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Assessment of Appropriateness of Diagnostic Lymph Node Tissue Collection from the Operating Theater and by Interventional Radiologist. A Clinical Audit

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Abstract

Background: Appropriate sample requesting, collecting and timely dispatch to the appropriate laboratory is essential in establishing diagnosis of pathologies with lesions. Much time and effort may be wasted if this is not done according to certain standards. We conducted this study to assess the route of lymph node samples from requests to reaching the laboratories. **Methods:** We conducted an audit over a period from 4th June until 10th Aug 2023. Data for all the procedures performed over this period on lymph node samples (was entered into and analysed using Excel. **Results:** A total of eighteen samples for sixteen patients were obtained during this period. Median age of the patients was 34 years (19 - 73) with a M:F ratio of 5:11. Among the IR samples, nine samples were from the neck, three from inguinal area and one from axilla. Seven samples (53.8%) were tru-cut biopsies, six samples (46.15%) were FNA. All samples were sent to the pathology laboratory fixed in formalin. Samples for TB were sent only for five cases (31.25%) and for only two cases (12.5%) were samples sent for bacterial culture. For the OR samples, none were sent for either bacterial culture or TB. Overall, eight patients (50%) were not investigated for any infectious etiologies like brucella, toxoplasmosis, CMV, EBV plus other possible causes. Repeat sampling was required for 25% of patients (within and out of the audit period). **Conclusions:** to avoid delays in making diagnoses, it is paramount to consider infectious etiologies as possible diagnosis for lymphadenopathy and request appropriate investigations. This requires liaising with infectious diseases/clinical microbiology experts to guide regarding types of samples, types of media and timely dispatch

to the correct laboratory.

Keywords

Clinical Audit, Clinical Samples, Biopsies, Lymph Nodes, Saline, Formalin, Quality Improvement

1. Introduction

The work of infectious diseases experts relies heavily on the cultures of samples. [1] Lymphadenopathy has a long list of differential diagnosis including infections, malignancy and autoimmune diseases. [2] Therefore, thinking of infectious etiology as a possible cause of a pathology and sending appropriate samples in the correct medium in a timely manner is crucial. Not infrequently we in the infectious diseases (ID) team get referrals for management of results of lymph node (LN) fine needle aspiration (FNA) or biopsies especially when the report mentions necrotising granuloma. For many of such LN, only formalin fixed samples had been sent and no samples in saline had been sent to the microbiology laboratory for culture or for tuberculosis specifically. Here, we present the results of the first round of an audit we conducted at Sultan Qaboos University Hospital from 4th of June until 10th of August to assess the fate of LN samples obtained from the IR and OR.

2. Material and Methods

This is an audit conducted at Sultan Qaboos University Hospital over a period from 4th June to 10th August 2023. We obtained a list of the procedures performed in the OR and in the IR from our institute by allocating two members of staff (nursing and radiology technicians). The samples had been requested by various teams in the departments of medicine and surgery.

We used Excel to enter the data and analyze it. Inclusion criteria: all samples collected from operating room (OR) and interventional radiology room (IR) for LN of any area (cervical, axillary, inguinal) of adult patients (age > 12 years) or any neck mass of unknown tissue origin. Exclusion criteria: patients younger than 12 years.

Relevant information was obtained from the electronic medical records of the patients following approval of ethical committee under number *MREC#3280.*

3. Results

From 4th June to 10th August 2023 we found a total of eighteen procedures done on sixteen patients on lymph nodes from various sites or neck masses if tissue origin of mass was not identified. Thirteen samples were sent from IR and three from OR. Median age of the patients was 34 years (19 - 73) with a M: F ratio of 5:11. Among the IR samples, nine samples were from the neck, three from inguinal and one from the axillary area. Seven samples (53.8 %) were tru-cut biopsies and six

samples were FNA (46.15%). Of the seven tru-cut biopsies, one was done two days after excisional biopsy of another LN and was done three months after previous FNA and excisional biopsy. For only three patients, samples were also sent for tuberculosis (TB) and only two samples were sent for other bacterial infections. Four of these biopsies were lymphomas (three of whom had a previous history of lymphoma), one was multiple myeloma (MM) in a known case of MM and one showed caseating epithelioid granuloma that was negative for TB and the lymphadenopathy resolved spontaneously. Regarding the six FNA samples, for only one case were samples sent to the microbiology laboratory for bacteria and TB. One sample was followed by a tru-cut biopsy five months later and one was followed by excisional biopsy two months later due to inadequate sample. Results of the samples were inadequate for one sample, reactive for two samples, suppurative granuloma for one sample that resolved on azithromycin and unidentified tissue for one sample without established diagnosis as the patient failed to follow up. One patient had undergone FNA and excisional biopsy three months before our period of study that were sent only for histology and not for microbiology. As his lymphadenopathy persisted, a second biopsy was repeated during our study period and this time samples were sent for TB in saline but diagnosis was not established. An additional excisional biopsy had to be sent two months after our study that came positive for TB. From the OR, five excisional biopsies were carried out all of which were sent to the pathology laboratory in formalin and none to the microbiology laboratory for TB or other organisms. Two of them proved to be of malignant origin in patients with previous thyroid malignancy and one sample remained of unknown tissue origin.

