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Efficacy of Mediastinoscopy in Patients With Isolated Mediastinal Lymphadenopathy

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ABSTRACT

Background: Since its introduction in 1959 by Carlens (1), Mediastinoscopy has been, for long, used for assessment of the mediastinum (superior and middle) for establishing a histological diagnosis of mediastinal masses of undefined cause, and for Lung carcinomas staging. The use of Mediastinoscopy has been decreasing lately due to the introduction of other less invasive techniques (e.g., endoscopic ultrasound-directed fine needle aspiration cytology), however, it is still a cheap and effective tool that can be utilized in underprivileged centers. **Objective:** To emphasize how does Mediastinoscopy plays an important role in confirming the clinical diagnosis of isolated mediastinal lymphadenopathy and reviewing its utility. **Methods:** These are a retrospective analysis of medical charts for patients who underwent diagnostic cervical mediastinoscopy during (2012 – 2018) at a University hospital in Saudi Arabia. The included patients are presented with an isolated mediastinal lymph node enlargement, in the absence of underlying cause and was found to be significant (>1cm in its short axis) by computed tomography. The patient who had a known cause (e.g., Sarcoidosis) or were diagnosed via other tools, was excluded. **Results:** Mediastinoscopy was performed on 56 patients, 38 of them were males (68%) and 18 females (32%), with a mean age of (37.5 ± 10 years). The patients' most common presenting symptoms were persistent cough (49%), fever of unknown origin (38%) and weight loss (36%) with an average of 2 symptoms per patient, while in 4 patients (7%) lymphadenopathy was discovered incidentally during the CT scan for other reasons. In addition, the histopathological examination of specimens obtained confirmed the most common diagnoses, Sarcoidosis in 17 patients (30%), lymphoma in 12 patients (21%) and TB in 10 patients (18%). The mean hospital stay (calculated from the day of the procedure) was (2.5 ± 4 days) including work up, with only one mortality (2%) and 3 patients (5%) had experienced post-operative complications. **Conclusion:** The diagnostic Mediastinoscopy is both safe and efficient in the diagnosis of patients with isolated mediastinal lymphadenopathy, requiring a minimal surgical setup and is considered cost-effective. Therefore, it is a valid choice of investigating such cases in other underprivileged centers, as it reaches a tissue-based diagnosis, while other techniques are used for staging purposes.

Keywords: Biopsy, Isolated, Lymph node, Mediastinoscope, Mediastinal.

1. BACKGROUND

Isolated mediastinal lymphadenopathy (IMA) is mediastinal adenopathy which is not associated with any disease elsewhere in the body, increasingly found on Computed tomography (CT) chest that is performed for different indications (e.g., Lung mass). Clinicians are faced with difficult clinical decisions regarding the investigation to be done for a patient with non-specific symptoms (e.g., cough, low-grade fever) (2). In the 1950s, the Mediastinoscopy (MDS) was introduced by Carlen and since then it has long been held a position of "splendid isolation" in terms of diagnostic ability in approaching diagnosis in patients with undiagnosed mediastinal lymphadenopathy and in staging lung cancer (3). Neither CT nor Positron emission tomography (PET) scan, is sensitive or specific enough in detecting nodal pathology, a normal CT may have metastatic disease in 13% of patients (4,5,6). The radiological images provide limited information about the pathology of a given lesion and this makes it an adjunct rather than a diagnostic tool. Nonetheless, there are minimally invasive cytologic techniques (e.g., endoscopic ultrasound-directed fine needle aspiration cytology) that require an increased

number of staff with special training and working hours to stage conditions (e.g., lung carcinoma), not to diagnose it which deems the techniques to be cost ineffective in comparison to MDS. The mediastinal exploration through a MDS can provide a definitive histopathologic diagnosis as it permits full survey of the mediastinal lymph nodes (LN), palpation of the lesion and taking biopsies (7). The precise histopathologic diagnosis obtained by MDS is the key for applying definitive management in patients with IMA, aiding in the diagnosis and early management of life-threatening conditions (i.e., diagnosing Lymphoma and preventing the mismanagement of patients with Sarcoidosis). Therefore, this study discusses the presenting symptoms, diagnostic processes' utility and complications of IMA patients, in the eastern province of Saudi Arabia.

