RESEARCH ARTICLE

SELECTION OF MODE OF BIOPSY IN HISTOPATHOLOGICAL DIAGNOSIS OF SOFT TISSUE SARCOMA DEPENDING ON DIAGNOSTIC ACCURACY AND FEASIBILITY: DEBATABLE ISSUE IN MODERN ERA

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ABSTRACT

Background: Biopsy method of choice is a controversy issue for diagnosis of soft tissue sarcoma which are traditionally been managed by wide excision surgery and radiotherapy. Chemotherapy is reserved for advanced cases.

Aims & Objective: The objective of study was to evaluate diagnostic accuracy of various modes of biopsy focusing on image guided core needle biopsy (CNB).

Material and Methods: Current study includes 50 cases of soft tissue sarcoma from January 2010 to October 2012. The Mode of biopsies included image guided CNB, open and excision biopsy. Effective accuracy of each was determined by accuracy of biopsy to provide adequate tissue for histopathological and other special examinations like immunohistochemistry to reach final diagnosis.

Results: Out of total 50 cases CNB was done in 13 cases, open biopsy in 2 cases and in 35 cases excision biopsy was done. CNB was adequate in 92.31 % cases and 7.69 % cases it was inadequate. Open and excision biopsy were 100 % adequate.

Conclusion: Image guided CNB is very helpful in early diagnosis and shows high accuracy especially for high-grade sarcoma. It is less invasive compared to others and differentiate benign from malignant. It is handful when preoperative diagnosis is essential for planning pre-operative chemotherapy especially in patients with primarily inoperable, advanced tumour with compromised performance status or recurrent tumour. But it should be properly directed and representative of whole tumour and require full radiological correlation by experienced hands. Tumours with myxoid pattern, lipomatous tumours and low grade sarcomas encounters lower diagnostic accuracy on CNB.

Key-Words: Soft Tissue Sarcoma; Core Needle Biopsy; Excision Biopsy; Preoperative Diagnosis

Introduction

Due to growing tendency to perform least radical surgery and least invasive treatment number of major radical surgery specimen received to surgical pathology laboratory has decreased since last two decades. Given the prognostic and therapeutic importance of accurate diagnosis, a biopsy is essential and appropriate method to establish malignancy, to assess histological grade, and to determine the specific histological type of sarcoma, if possible. A treatment plan can then be designed that is tailored to a lesion's predicted pattern of local growth, risk of metastasis, and likely sites of distant spread.[1] Representative and enough sample from a viable area of sarcoma is usually required for definitive diagnosis and accurate grading.[1] Tissue sampling can be accomplished by open incisional biopsy, fine-needle aspiration (FNA), image guided core needle biopsy (CNB) and excision biopsy. The choice of technique balances the invasiveness, risk, and cost of the procedure against the total amount of tissue obtained. Although open surgical biopsy is considered the reference standard, it is more expensive, may require hospitalization, and has a higher complication rate than image guided core needle biopsy.[2-4] Most limb masses are generally best sampled through a longitudinal incision, so that the entire biopsy tract can be completely excised at the time of definitive resection. Excisional biopsy should be avoided, particularly for lesions greater than 2 cm in size, since such an approach will make definitive re-excision more extensive due to the contamination of surrounding tissue planes.[1] For deep-seated lesions, image guided core needle biopsy approach may be used to establish a diagnosis.[1] When performing FNA, one runs the risk of insufficient tissue sampling. FNA is likely

adequate for metastatic lesions; however, its utility in the diagnosis of primary sarcomas of soft tissue is limited and controversial.[2,5-7] Because fine needle aspirates show only the cytological features of the lesion and do not show tissue architecture, accurate pathologic diagnosis is often not possible.[2,7] Also Immunocytochemical assessment is cumbersome and need special care on FNA smears. CNB of soft-tissue lesions is minimally invasive, can be performed in an outpatient setting, and is less expensive than surgical biopsy.[6,8,9] Moreover, CNB creates a smaller biopsy track than open surgery, facilitating subsequent resection of the track at definitive surgery.[10,11] Complication rates are low and are estimated at 0.2%, with a range of 0%–10%.[6,7,10,12-20] The diagnostic yield and diagnostic accuracy of CNB are high and have improved over the years as the procedure has becoming increasingly practiced.[4-6,10,14-16,20-23] Currently, to our knowledge, no published guidelines exist on the size or number of specimens that should be obtained during CNB of soft tissue lesions to optimize the diagnostic yield. Practice patterns vary widely. Some authors advocate the acquisition of three or fewer specimens.[12,15,16,24] Other authors advocate minimum of three specimens[5,6,25] while still others routinely acquire five to 10 specimens with few complications[8,17]. To our knowledge, no prior study has systematically evaluated the influence of specimen size or number on the diagnosis of soft-tissue lesions keeping in mind that biopsy should be appropriately directed and representative of whole tumor and done after full radiological correlation by experienced hands.. Current study shows that the image guided core needle biopsy less invasive as compared to open and excision biopsy and vital in patients with primarily inoperable pelvic tumor, advanced tumor and compromised performance status, or recurrent pelvic tumor. Tumors with myxoid pattern, lipomatous tumors and grade 1 sarcomas are associated with lower diagnostic accuracy on CNB.