Overall samples for TB were sent only for five cases (31.25%) and for other bacterial infections only for 2 cases (12.5%). Repeat sampling was required for four cases (25%). See Table 1.

Table 1. Lymph node/cervical mass samples sent form IR and OR during the period from 4th June until 10th August 2023. It shows the poverty of requests made for the microbiology laboratory for bacteria culture or for TB. LN; lymph node, Bx; biopsy, HL: Hodgkin's lymphoma, DLBCL: diffuse large B cell lymphoma, MM; multiple myeloma.

Age/Gen	Tissue	Background	Bx pathology	Microbiology sample	TB/NTM sample	Other tests	Outcome
73/M	inguinal LN	B cell Lymphoma	14/6: tru-cut: low grade B cell lymphoma	no	TB PCR and culture negative	No	Started treatment for lymphoma
19/M	inguinal LN	HL	2/8/23: tru-cut: reactive + large atypical cells. EBV and scattered CMV positive	no	no	EBV, CMV.	Started on treatment for lymphoma
33/F	Cervical LN	thyroid nodule	20/6/23: FNA reactive,	no	no	no	Reactive LN
28/F	cervical LN	Family history of thyroid ca	8/8/23: FNA	no	n	no	Reactive. LN regression. f/u US planned after 6/52 but pt defaulted

Continued

52/F	Cervical LN.	MM	6/6/23: tru-cut: MM	Few pus cells, no pathogens	AFB and culture: negative	HIV	On treatment for MM
30/F	Inguinal LN	eczema	Tru-cut	n	n	EBV, CMV, adenovirus: negative, IGRA: negative	On treatment cutaneous large cell lymphoma
30/F	cervical LN	post parotidectomy	18/6/23: excisional; OR carcinoma 18/7/23: FNA: reactive LN, no malignancy	n	n	no	acinic cell parotid ca. Referred for treatment
56/M	cervical LN	DM, HTN	24/7/23: FNA: inadequate sample 26/9/23: excision Bx: reactive, no granuloma, no necrosis no malignancy	no	n	EBV, CMV: negative	Inadequate sample
25/F	Cervical LN	Nil known	13/6/23: excision: necrotising granuloma OR 15/6/23: tru-cut caseating epithelioid granulomatous inflammation 18/9: excision Bx: necrotising granuloma	n	TB negative on 15/6	no	resolution of the LN,
26/F	Cervical mass	Nil known	FNA: suppurative granuloma	Pus cells but no pathogens	AFB, PCR and culture: negative	brucella, done	Resolved after azithromycin
46/F	cervical LN or parotid tissue	Grave's disease	FNA: LN or parotid? cystic squamous	no	no	no	Patient defaulted
65/M	axillary LN	DLBCL	24/7/2023: tru-cut: lymphoma	no	no	CMV, EBV negative	Started on treatment for lymphoma
28/M	Cervical LN	Nil known	14/3: FNA : necrotising granuloma 29/3: excisional Bx: necrotising granuloma 5/6/23: tru-cut 24/10:exc: necrotising granuloma, no malignancy	no	5/6/: TB AFB and culture negative Oct: TB positive	n	TB on treatment
35/F	cervical LN	Thyroid ca with metastasis	Metastatic papillary CA	no	no	none	referred to cancer center
39/F	cervical LN	Thyroid ca	Malignant nodule, residual papillary Ca	no	no	none	Referred to cancer center
37/F		Papillary thyroid ca, Behcet's disease	no identifiable LN tissue	no	no	none	No other action

