operation on metastatic fractures is usually prompt.

Hyperuricaemia may be precipitated by the injudicious use of radiotherapy or when highly cytotoxic chemotherapeutic agents have been used. This is particularly true with reticulum-cell sarcoma and may be of such proportions as to cause a fatal anuria as a result of the production of uric acid crystals in the kidney tubules.

Involvement of the Spinal Column

When metastatic disease occurs in the spinal column it is usually the pedicles that are first attacked, but any portion of the vertebra may be invaded and destroyed. If symptoms develop, radiotherapy should be instituted as an emergency. This is particularly true when there is evidence of neurological involvement. Even though the tumour may be relatively radioresistant, it is worth trying high doses of radiotherapy in the first instance.

In the event of paraplegia developing, if surgery is going to help, it must be carried out within the first 12 hours of the onset of symptoms. In order that the laminectomy may be carefully planned, myelographic examination is a necessary precursor. A word of caution should be sounded here: beware of performing a laminectomy when there is extensive bony destruction, since you may remove the only stabilizing portion of the vertebra and, instead of performing a decompression, all that will be accomplished is a transection of the cord. Likewise, the skull caliper, while offering considerable relief of pain in cervical metastatic disease, should be applied with caution in the unstable spine since its use may result in elongation of the neck with the usual tragic end-result. It is wise also, when inserting a skull caliper, to ascertain the integrity of the bone before the insertion of the prongs, since large areas of bone may be destroyed by metastatic disease and the cranial cavity inadvertently entered.

The Blackburn skull caliper, although the most tedious to insert, is safer than the other varieties and should be introduced under local anaesthetic. Approximately 5 pounds of traction is all that is required to ensure comfort.

Many of these cases are poor surgical risks by ordinary standards, but provided very careful preparation for surgery is undertaken, the mortality and morbidity rate is no higher than in any of the more common major surgical procedures.

Associated Conditions

Particular attention should be paid to the identification and correction of: (1) Total circulatory blood volume deficiency; (2) anaemia; (3) hypercalcaemia; (4) hyperuricaemia; (5) any bleeding tendency; (6) recent myocardial infarction; (7) respiratory insufficiency arising from (a) pulmonary infarction, (b) pneumonia, (c) metastatic disease, (d) pleural effusion; (8) diabetic states; and (9) pituitary or adrenocortical insufficiency.

The surgery should be carried out expeditiously and unimportant technical minutiae discarded in favour of speed. Blood loss may be reduced by the use of the diathermy cautery during the exposure and raw bleeding bone sealed with one of the cellulose mesh substances, which may be reinforced with crushed muscle with advantage.

Rehabilitation should be aimed at the rapid mobilization of the patient.

CONCLUSIONS

1. Metastatic cancer to bone is common and the incidence is increasing.
2. Any cancer can give rise to metastatic bone disease.
3. A pathological fracture is no longer a terminal event and is eminently treatable.
4. Treatment consists of internal fixation and X-ray

therapy in the majority of cases.

5. The nature of the tumour alters the prognosis.

SUMMARY

The prognosis in cancer of the breast, testicle, ovary and prostate, and leukaemia may be good (relatively speaking).

The prognosis in melanoma, cancer of the lung, pancreas, gastro-intestinal tract, head and neck, is always dismal.