Bone and Joint Diseases

Primary malignant tumours of bone

RODNEY SWEETNAM

British Medical Journal, 1976, 2, 1367-1369

There can be few more distressing conditions to treat than primary bone tumour in a child. Not all such tumours occur in childhood, but most do and then amputation followed by a prolonged course of often rather unpleasant chemotherapy strain to the utmost the resilience of patient, parents, and doctors alike.

Here, though, I shall discuss all primary malignant tumours of bone, not just the commonest—the osteosarcoma that tends to strike during adolescence. Chondrosarcoma and fibrosarcoma by contrast usually occur in the middle years of life, as indeed also does the giant cell tumour (osteoclastoma) that carries an often undeservedly benign reputation. Other tumours, such as myeloma, reticulum cell sarcoma, and Ewing's tumour, do not strictly arise from bone and, therefore, need not be considered here. Passing mention must, though, be made to the even more malignant variety of osteosarcoma that may occur in Paget's disease of bone, which is usually fatal within 18 months. Another less common variety, the so-called juxtacortical osteosarcoma, is correspondingly less malign, and even before modern treatment over half the victims survived. All malignant bone tumours are extremely rare, and many a general practitioner will never see one in his own practice during a professional lifetime. Most orthopaedic surgeons will treat a mere handful unless they happen to work with a medical oncology centre to which such patients are referred. Metastatic bone tumours, on the other hand, are common and thus form the largest and most important group in the differential diagnosis of a suspicious bony lesion in the older age range.

Diagnosis

Early diagnosis is important. The history is usually simply one of pain, and in most cases as we shall see later it is around the knee. Swelling too is an early complaint (fig 1). Suspicion should always be aroused by the complaint of constant pain at night. Transient occasional night pains are much more common and not normally a feature of bone malignancy. An x-ray examination, is essential and will usually give a good indication of the diagnosis that will later be confirmed by biopsy. It was once thought that open biopsy was dangerous and might disseminate tumour cells into the blood stream. Now we know that such fears are groundless, for such cells are probably being shed all the time, and almost all are destroyed by the body's defences. Even after biopsy some doubt as to the exact nature of the tumour may remain, for there are few areas in pathology where histological diagnosis can be so confusing. Often, of course, the diagnosis is clear, but almost as often there is some doubt or difference of

FIG 1—Visible swelling of a "typical" osteosarcoma.

opinion—even to the extent of uncertainty as to whether the tumour is benign or malignant. Nowhere is this seen more often than in the chondrosarcoma, where one part of the tumour may look quite innocent whereas in another part there are obvious areas of malignancy—hence the necessity for a generous and representative biopsy. Needle biopsy specimens are often difficult to interpret, although they may be of value in surgically relatively inaccessible areas such as the vertebral bodies.

Most malignant tumours occur at the knee. At least 60% of osteosarcomas occur here, mainly in the femoral metaphysis (fig 2). The position is quite different with osteosarcoma in the dog. Such tumours are apt to develop, particularly in large dogs such as the alsatian (fig 3). The forelimb, however, is the common site for them. Although most of these primary tumours occur in the limbs they may develop anywhere in the skeleton. Chondrosarcoma is the odd one out, for it is much more "common" in the pelvic and shoulder girdles. Seldom is it seen further afield than the proximal humerus or femur.

Radiologically most malignant tumours are characterised by varying degrees of bone destruction, reactive new bone formation, and the presence of a soft-tissue mass. It is the site and varying amounts of each component of these that make up the so-called "characteristic" appearance. Be warned, though, for mistakes are easy to make and just as with histological diagnosis it may sometimes be extremely difficult to say from x-ray examination alone whether or not a particular tumour is malignant. The osteosarcoma is characterised by metaphyseal

FIG 2—Incidence of osteosarcoma—many large series contain an even higher proportion around the knee.

destruction that is usually eccentric and beneath an overlying soft-tissue mass in which there may sometimes be seen spicules of new bone formation (fig 4). The sun ray spicules and Codman's triangles, so beloved of students, are, I am afraid, uncommon. The fibrosarcoma is usually more osteolytic, and new bone is seldom visible in its soft-tissue mass. Areas of irregular calcification are, though, common in the large mass so often seen overlying the area of destruction in the pelvis in chondrosarcoma. Every student is familiar with the locular often expanded appearance of the giant cell tumour extending right down to the joint margin (fig 5). Not a unique appearance, but in middle-aged patients in whom they usually occur it is rarely mimicked by anything else.

Treatment

Regrettably, for most amputation is still an essential part of primary treatment. The one exception is the giant cell tumour that is in most cases either fairly benign or no worse than locally invasive. It is included among malignant bone tumours simply because some are frankly malignant and many others, although not so at first, later become so. Sometimes local excision, as in the lower radius, ulna, or upper fibula, is possible, but at other sites thorough curettage and packing with bone chips is all that is needed. Recurrences, however, must be treated more aggressively.

