REVIEW ARTICLE

Biopsy principles of musculoskeletal tumours - when, where, who and how?

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Abstract

Histological assessment with a well representative adequate sample would be the key step in diagnosis of musculoskeletal tumors, but poorly performed biopsy remains a common finding in patients with musculoskeletal tumors who are referred to orthopaedic units. Success of a biopsy in musculoskeletal tumour pathology is based on the answers to several vital questions. These questions are when to biopsy? Who should perform the biopsy? where to take the biopsy? And How to biopsy? Errors in answers to these questions will lead to errors in biopsy, misleading the diagnosis and adversely affecting the survival of the patient. Subsequently patients may require an amputation to achieve an adequate surgical resection instead of a limb salvage procedure. In order to minimize the errors related to biopsy, it is mandatory to follow a set of guidelines during the biopsy procedure. This article will discuss the proper biopsy procedure by seeking answers to the above questions.

Introduction

The diagnosis of a musculoskeletal tumour is based on clinical, radiological and histological assessment. It is mandatory that all three parameters must fit in to each other for a final diagnosis. In the absence of such compatibility the accuracy of the diagnosis must be questioned. Among these parameters the key step in diagnosis would be the histological assessment via biopsy.

When to biopsy?

As stated by Jaffe the biopsy should be regarded as the final diagnostic procedure, not as a shortcut to the diagnosis [1]. Therefore always a tissue diagnosis should be considered when initial clinical, laboratory, and radiographic examination is unable to confirm the diagnosis.

Rougraff et al. has described several reasons why the biopsy should not be done until the clinical and radiological evaluation is completed in an evaluation of musculo-skeletal tumors [2].

- Biopsy may not be needed for the diagnosis, if a definitive diagnosis can be achieved with clinical and radiological evaluation alone e.g. benign latent lesions like non ossifying fibroma or enchondroma which can be accurately diagnosed with a simple plain X-ray.
- Initial imaging may help in planning the placement of the biopsy incision while providing more information leading to a more accurate pathological diagnosis.
- Histological diagnosis is more accurate if supported by appropriate imaging studies.
- A biopsy prior to a radiological evaluation may alter the interpretation of the imaging studies due to artificial radiologic changes at the biopsy site.
- The pathologist and surgeon may be more assured of a diagnosis made on frozen section analysis if supported by the preoperative evaluation. Thus definitive treatment can be carried out without undue delay Eg: If a giant cell tumor is suspected on clinical and radiographic grounds, definitive curettage can proceed immediately after confirmation of the diagnosis on frozen section.
- In highly vascular lesions, surgeon may wish to consider pre-operative embolization prior to biopsy in order to avoid excessive bleeding;
- If the lesion is a part of metastases of an unknown primary; another, more accessible lesion may be found which is more suitable and accessible for a biopsy.

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It is important that the surgeon and the radiologist, be familiar with the biological and radiological findings of musculoskeletal tumors. Ideally, if the results of the evaluation suggest a possibility of a primary malignancy, the patient should be referred to a unit specialized in musculoskeletal oncology before the biopsy. Preferably, this should be the unit where definitive treatment will take place. The value of such a referral was emphasized in two landmark studies conducted by the members of the Musculoskeletal tumour society. In 1982, they evaluated 329 patients who underwent biopsy for bone or soft tissue sarcomas. According to the study, nearly 18% of biopsies of musculoskeletal neoplasms resulted in an error in diagnosis and about 10% were poorly planned and executed or resulted in a non-representative sample. Of greater concern, almost 17% of biopsies resulted in some sort of skin, bone or soft-tissue complications, with 5% unnecessary amputations. [3]

When this study was repeated after 10 years in 1992, with 597 patients submitted by 25 surgeons from 21 institutions, the rates of complications, errors, and deleterious effects related to biopsy, were essentially the same. It was evident that these events occurred with far greater frequency when the biopsy was performed in a referring institution, rather than in a specialized oncology center [4].

Who should perform the biopsy?

Biopsy should be planned as carefully as the definitive procedure, because in planning the definitive surgery, it must be assumed that the biopsy tract is contaminated with tumour cells and thus should be resected with the same safety margins as the primary tumour (wide margins).

Although some have stated that seeding of needle biopsy tracts with sarcoma is rare, suggesting that needle tracts do not need to be resected *en bloc* with the final specimen, this remains controversial as there are reported cases of recurrence within needle tracks [5-7]. Therefore it is always safe that the incision of an open biopsy or the needle puncture hole of a closed biopsy, must be made with consideration of the planned surgical incision site so this could be excised with the future surgical specimen.

The surgeon performing the biopsy should be familiar with incisions for limb salvage surgery and amputation flaps. In order to fulfill these requirements it would be best if the biopsy is performed or directed by the surgeon who will ultimately provide definitive surgical care for the patient [3,4].