Materials and Methods

Total 50 cases of soft tissue sarcoma from January 2010 to October 2012 were studied. For histopathological examination mode of obtaining tissue were Excision biopsy, Image guided core needle biopsy and open incisional biopsy. Being tertiary care hospital referred cases of soft tissue sarcoma managed according to available facility. After routine clinical, thorough radiological, other investigations and considering other factors mode of biopsy chosen. Excision of whole soft tissue lesions in 35 cases and Open biopsy was done in 2 cases by experienced surgeons of our institute. Core needle biopsy was done in 13 cases after thorough evaluation by radiological procedures like x-rays, Ultrasonography (USG), CT scan, Magnetic resonance imaging (MRI) and others required. Each core needle biopsy was performed under complete imaging guidance which include USG and CT guidance. 14 or 16-gauge coaxial automated biopsy gun system was used. Patients were in a state of conscious and given Atropine and Diclofenac injections were given before the procedure to avoid vasovagal shock and to reduce pain during the procedure. Procedures were performed by experienced radiologist and surgeons under imaging guidance and representative cores from whole tumor were taken averaging 3-5 in majority. Considering possibility of complications all precautions were taken and all appropriate facility made available at site to manage any complications but no major complications were documented. We placed biopsy cores in neutral buffered formalin-filled container immediately, processed and interpreted by histopathology section of department of pathology. Apart from histopathological examination by Haemotoxylin and Eosin and other special stains, panel approach of Immunohistochemistry (IHC) was also used to accurately diagnose soft tissue sarcoma. Adequacy of each mode of biopsy was determined by accuracy of mode of biopsy in providing adequate tissue for histopathological examination and whether enough tissue was obtained for routine and special examinations especially IHC to reach final diagnosis.

Results

Out of total 50 cases 35 cases (70 %) were assessed by excision biopsy, 13 cases (26%) cases by image guided core needle biopsy and 2 cases (4%) by open incisional biopsy. No major complications were noted especially during image

guided core needle biopsy. Excision and Open incisional biopsy approach yielded 100% adequate tissue for routine and special examinations especially IHC. Adequate panel of IHC was applied after assessing histopathological morphology in representative portion of biopsy. It was possible to reach a single final diagnosis in all these cases. So accuracy of Open and excision biopsy is 100%.Image guided core needle biopsy was adequate in 12 cases (92.31%) and in 1 case it was inadequate as only 2 cores with very tiny bits were available because patient denied further procedure. In that case on histopathological examination it was pleomorphic sarcoma with only one IHC marker Cytokeratin was done which was negative and final diagnosis of pleomorphic undifferentiated sarcoma made considering morphology other data. In rest of 12 cases biopsy was adequate enough for examination and panel of IHC providing final diagnosis. So that the further plan of management can be followed. Quality control simultaneously been ensured by positive control of IHC while making the diagnosis. One of the case of Lung mass with past history of chronic obstructive pulmonary disease accidently detected 11cm X 9cm X 6cm on x-ray and CT scan of chest. Image guided CNB from lung mass was taken and it was synovial sarcoma by histopathology and IHC. Such result was supported by cytogenetic and molecular analysis like by Fluorescence In Situ Hybridization (FISH) with DNA Probes on the tissue of core needle biopsy shows SYT 18q11.2 gene rearrangement t (X;18) confirming the reliability of diagnosis made on core needle biopsy.

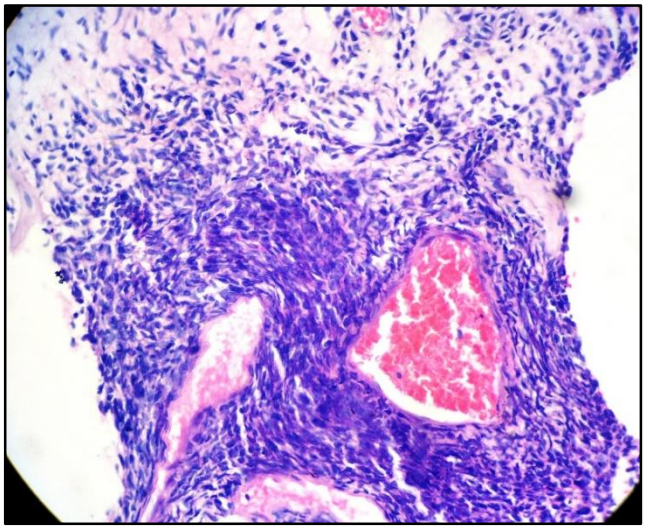

Figure-1: H & E of CNB in Synovial Sarcoma of Lung (X40)