2. OBJECTIVE

The aim of the study was to emphasize how does Mediastinoscopy plays an important role in confirming the clinical diagnosis of isolated mediastinal lymphadenopathy and reviewing its utility.

3. PATIENTS AND METHODS

This is a retrospective study that included 56 patients who underwent diagnostic cervical MDS during a period of 7 years (2012 to 2018) at a University hospital in Dammam, Saudi Arabia. The inclusion criteria were patients with isolated mediastinal lymphadenopathy which was found significant on CT scan (>1cm in its short axis is indicating a significant enlargement) with one or more station of LN involved. On the other hand, patients with known bronchogenic carcinoma or any other associated parenchymal lung lesion, patients with previous history of MDS or mediastinotomy, were excluded. The included patients had extensive pre-procedural investigations including laboratory tests (e.g., complete blood count, prothrombin time), chest x- rays, CT scans of the chest, sputum stains and cultures for acid fast bacilli (AFB). Moreover, the procedure was done according to standard techniques described by Kirshner (8) through a 2cm incision in the suprasternal notch dissecting the pretracheal fascia, the advancement of the mediastinoscope was helped by finger dissection proceeding gently in both pretracheal and paratracheal planes. The visualized LN's intended for biopsy were aspirated fist, through a long needle to prevent inadvertent vascular injury, then taken encapsulated as much as possible, otherwise multiple punch biopsies from various sites were obtained. The specimens were sent for histopathological examination, gram stain, AFB stain and cultures. In addition, data relating to indications, histopathology result, operative complications, and length of hospital stay were collected and statistically analyzed. The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 27. The descriptive statistics were in the form of frequency and percentages representing the categorical variables (e.g., gender, presenting complaint), while the mean and standard deviation were computed for the numerical variables (e.g., age).

4. RESULTS

A total of 56 patients, 38 (68%) were males and 18 (32%) females with an age range (17-58 years) and a mean of (37.5 years). Among the patients, 52 had symptoms on admission and 4 were asymptomatic where LN's enlargement was incidentally discovered during routine radiological examination. The most common symptoms were persistent cough (n=27; 49%), fever of unknown origin (n=21; 38%), weight loss (n=20; 36%), dyspnea (n= 16; 28%), chest pain (n=10; 17%) and easy fatigability (n=11; 19%), the average symptoms for each patient were 2 symptoms (Table 1).

The lower paratracheal LN were the most presenting enlarged group in CT and in MDS, as they were enlarged in (55%), followed by the subcarinal group in (36%), then the upper paratracheal in (30%) and lastly the preoartic group in (19%). Consequently, the histopathological examination of specimens confirmed the diagnosis of Sarcoidosis in 17 patients (30%), lymphoma in 12 patients (21%), TB in 10 patients (18%), thymoma in 2 patients (4%), nonspecific lymphadenitis (reactive enlargement) in 8 patients (14%), metastatic carcinoma in 4 patients (7%) and only 1 patient (2%) for germ cell tumor, schwannoma and Kikuchi's disease (Table 2). The

Variable		N	%
Age (mean ± SD) Years		37.5 ±10.2	
Gender	Male	38	(68%)
	Female	18	(32%)
Chief complaint:			
	Persistent cough	(%49)	27
	Fever	(%38)	21
	Weight loss	20	(36%)
	SOB	16	(28%)
	Easy fatigue	11	(19%)
	Chest pain	10	(17%)
	Incidental	4	(7%)
LN involved;			
	Lower Paratracheal	31	(55%)
	Subcarinal	20	(36%)
	Upper Paratracheal	17	(30%)
	Preaortic	11	(19%)