CHEMOTHERAPY

The great advance in the treatment of bone tumours and, in particular, osteosarcoma is the use of prophylactic adjuvant chemotherapy. This kills any occult micrometastases, or perhaps even more descriptive of their minute size, "pico-metastases". We now believe that these are present at the time of diagnosis in those who subsequently die of their disease. Our experience has been mainly in the treatment of osteosarcoma. There is as yet no evidence that similar chemotherapy is of value in fibrosarcoma or chondrosarcoma, the sheet anchor of treatment of both still being primary amputation, although in the relatively less virulent chondrosarcoma radical local excision with prosthetic replacement of the adjacent joint is sometimes possible.

To be effective, chemotherapy must be given as early as possible, and in practice this means within two weeks of amputation. Bone tumours are relatively resistant to chemotherapeutic agents and, therefore, bulk disease cannot be controlled. The primary tumour, therefore, must be destroyed quickly and certainly. Radiotherapy, being less effective than amputation, is therefore no longer one's choice in treating limb tumours. The otherwise excellent regimen of the late Sir Stanford Cade, in which limbs were amputated only in those most likely to survive (as shown by an absence of lung metastases some six months after a full course of irradiation), is no longer advisable. Once amputation has been performed, and usually just before the stitches are removed, the regular administration

FIG 3—Osteosarcoma in an alsatian dog. (By permission of Dr L N Owen, department of clinical veterinary medicine, University of Cambridge.)

FIG 4—Ossification in the "soft-tissue" mass of an osteosarcoma.

FIG 5—Giant cell tumour (osteoclastoma) treated by local resection.

of adjuvant chemotherapy can begin. It is not strictly "prophylactic" because to be effective and necessary, occult "picometastases" must already be present. The course lasting at least a year is arduous and necessitates admission for a day or so every three weeks.

The commonly used drugs are methotrexate, a folic acid antagonist, or doxorubicin, but others may be used either alone or in combination. The Medical Research Council are at present co-operating with clinicians throughout Britain in a national trial of two drug regimens. In the first trial a moderately high dose of methotrexate is used with vincristine. The patient's normal cellular activity (and incidentally, therefore, also his life) is subsequently rescued by taking a reduced form of folic acid known as citrovorum factor some hours later. In the second trial the same dose of methotrexate is alternated every three

FIG 6—The two regimens of adjuvant "prophylactic" chemotherapy used in the Medical Research Council's trial.

weeks with doxorubicin (fig 6). All these drugs are potentially dangerous and may have unpleasant side effects—for example, total but, fortunately, temporary alopecia is almost invariable with doxorubicin. Deaths may occur from renal or cardiac toxicity, and therefore these drugs are only given under the supervision of a medical oncologist.

It is too early to say whether chemotherapy used in this way will save lives. Quite certainly, though, it prevents many patients from the early development of metastases, and with increasing experience it is beginning to look as though many of these will be cured.

Looking to the future I think that better and possibly more selective chemotherapeutic agents will probably be developed, and hope that they will be sufficiently effective to act against bulk disease, possibly in combination with irradiation or even local resection without therefore the need for amputation. Already local resection is beginning to be advocated by some for osteosarcoma, but the wisdom of this has not yet been shown by long-term results. Various treatments based on enhancing active or passive immunity are under clinical trial—so-called immunotherapy. Results are awaited, but chemotherapy still appears to be the more effective.

Finally, in any consideration of the management of primary bone tumours one cannot ignore the proved value of resection from the lung of solitary metastases. Such single metastases are rare, but many lives have been saved by their resection and thus close radiographic surveillance during treatment is essential.

Recent developments in adjuvant treatment suggest that we are on the threshold of an important advance in the treatment of malignant bone tumours. However great such improvement may seem when compared with the 80% early death rate from osteosarcoma before such treatment, much more progress has to be made before most malignant tumours can even compare in terms of survival with most other tumours. We may now have reached that stage with the use of adjuvant chemotherapy, but it is still too early to be sure.

Aspects of Student Health

Health and safety in a university

D BUSH

British Medical Journal, 1976, 2, 1369-1371

Accident statistics for universities show that, taken overall, students are less at risk than employees both in terms of the probability of being in an accident at the university and also in terms of accident severity. Accidents affecting students are relatively few, and they tend, generally, to be not too serious from the medical point of view.

This account is based largely on my experience of safety at the University of Birmingham, and it deals with legal aspects, hazards, safety organisation, typical accidents, medical treatment, and health surveillance.

Legal

Until 1 April 1975, when the Health and Safety at Work etc Act, 1974, came fully into operation, few university activities were controlled by safety legislation. One of the earlier pieces of legislation that did apply to limited parts of universities was the Offices, Shops, and Railway Premises Act 1963, which specified suitable and safe conditions for workers in offices. Another area covered by earlier legislation was the storage and use of certain highly flammable liquids under the Petroleum (Consolidation)

University Safety and Radiation Protection Service, University of Birmingham, Birmingham B15 2TT

D BUSH, BSc, university safety adviser and radiation protection officer