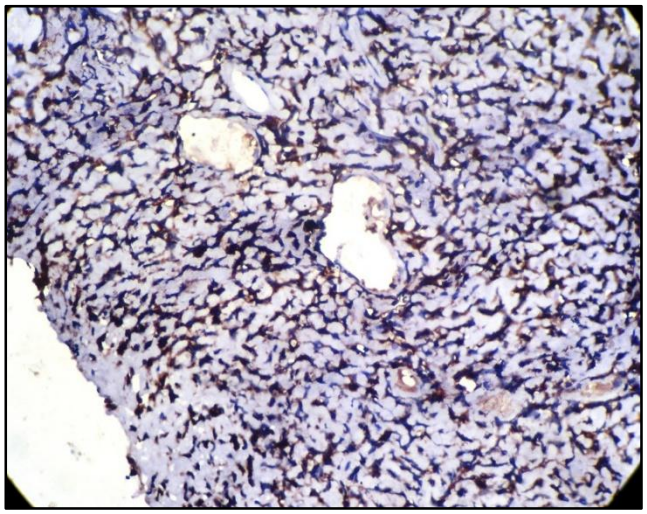

Figure-2: BCL-2 Positivity in Synovial Sarcoma of Lung (X 40)

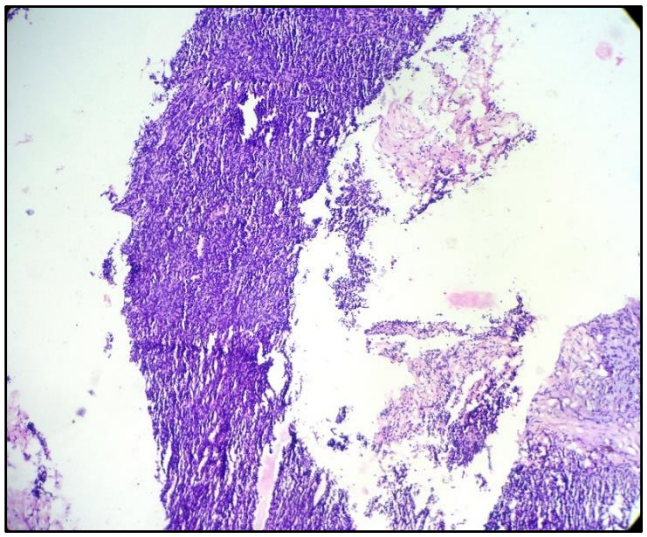

Figure-3: Multiple Cores in CASE of Ewings Sarcoma (X10)

Discussion

Due to increasingly growing tendency to perform limb-sparing and less radical surgery for sarcomas of all types, the number of major radical surgery and amputation specimens received in the surgical pathology laboratory has markedly decreased. Whatever may be the mode of biopsy it should provide adequate tissue for histopathological and other special examinations like IHC to reach final diagnosis. Enough tissue is usually required for use in several other diagnostic tests, such as electron microscopy, IHC, cytogenetic analysis & flow Cytometry to accurately type the sarcoma. In the past the choice of biopsy technique for soft tissue masses was decided by the size and location of the lesion. Incisional biopsy was considered the gold standard for large, deeply situated masses and provided ample material for diagnosis and