Table 1: Preoperative patient characteristics

Pathological diagnosis	N	%	Male	Female	Presenting symptom
Sarcoidosis	17	(30%)	8	9	chest pain, cough
Lymphoma	12	(21%)	9	3	Weight loss, cough
Tuberculosis	10	(18%)	8	2	Fever, cough
Thymoma	2	(4%)	2	-	Weight loss, fatigue
Non-specific (reactive)	8	(14%)	6	2	Cough, SOB
Metastatic	4	(7%)	3	1	Weight loss, SOB
Germ cell tumor	1	(2%)	1	-	Weight loss, fever
Schwannoma	1	(2%)	1	-	Chest pain, cough
Kikuchi disease	1	(2%)	-	1	Fatigue, Fever

Table 2: Post-operative histopathological diagnosis

AFB stain for TB was positive in only two patients in whom diagnosis was confirmed histopathologically as none of the cultures were positive.

Sarcoidosis was common in patients presenting with chest pain (6 out of 10 were diagnosed) and was associated with paratracheal lymphadenopathy (10 out of 31 found) while in TB, patients were presenting with fever, cough and was associated with paratracheal and subcarinal LN groups. the Lymphomas were associated with weight loss and the preaortic lymph node enlargement (7 out 11 cases of preaortic group were lymphomas). Nonetheless, 20 diagnoses of malignancy (36%), and 36 (64%) of benign pathology. The incidence of benign pathology was higher in females than in males as out of 18 females, 14 (78%) had benign pathology and 4(22%) had malignant conditions, while out of 38 males, 16 (42%) had malignancy and 22(58%) had benign conditions with most of preaortic LN enlargement was due to malignant pathology (9 out of 11; 81%) (Table 2).

The mean hospital stay (calculated from the day of the procedure) was (2.5 ± 4 days) including work up, with 3 patients (5%) developing post-operative complications, in one had an immediate post-procedural pneumothorax on the right side which was mild and treated conservatively. The second patient developed hoarseness of voice with recurrent laryngeal nerve palsy and he was recovered after six weeks. The third patient had deep wound infection with sinus formation, this patient was diagnosed as TB by histopathology and the sinus was closed after 4 month of anti-TB therapy. Lastly, we had one case of mortality after 10 days of the procedure, it was attributed to massive pulmonary embolism in a 56-year-old patient who was diagnosed with non-Hodgkin's lymphoma.

5. DISCUSSION

Cervical MDS is performed under general anaesthesia and is safe enough to be done as an outpatient procedure. For many years it was the gold standard for invasive staging of patients with potentially operable lung cancer (9). The use of video assisted mediastinoscopy (VAM) was introduced in 1995 and had led to improved visualization of the surgical field and teaching for both the surgeon and the trainee who can share the magnified picture on the video-screen (10). An accurate histopathological diagnosis is the key to plan the further management and this creates a strong indication for MDS in cases where there is IMA. As a minimally invasive procedure, MDS should not be taken lightly, as lethal complications were documented in literature (i.e., intra-operative hemorrhage, post-operative wound infection, pneumothorax and recurrent laryngeal nerve injury are frequent complications, while tracheal and esophageal injuries were reported as rare complications) and the benefits obtained from a precise histological diagnosis should be weighed against the risk of this technique (7,11,12).

Recently, there cytologic studies that are the endoscopic ultrasound-directed fine needle aspiration cytology (EUS-FNAC), endobronchial ultrasound directed FNAC (EBUS-FNAC), and CT guided FNAC which are alternative effective, less invasive methodology for obtaining tissue biopsy and may replace MDS (13). Although the CT-guided FNAC is a more commonly available tool, it is not so popular because of the risk of injuring a major vascular structure in the mediastinum. However, the histopathological results of the obtained tissue biopsy are more sensitive and gives less false negative results, than the cytology smears obtained through FNA even with core biopsy, as its role is prominent in cases of bronchogenic carcinoma (14,15,16). The EUS-FNAC is a minimally invasive procedure for the diagnostic approach to mediastinal lymphadenopathy that is safe, effective and when used in combination with EBUS-FNAC its diagnostic utility approaches that of cervical MDS (17).