Where to biopsy

Positioning of the biopsy tract of bone and soft tissue tumours should be predetermined by identifying the most representative part of the lesion for the biopsy, usually by imaging. The biopsy tract must be the shortest way to the lesion; however, the deep incision should go through a single muscle compartment rather than contaminating inter-muscular planes. The main neurovascular bundle must be avoided during the procedure since their exposure places them in a contaminated tract of tissue that may require resection. When a needle biopsy is performed with or without image guidance it is extremely important that the treating surgeon communicate clearly with the radiologist about the approach and direction of needle tract [8-10].

Even though bone and soft tissue sarcomas have a common origin from the mesenchymal elements, the type of mesenchymal proliferation is determined by the anatomical location of the lesion i.e. soft tissue tumors stimulate a fibrous reaction, and intraosseous lesions stimulate a bone forming reaction. Thus the same lesion will stimulate different mesenchymal responses in different areas i.e. the reactive region around an intraosseous lesion matures into reactive bone, whereas if the lesion penetrates the soft tissues, the mesenchymal response is fibrous [11,12]. This emphasizes the importance of taking multiple samples when obtaining a biopsy specially with the technique of needle biopsy.

Most importantly the biological behavior of a sarcoma is different to that of a carcinoma. Carcinomas usually infiltrate the surrounding tissues but a sarcoma may push the surrounding tissues to the periphery with its centripetal pattern of growth, creating a reactive zone between the tumor and the compressed surrounding normal tissue. This reactive zone is composed of proliferating mesenchymal cells, neovasculature, and inflammatory process [13,12]. Therefore to obtain an adequate well representative sample of the tumor, care should be taken to sample more than just the reactive zone surrounding the lesion by reaching an adequate depth in to the lesion.

As a rule, the extraosseous component of a malignant bone tumor is as representative of the tumor as is the bony component. Thus it is not necessary to disturb the cortex of a bone that harbours a malignant tumor unless there is no significant extra-osseous soft tissue extension, because such disturbance may predispose the patient to a pathological fracture.

It is always advisable to send a frozen section intra-operatively to verify the presence of representative tumor material in the specimen. The value of a frozen section diagnosis would be to confirm the clinical and radiographic diagnosis. Thus in a situation where we can proceed with definitive treatment, it is possible to complete the treatment at the same time. For example, if a giant cell tumour is suspected on clinical and radiographic grounds, definitive curettage can proceed immediately after confirmation of the diagnosis on frozen section. Conversely, In cases of discrepancy or doubt or if the frozen section exhibited any atypical cells that might represent a sarcoma, definitive surgery should be delayed until the final pathological evaluation is complete.

How to biopsy?

A biopsy can be performed either as an open incisional biopsy or a closed procedure like fine-needle aspiration biopsy or core needle biopsy. Excision biopsies are rarely performed for musculoskeletal tumours unless direct primary excision of the lesion is possible. When the lesion is a small (<3 cm) subcutaneous mass which is unlikely to be malignant or if the lesion is definitely a benign bone lesion according to some characteristic radiographic appearance (eg: osteoidosteoma and osteochondroma) primary resection without a biopsy is possible. Also painful lesion in an expendable bone, such as the proximal fibula or distal ulna when the lesion is confined to the bone, a primary excision can be performed without biopsy. But even the slightest doubt regarding the diagnosis at the end of a clinical evaluation one should not be hesitant to go for a tissue diagnosis.

There is no good quality evidence to suggest that biopsy promotes accelerated growth or metastatic dissemination of a malignant tumour, with any of these techniques. But it is reasonable to suppose that technically there is a risk of spread of tumour cells and local recurrence with open and needle biopsies [14-16, 7].

Incisional biopsy

Incisional biopsy is the gold standard for biopsy of bone and soft tissue tumours, since it is least likely to be associated with a sampling error due to the large volume of tissue it provides. Because of such volume an accurate evaluation of cellular morphologic features and tissue architecture from different sites of the lesion is possible as well as providing adequate sample sample for additional diagnostic studies, such as immune histochemical analysis, cytogenetics, molecular genetics, flow cytometric analysis, and electron microscopic examination. These additional studies may help in sub-classifying the tumours increasing the accuracy of the diagnosis and deciding the definitive treatment.

Longitudinal incision as small as necessary to obtain an adequate specimen would be the ideal to minimize the surrounding tissue contamination .Transverse incisions should be avoided because they are extremely difficult or impossible to excise with the specimen [3,4,17]. When obtaining the specimen, a knife or curette should be used to avoid crushing or distorting the specimen's texture. Use of diathermy around the biopsy will disturb the tissue architecture.