ancillary studies. Its principal disadvantages included spillage of tumor into adjacent compartments due to poor hemostasis or faulty biopsy placement, complications of wound infection, and the usual requirement for hospitalization of the patient. Excisional biopsy, while invasive and providing the entire lesion for examination, could only be performed on small, superficial lesions amenable to complete resection.[26] Most extremity sarcomas are removed with a wide local excision usually combined with preoperative or postoperative radiotherapy. There are no dogmatic guidelines for sampling soft tissue tumors; to some extent, sampling is decided by various factors in specific case.[27] The current reliance is on minimally invasive techniques to obtain tissue has changed the biopsy paradigm in the direction of the use of core needle biopsy. Based on the Memorial Sloan-Kettering Cancer Center experience, the incidence of core needle biopsies increased from less than 10% to nearly 80% during the early 1990s[27], and according to others it currently exceeds 90%[26]. Consequently, the amount of material available to type and grade sarcomas has decreased and this trend is likely to continue unabated due to the emphasis on less costly and less invasive outpatient care. Therefore, it is important to be aware of the limitations and pitfalls of core needle biopsy and to keep in mind a few basic principles.[28] First, the pathologist should be aware of the expectation of the clinician. In some instances the goal of a core needle biopsy may be simply to establish that a soft tissue mass is a primary mesenchymal neoplasm as opposed to a lymphoma or metastatic lesion; a distinction usually easily made in a majority of cases with the use of adjuvant immunohistochemistry. If definitive surgery will be performed following the needle biopsy, then the most important priority is to determine if the lesion is a sarcoma or not. If, however, the intention is to provide preoperative (neoadjuvant) radio- or chemotherapy, every attempt should be made not only to make the diagnosis of sarcoma but also to classify and grade the lesion. It is not always possible to reliably grade a sarcoma on the basis of a core needle biopsy, however. In particular, it is difficult to discriminate a grade 2 from a grade 3 lesion. Pathologists may find that the best assessment they can give is the designation “low grade” or “high grade”. Current study indicates that the image guided core needle biopsy if appropriately taken and representative of the whole tumor will be a great tool in the form of rapid, least invasive, short outpatient based procedure and good alternative mode of obtaining tissue which even doesn’t require the anaesthesia. Other modes including open incisional biopsy and excision biopsy provide 100% adequate material for final diagnosis though they carry the risks including haemorrhage, surgical and anesthetic complications, spillage of tumor during procedure with wide spread dissemination and other complications. It also very time consuming and often delays the diagnosis in cases when patients are not fit for procedure. Few of the cases including the inoperable pelvic tumor, advanced tumor and compromised performance status, or recurrent pelvic tumor in such cases open incisional biopsy and excision biopsy are not feasible. It is important to note that, soft tissue tumors often are spatially heterogeneous with respect to tumor grade and histologic features, and tumor necrosis may be widespread. For these reasons, the limited and unrepresentative sampling that is possible at needle biopsy may be a source of problems or may limit confidence in diagnosis. Hence, patients with masses suspected to be primary neoplasms of the soft tissue lesion should be thoroughly evaluated and representative biopsy is must to avoid false diagnosis. For e.g. Tumors like Neuroblastoma if assessed by core needle biopsy may have heterogeneous components like schwannian stroma, ganglion cell component, and neuroblastic components and if the core needle biopsy not taken from the representative areas will results in false diagnosis. So tumors with different heterogeneous components caution need to be exercised. According to various studies adequate tru cut biopsy along with IHC is effective in diagnosis and correct typing of tumors in more than 85 % of cases. On an average it provides about 85-90 % of accuracy.[29-36] In the multicenter survey by Mankin et al[37] of soft-tissue tumors in patients referred to major treatment centers, the accuracy of core-needle biopsy was 69% (43 of 62). In the experience of Heslin et al[27], core-needle biopsy findings resulted in the correct histologic diagnosis in 70% (42 of 60) of soft-tissue masses. In a combined

series of suspected mesenchymal tumors of soft tissue and bone reported by Skrzynski et al[38], the accuracy of core-needle biopsy results for correct histologic features and tumor grade was 77% (48 of 62). Wu et al[39] having adequacy of 76% (48 out of 63). Yang et al[40] study showed adequacy of 83%. Current study shows adequacy of tru cut biopsy in 92.31 % which is supported by above mentioned studies and suggest that core-needle biopsy could be effective primary tool for evaluation of soft tissue tumors and its accuracy is been rising and in future CNB will be practiced as a primary tool as the preoperative diagnosis is been considered essential to plan preoperative chemotherapy.

Table-1: Comparison of Current Study with Others Studies

Study	Adequate	Inadequate
Yang & Damron et al (2004)[40]	83%	17%
Skrzynski et al (1996)[38]	77%	23%
Wu et al (2008)[39]	76%	24%
Mankin et al (1996)[37]	69%	31%
Heslin et al (1995)[27]	70%	30%
Current Study	92.31%	7.69%

Conclusion

Image guided Core-needle biopsy is a safe, accurate, and economical procedure compared to open incisional biopsy for diagnosing soft tissue sarcomas. Also it is less time consuming, require no anaesthesia and can be performed as an outpatient procedure. So it should not be reserved for special situations in which other mode of biopsy not feasible. In recent years, the numbers of techniques, needle sets, and imaging guidance systems have improved. The most common reported reason for inaccurate results is failure to obtain enough tissue for histologic analysis; thus, a strategy is needed to maximize the amount of biopsy tissue that can safely and easily obtained via image-guided core needle biopsy procedures. The use of CT or sonography to guide a core-needle biopsy can increase the yield of tumour tissue by more accurately pinpointing the location of the tumour. Obviously, it is particularly important to precisely locate the needle in the tumour mass to avoid sampling necrotic or cystic areas of the tumour that are of no diagnostic value. Current study indicates that the use of well-directed and representative image guided core needle biopsy for primary evaluation of soft tissue sarcoma can be handful.

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