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THE ROLE OF FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF BONE TISSUE LESIONS

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Summary

FNAC for the diagnosis of cancer has been used for over a half century to diagnose tumors of almost any organ. In bone however FNAC has not been widely applied because of concerns about its diagnostic accuracy. The present study aimed to determine the value of FNAC in the diagnosis of bone lesions.Between October 2000 and September 2001, FNAC was performed on 60 patients with bone lesions. The material was smeared on glass slides fixed in 95% ethanol stained with Haematoxylin & eosin or Papanicolaous stains. In 54 out of the 60 cases open biopsies were performed and the results were statistically analyzed. Of the 60 patients with bone lesions, the male to female ratio was 1.07:1 The age ranged from 6 to 93 years and the mean age was 37.2 years. Most of the cases were in the second and third decades of life. The cytological diagnoses were malignant in 33 cases (55%) including 25 primary malignant and 8 metastatic tumors. Benign diagnoses were found in 16 cases (26.7), suspicious in 2 cases (3.3%) and unsatisfactory results in 9 cases (15%). Two false positive (3.3%) and two false negative (3.3%) results were encountered.. The sensitivity and specificity were 86.2% and 87.5% respectively; while the overall accuracy was 86.7%. FNAC is a simple, safe and relatively accurate screening procedure for differentiating benign from malignant bone lesions. However specific diagnosis and grading are often difficult to make and therefore it must never be regarded as a substitute for histopathological diagnosis.

Introduction

Sarcomas are rare mesenchymal neoplasms. In bone tissues they constitute less than 1 % of the newly diagnosed cancer per year. They are one of the most common solid tumors of childhood and are the fifth more common cause of cancer death in this age group[1,2,3].

In our country the results of Iraqi cancer registry of years 1995-1997 found that bone sarcomas are rare; representing only 1.2% of all newly diagnosed cancer per year; while in children they constitute 5.1% of total malignancies[4].

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A correct diagnosis of bone lesion can usually be made by combined clinical, radiological and pathological features[5,8]. Open biopsy has been the conventional procedure for obtaining adequate and representative samples of tissue for diagnosis. It requires an operation which needs general anesthesia, increased cost and associated with higher rate of complications, local dissemination of tumor cells and discomfort associated with surgery[9-14].

Core needle biopsy (CNB) is a reliable technique for evaluation of bone lesions by providing tissue for histological examination and for cytological analysis. It is preferred if limb sparing is an option, since it entails less local contamination than open biopsy. It is especially helpful in difficult areas such as the spine, pelvis and hips with less complications and high diagnostic value[6,15-17].

Aspiration cytology has been employed in the diagnosis of bone lesions in several studies since 1930 [17- 19]. In these earlier studies, needles gauge-18 and larger were used, which necessitated local anesthesia and often skin incisions, with the resulting morbidity and discomfort. With the introduction of FNA of bone lesions, the procedure has become easier to perform, kinder to the patient, and less invasive than a large CNB or an open biopsy; but has not gained wide application, presumably because of anticipated difficulties in obtaining adequate tissue material, partly due to technical problems but also to morphological heterogeneity of bone tumours[20-22]. FNA is particularly useful in delineating patients with metastatic or primary tumours such as multiple myeloma or lymphoma to avoid unnecessary surgery as most instances can be managed by radiotherapy or chemotherapy [23]. This study is done to assess the current role of FNAC in the diagnosis of bone lesions and to provide a preoperative diagnosis, which is essential in planning the operative procedure

Materials and Methods

Between October 2000 and 2001, a prospective fine needle aspiration cytology (FNAC) was done on 60 patients presented with bone lesions. The majority of cases were admitted to the orthopaedic ward in Basrah General Hospital. Most patients had x-ray films showing bone destruction or other changes (periosteal reaction, cystic changes.... etc.).

Fine needles (19-22 gauge) with a length varying from 2.5 to 8.8 cm, attached to a disposable plastic syringes 10 or 20 ml were used. No local anesthesia was required in most of the cases. In some patients especially those with vertebral lesions FNA was performed under general anesthesia before open biopsy. The site and depth of aspiration were determined by carefully studying the anterio-posterior and lateral x-ray films and CT or MRI when necessary. After locating the optimal site for aspiration, the patient turned to the most advantageous position to obtain the shortest possible path of the needle and to prevent damage to the underlying structures. The needle was generally introduced perpendicularly to the cortex of the bone to be aspirated. Lack of resistance was felt when the needle reaches the lesion. Before removing the needle from the lesion the suction was released. If aspirated material was not sufficient, the procedure was repeated once again [17,24].

The content of the needles were smeared on 2-4 glass slides and immediately fixed in 95% ethyl alcohol for 20-30 minutes. The slides were stained with Papanicolaou's stain or haematoxylin and eosin [25]. The lesions were cytologically classified into four groups [23].