Tourniquet is indicated for an open biopsy procedure since achieving adequate hemostasis during the procedure will be a difficult task due to increased vascularity of musculoskeletal tumours. If a tourniquet is used, the limb may be elevated before inflation but should not be exsanguinated by compression since there is a theoretical risk of forcing tumour cells in to the proximal aspect of the extremity and in to the bloodstream. As a general rule it is necessary to 'culture what we biopsy and biopsy what we culture', because osteomyelitis may mimic a bone tumour. Therefore part of the specimen should be sent for aerobic, anaerobic, and acid-fast bacterial culture, along with fungal culture.

Biopsy from a purely intraosseous bone lesion will be definitely through a cortical window. Clark et al evaluated the impact of three types of biopsy hole shapes namely, rectangular hole with square corners, rectangular hole with rounded corners, and oblong hole with rounded ends on the breaking strength of human femora . They found that an oblong hole with rounded ends afforded the greatest residual strength. Significant

reduction in strength was observed by increasing the width of the hole than the length. According to these results for a small cortical window a circular shape and for a larger window an oval shape would be the best considering the amount of stress risers [18].

It is vital to prevent a haematoma formation since such haematoma will be invariably contaminated with tumour cells and may dissect the soft and subcutaneous tissues to contaminate the entire extremity, leaving the chance of limb salvage at risk. In order to minimize this risk, methylmethacrylate (bone cement) can be used to plug the cortical defect in order to limit hematoma formation but care should be taken not to use a large amount of methacrylate needed to plug the hole since excessive amounts push the tumor up and down the bone.

At the same time it is important to ensure meticulous hemostasis prior to closure once the tourniquet has been deflated with or without a drain. If a drain is used, it should exit in line with the incision or through the biopsy incision so that the drain track also can be easily excised en bloc with the tumor. The wound should be closed tightly in layers avoiding the use of wide retention sutures

However complications such as bleeding, hematoma formation, wound Infection, tissue contamination and pathological fracture are relatively higher with incisional biopsy when compared to closed biopsy techniques [3, 4].

Needle biopsy

Closed biopsies offer several advantages over open biopsies. Obviously, closed biopsy would be less invasive, less painful, less costly and theoretically carry a lower risk of tissue contamination with tumour cells. Needle biopsy will extremely useful when the patient is obese and also in a situation where the tumor is in in a difficult location like pelvis or in close proximity to neurovascular structures [17]. When the tumour is palpable and remote from the neurovascular bundle, a needle biopsy can be performed even in a clinic setup.

The disadvantages of needle biopsy are more crucial than these advantages, however since these may directly affect the diagnostic ability of the procedure. When compared with an open biopsy, in closed biopsy procedure the amount of tissue that the procedure can obtain is less. Especially when evaluating heterogeneous lesions such inadequacy may adversely affect the quality of diagnosis underestimating the tumour grade since it is not possible to gather enough details on tissue architecture and matrix formation. Such error will have a profound effect on a patient's prognosis and treatment. Thus it is mandatory to perform the procedure with a proper technique by an experienced person. These disadvantages are more with fine needle biopsy than Core needle biopsy. Therefore excep in a few specialized centers, [19, 2, 21] fine needle aspiration is not used commonly to diagnose primary bone tumours [22].

It is important to plan well and adopt the correct technique of biopsy in order to overcome these errors. More importantly the interpretation of the biopsy should be done by a well experienced pathologist on musculoskeletal tumors [3, 17, 9, 6, 23-25]. According to some studies 22 gauge needle will provide a reliable and sufficient biopsy sample during fine needle aspiration of soft tissue tumors [19, 26-28]. Diagnostic accuracy was higher when cell type of the tumour is homogeneous, as in the case of multiple myeloma or metastatic carcinomas.

A core needle biopsy uses a larger-gauge needle than a fine-needle aspiration, providing for tissue and preservation of the tissue architecture. Core needle biopsy, using a 14-gauge needle that provides a core of tissue with a maximum length of 20 mm, was shown to be more than 90% accurate in differentiating malignant from benign lesions [29]. In some centers core needle biopsy is performed as the first biopsy modality for suspected bone or soft tissue sarcomas [29].

Open biopsy is performed when the pathologic diagnosis is inconclusive or does not correlate with the clinical presentation and radiologic findings. Needle biopsies can be performed with image guidance (e.g.; CT, USS) when the tumour is deep seated like in pelvis. For bone lesions, CT guidance is frequently used because it allows the physician to visualize the cortical integrity and matrix characteristics of the lesion that may lead him or her to an area of the lesion that is most likely to contain pathologic tissue. CT-guided biopsies of lesions in the spine and pelvis can be much more accurate and safe than open biopsies of these lesions [30, 31].

Conclusion

When handling musculoskeletal tumours, biopsy principles must not be violated at any cost, since such violation will affect the outcome of the patient. Simply stated, the musculoskeletal tumours should be handled by the same expert from the biopsy to the definitive management.

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