The cost-effectiveness of any used technique to sample the IMA is dependent upon the increased prevalence of the disease, the severity, the resources available to the center and the price of the devices used. The utility of MDS was found to be cost ineffective in cases of stage 1 non-small cell carcinomas, in which the cost per gained life-year was 250,989$ with an increase in the survival rate by 0.008 years (24,25). In addition, EBUS-FNAC, solely, is a less invasive technique with a lower mean cost by a 2,211$ difference (i.e., the mean cost derived, of the MDS vs EBUS-FNAC was 9,023$ vs 6,816$, respectively), yet the installation of the EBUS-FNAC device is more expensive (26). Although the least costly technique is an EBUS- transbronchial needle aspiration (TBNA), there is a group of cases that will require an added diagnostic technique (e.g., the performance of MDS, after EBUS-TBNA in selected patients) (27,28). These studies and protocols are developed to identify patients in developed countries, hence, requiring other cost-effectiveness studies in underdeveloped countries to appreciate the economic burden and the obstacles to reach life-threatening diagnoses (e.g., the utility of these techniques to rule out lung cancer-related lymphadenopathy in regions of high TB incidence) (29,30). he most common presenting diagnoses of IMA in our study were Sarcoidosis and lymphoma (51% of the cases) which are tissue-based diagnoses and not cytology-based, deeming the FNAC techniques devalued, diagnostically.

Similarly, the results of Reich (11), Nuria (18) and Leavitt (19), on our commonest results of histological examination of mediastinal lymphadenopathy was Sarcoidosis (30%). The etiology of mediastinal lymphadenopathy may differ significantly with different places and populations, other research has defined Lymphoma as the most common pathological cause (20). This variation could be due to the used inclusion criteria or an actual incidence variation in various ethnicities and although the proportion of each diagnosis differ according to various factors (e.g., age, drugs used, comorbidities), this fact does not prevent need for a precise histologic diagnosis in all cases. The mean period of hospital stay calculated in our hospital was (2.5 days), calculated from the day of the procedure to avoid over estimation, and

this coincide with the results of McManus (2), Reich (11) Rodreguez (21).

Regarding the safety of MDS, we experienced three cases of post-operative complications, none of them were life threatening and were self- limited. There was an encountered case of mortality (2%) that was not related to the procedure itself, in which the patient had massive pulmonary embolism at the 10th day, post-operatively. Lemaire and colleagues (7), in a review of series of 2145 patients who underwent MDS recorded 1.07% of patients who had complications in the form of hemorrhage, pneumothorax, tracheal injury, and vocal cord dysfunction and one case of mortality from pulmonary hemorrhage. In comparison, the published mortality and morbidity of Hammoud (12), Rodrigues (21), Porte (22), and Hajjar (23), were comparable to our results. The relatively low incidence of complications in our study is likely due to the safety, effectiveness of the procedure itself and the specificity of the center where it was done. There are limitations in this study, with a relatively low number of cases, being a retrospective study, thus making recording of the clinical picture and clinical diagnosis affected by each individual physician's opinion, approach and that is why we didn't include the provisional clinical diagnosis of the physicians.

6. CONCLUSION

The cervical MDS is a time-tested minimally invasive procedure that can reach a precise histopathological diagnosis and is still useful, regardless of recent advances. Its safety, high sensitivity and specificity increases its utility in patients with IMA. Therefore, in an underprivileged center that has a case presenting with nonspecific respiratory symptoms and radiological evidence of IMA, MDS is still a valid choice as various conditions (e.g., Sarcoidosis) are a biopsy-based diagnoses, rather than cytology-based which makes MDS cost-effective in the diagnostic process.

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