1-Benign: If no malignant or atypical

cells were present in the aspirate.
2-Suspicious: Based on presence of few or degenerated atypical cells.
3-Malignant: if the aspirate contained considerable number of malignant cells with statement to the type of malignancy if possible.
4- Unsatisfactory: If the aspirate had very scanty unremarkable cells or contained blood

Open biopsies for histopathological diagnosis were performed on 54 cases.

For statistical analysis all cases with no histological examination and unsatisfactory results were excluded. Cytologically suspicious cases considered as false negative.

Results

FNA was obtained from 60 patients. There were 31 males (51.7%) and 29 females (48.3%) with male to female ratio of 1 07:1.

The age ranged from 6 to 93 years with a mean of 37.2 years. Fig.1 shows the age distribution of patients with various bone lesions. Most of the cases were in the second decade, and 40% of patients were in the second and third decades of life.

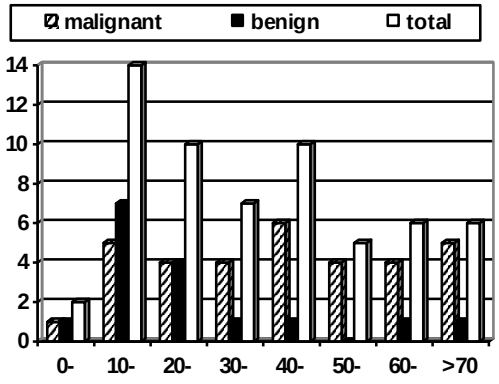

Figure 1. Age distribution of patients with bone lesions

The femur was the most frequently aspirated site contributing to 14 cases (23.4%) followed by the vertebrae 11(18.3%), humerus 8(13.3), sacrum 5(8.3%), pelvis 5(8.3%), scapula 3(5%), ribs 3(5%) and others 11(18.3%) (Table I).

The cytological diagnoses were summarized in Table II. Malignancy were diagnosed in 33 cases (55%); of these 25 (76%) were primary bone tumors and 8 (24%) were metastatic. Benign lesions were diagnosed in 16 cases (26.7%), suspicious in 2 cases (3.3%) and unsatisfactory for diagnosis in 9 cases (15%).

Histological diagnosis was available in 54 cases, 19 were benign and 35 were malignant.. Of 35 malignant lesions the diagnosis was primary in 29 cases and metastatic in 6 cases. In six cases, there was no histological confirmation and the diagnosis was based on cytological, radiological and clinical features.

Table III shows the correlation between cytological and histological bone lesions. Of 16 lesions diagnosed as benign by FNAC, the histological diagnoses were benign in 14 cases and malignant in 2 cases (false negative). The two suspicious results were subsequently proved by histology as malignant. Of 33 cytologically malignant cases, the histological examination was available in 27; of these 25 cases were confirmed as malignant (20 primary malignant cases and 5 metastatic carcinomas); the remaining two were benign (false positive). Open biopsy was done for all 9 patients with unsatisfactory aspirates, which proved to be benign in 3 cases and malignant in 6 cases.

Table IV shows the statistical analysis of bone lesions. Sensitivity and specificity were 86.2% and 87.5% respectively, PPV was 92.6% and NPV was 77.8%. The accuracy of FNAC was 86.7%.

Site	Benign	Suspicious	Malignant	Unsatisfactory	Total No. (%)
Femur	3	1	7	3	14 (23.4)
Vertebrae	3	0	5	3	11 (18.3)
Humerus	1	1	5	1	8 (13.3)
Sacrum	0	0	4	1	5 (8.3)
Pelvis	1	0	4	0	5 (8.3)
Scapula	1	0	2	0	3 (5)
Rib	1	0	2	0	3 (5)
Tibia	1	0	1	0	2 (3.4)
Others	5	0	3	1	9 (15)
Total	16	2	33	9	60 (100)

Hip joint (2), Fibula (1), Radius (1), Skull (1), Calvicle (1), Phalanx (1), Matatrasal (1) and Jaw.

Table I. Distribution of 60 bone lesions according to the anatomical site

Cytological diagnosis	Patients		Age range (years)	Mean age (years)
	No.	%		
Benign	16	26.7	7-80	25.6
Suspicious	2	3.3	18-60	39
Malignant	33	55	6-93	43
unsatisfactory	9	15	17-50	35.9
Total	60	100	6-93	37.2

Table II. The range and mean of FNAC diagnosis in 60 bone lesions.