4. Discussion

Awareness of infectious etiologies as being a possible cause of any tissue lesion is of paramount importance as it then guides to the correct requesting, sample collecting and timely dispatching to the correct destination. We have come across patients referred to our team for management of patients with histological results mentioning necrotising granulomas from fixed LN biopsies with or without caseation. No samples had been sent for such patients in saline to the microbiology laboratory for bacterial culture or TB specifically. As there is a long list of differential diagnoses for necrotising granulomas including infectious aetiologies such as TB or non-tuberculous mycobacteria (NTM) and non-infectious aetiologies like sarcoidosis which is reported to account for 1.7% of all head and neck LN [3] [4] [5] [6] Such pathologies should be considered in the differential diagnosis by parent teams and appropriate samples should be requested with the use of appropriate media. Unestablished diagnosis has also been reported for necrotising granuloma as found in our audit. [7] Sending samples fixed in formalin to the pathology laboratory only is by no means adequate as even if acid fast bacilli (AFB) are seen in the formalin-fixed biopsies, culture of the AFB is still mandatory for both differentiation between TB and NTM and for sensitivity testing. This is also true if TB PCR is positive as sensitivity testing is still required. In the past, we had also faced the problem of samples being sent to the microbiology laboratory but in formalin rather than saline. In our small audit, we show a number of cases of lymphadenopathy that were due to lymphoma. No samples had been sent for bacterial culture and for TB testing (PCR/culture) from such cases. Most of these cases were in patients with a previous history of lymphomas and the samples were most probably obtained looking for relapse. However, more than one pathology could co-exist such as TB and Lymphoma, hence seeing malignant cells alone may not suffice to make a final diagnosis. [8] Moreover, difficulty in distinguishing lymphoma from TB on histology alone has also been reported. [9] In some cases where samples had not been sent for microbiology processing, multiple sampling had to be done due to unidentified diagnosis and eventually TB was found to be the diagnosis. Samples sent in saline are valuable in establishing the diagnosis by doing tests like 16S rRNA should bacterial cultures come back negative. Repetition of sampling causes much loss of resources and efforts and leads to delays in diagnosis. It also causes inconvenience to the patient in addition to leading to miss trust towards the clinicians that itself might lead to health care shopping by the patient and further delays in diagnosis. [10] In Oman, the incidence of lymphoma (HL + NHL) was reported to be 5/100 000. [11] On the other hand, TB incidence is 400 new cases/year with a prevalence of 9.3/100 000 in 2022 [12]. Incidence of TB adenitis is not mentioned specifically in the national TB manual 2022 but it is estimated to be 0.3 - 0.6/100 000. [13] Comparing these results to our audit finding suggests that there might be an underestimation of our audit results due to the low rates

of LN sampling for TB.

In this small audit, it is not possible to study the impact of age on the diagnostic outcome as can be seen from two female patients ages 28, 33 years having reactive LN while another female patient aged 30 year old had a diagnosis of acinic cell parotid carcinoma.

This audit indicates that there is a lack of a standard algorithm regarding investigations for lymphadenopathy. When our ID team is consulted for lymphadenopathy, after a thorough history taking which includes demographics of the patient and physical examination, we advise for a number of tests that include serology for brucellosis, EBV, CMV, HIV and other infections that could be compatible with the case presentation. Regarding sampling we ask for samples to be sent to the microbiology laboratory in saline in a plain sterile container for bacterial culture, TB and also a sample for 16s rRNA in case culture results come negative. We advise the sampling to be done while the patient is off any antibiotics for at least 48 hours to increase the yield of the culture. We also suggest tests for non-infectious causes like SLE.

Following completion of the data, we discussed our findings with a surgical team and provided recommendations regarding the handling of the samples which included advice on the numbers and types of samples required, the medium that should be used in the container and the timely dispatch to the appropriate laboratory. We learned that the surgical specialists focus more on their skill of surgery and complications that might arise rather than on the differential diagnosis of lesions. This was evident from the number of samples not sent to the microbiology laboratory and from 50 % of cases that had no other blood tests like serology of various possible infections. We explained that this gap could easily be closed by making a routine request for microbiology with samples sent in saline and by involving the ID team or the clinical microbiologist in the care of the patient. Moreover, we elaborated on the point of collecting samples out of microbiology laboratory hours for processing samples to store them in them at 4°C for dispatch the next morning. We also provided a protocol of investigating lymphadenopathy to the surgeons and the radiology department to refer to.

5. Conclusion

This small audit clearly demonstrates the need for different medical disciplines to work in concert rather than individually to better serve the patients. Planning a protocol for investigating lymphadenopathy is a clear example as is shown by this audit.

Limitations

Our sample size is small, however, it does show the need for improvement of our services regarding investigations and management of cases presenting with lymphadenopathy.

Funding

Not required.

Conflict of Interest

None.

Protocol for LN Sample Collection and Dispatch

Samples should be obtained while patient is off any antimicrobials to increase the chance of any culprit growth.

Samples should be divided into two parts:

1. For microbiology laboratory: Send samples in sterile saline in a sterile plain tube.

2. for pathology laboratory: Send samples in formalin in a sterile plain tube.

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