Cytological diagnosis	Total No.	No. biopsied	Histological diagnosis	
			Benign	Malignant
Benign	16	16	14	2
Suspicious	2	2	0	2
Malignant	33	27	2	25
unsatisfactory	9	9	3	6
Total	60	54	19	35

Table III. Correlation between the results of FNAC and histological examination of bone lesions.

FNAC diagnosis	60
Histological diagnosis	54
Satisfactory FNAC and histology	45
True positive (TP)	25
True negative (TN)	14
False positive (FP)	2
False negative (FN)*	4
Sensitivity	86.2%
Specificity	87.5%
Positive predictive value (PPV)	92.6%
Negative predictive value (NPV)	77.8%
Accuracy	86.7%

**Suspicious results considered as false negative in two*

Table (4): Statistical analysis of bone lesions (cytological vs. histological diagnosis)

Authors	Patients No.	No. of false positive	No. of false negative	Sensitivity (%)	Specificity (%)	Accuracy (%)
Layfield et al.[27]	29	0	0	100	100	100
Humphrey et al [35]	217	1	19	88	99.5	-
Kreicbergs et al [12]	300	1	8	94	99	95
Bommer et al.[20]	427	1	10	95.7	99.3	97.1
Saifuddin et al.[13]	144	1	10	92.9	66.7	92.4
Wedin et al.[11]	110	0	8	-	-	93
Present study	60	2	2	86.2	87.5	86.7

Table V. FNAC results in literature compared to the present study (Bone lesions)

Discussion

Since the initial description of the needle aspiration technique in 1930[17] several series describing needle aspiration of bone lesions have been published. The acceptance and development of bone FNA have been hampered by difficulty in obtaining adequate samples as seen in most series[13,19,20,23]. However, the reported 10-33% range of insufficient aspirates by Feldman[24] and Stormby[19] compares favorably with 9-33% published for open biopsy and for cutting needle biopsy [10,15,28].

The current study shows that the rate of inadequate sampling was 15%, which is similar to those reported by Bommer[21] and Ottolenghi[4] (14.4% and 16% respectively). Tumors that yield scant cellularity due to fibrotic nature, marked osteoblastic component, or cellular dilution by blood are frequently viewed as pitfall[28] or attributed to faulty technique[13]. Additionally, some patients are poor candidates for aspiration cytology since some lesions are either surrounded by intact cortical bone or the neoplasm itself is sparsely cellular[29]. Needle diameter as isolated variable does not seem to explain the differences in adequacy of diagnostic material, while greater experience and repeated aspiration when necessary might reduce the rate of failure and/or mistakes [29,31].

In this study, the benign lesions were less frequent than the malignant tumors in a ratio of 16 to 33. Of 33 malignant aspirates 25 (75.8%) were primary bone malignancies and 8 (24.2%) were metastatic carcinomas. Similar results were noted by Kumar et al.[32] where primary bone tumors constitute (77%) of aspirates. In other series, James and Frable[33] reported (18) benign and (79) malignant aspirates including (20) primary malignant and (59) metastatic tumors.

Several reported studies show a false positive rate of 0-0.3% [13,24,33], however in this study false positive results were found in 2 cases (3.7%) which were diagnosed histologically as healing fracture in one case and osteoblastoma in the other. Regarding the first one, the smears were moderately cellular with a single and loosely arranged oval to spindle cells, pleomorphic and hyperchromatic nuclei. In the second case, the predominant cells were single with plasmacytoid appearance (oval with eccentric nucleus) which misdiagnosed as plasmacytoma.

False negative diagnosis was noticed in 2 cases (3.7%), which was nearly equal to a rate of (3%) reported by Kreicberg[12] however, it was much lower than other series[34] (18%). In the present study the false negative diagnosis were seen in 2 cases of lymphoma. It has been reported that the diagnosis of lymphoma was difficult to establish even by CNB[18].

In many instances metastasis appear before the site of primary tumor is known; especially in the vertebrae and on many occasions these metastases had

both clinically and radiologically the appearance of a primary malignant tumor[6]. In this study a metastasis of follicular carcinoma of the thyroid were initially diagnosed by FNAC before the site of origin was suspected. Therefore FNAC may be used not only to give a correct diagnosis but also to detect the origin of the tumor.

Comparison of the cytological studies with the histopathology in 54 cases showed an accuracy rate of 86 7% other studies reported a range of 92-100% [11-13,21,27,36]. The sensitivity and specificity were 86.2% and 87.5% respectively. Higher rates reported by Layfield[27] where both sensitivity and specificity were 100% (Table V).

Therefore, FNAC proved to be an easy, sensitive and specific procedure. Its relative high accuracy and lack of complications may make it a good initial diagnostic method for skeletal lesions of unknown origin. However, specific diagnosis and regarding are often difficult to make and therefore it must never be regarded as a substitute for histhopathological diagnosis.

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