Diagnostic Accuracy of Multi-Detector Computed Tomography in the Evaluation of Mediastinal Masses- A Prospective Observational Study

Radiology Section

MANGALANANDAN SREENIVASAN¹, MEERA K VIJAYAN², GEENA BENJAMIN³

(CC) BY-NC-ND

ABSTRACT

Introduction: The introduction of Multi-Detector Computed Tomography (MDCT) has revolutionised clinical practice. Mediastinal lesions represent challenging problems faced by the radiologist and often a chest radiograph is inadequate for answering the queries of clinicians. MDCT is employed to diagnose various causes of mediastinal widening and often correct diagnosis is obtained using CT alone, thus obviating invasive diagnostic procedures.

Aim: To assess the diagnostic accuracy of MDCT in mediastinal mass lesions compared to histopathology.

Materials and Methods: A prospective observational study comprised of 52 patients who underwent MDCT examination for evaluation of mediastinal masses. All these patients subsequently

underwent histopathological examination either by CT-guided biopsy, transthoracic needle aspiration, endoscopic biopsy or by surgical resection. Sensitivity, specificity and accuracy of each type of lesion was calculated and tabulated.

Results: The study population comprised of 52 patients out of whom 43 cases (83%) were predicted correctly by CT when compared with histopathology diagnosis. The sensitivity of detecting malignancy was 100% and specificity was 92.6%. The present study had accuracy of 96.2% in differentiating malignant mediastinal masses from benign lesions.

Conclusion: MDCT is useful in evaluating the distribution of mediastinal masses and their relationship to adjacent structures and differentiating between malignant mediastinal masses from benign lesions.

INTRODUCTION

Multi-detector computed tomography helps to diagnose various mediastinal pathologies and often correct diagnosis is obtained using CT alone, obviating invasive diagnostic procedures. ITMIG definition of mediastinal compartments is suitable for cross-sectional imaging which consists of a three-compartment model of the mediastinum including prevascular (anterior), visceral (middle), and para-vertebral (posterior) compartments [1]. The presence of fat, cystic components, calcifications and precise location within the mediastinal compartments helps to narrow down the differential diagnoses of mediastinal masses [2]. In the anterior mediastinum, cystic lesions are diagnosed by their characteristic location [3]. Germ cell tumour usually has fat attenuation. A purely fat lesion is more likely fat pad or morgagni hernia or rarely thymolipoma [4].

Most middle mediastinal masses are lymphadenopathy, duplication cysts, vascular lesions, or oesophageal masses. The hypervascular lymph nodes can be seen in melanoma, castleman's disease, kaposi sarcoma, thyroid and renal cell carcinoma metastases [5]. Most posterior mediastinal masses are neurogenic in origin. Fat containing lesion in the posterior mediastinum may be- extramedullary haematopoiesis [5]. The long scan range, high spatial resolution, thinner collimation, short scan time and less movement artefacts are the advantages of MDCT. Multiplanar reformations with high resolution are reconstructed from the data volume [6].

Mostofthestudiespublishedinliterature demonstrated the effectiveness of CT in characterisation and localisation of mediastinal masses and showed that middle and posterior mediastinal masses constituted nearly 50% of primary mediastinal masses [5,7-9]. Mesenchymal neoplasms account for about 55% of mediastinal tumours and the radiological pattern of these masses are quite characteristic [10-13]. With this background, the present study was conducted with an aim

Keywords: Biopsy, Histopathology, Mediastinal mass

to assess the diagnostic accuracy and validity of MDCT findings in mediastinal mass lesions compared to histopathology.

MATERIALS AND METHODS

A prospective observational study was conducted in a tertiary care hospital from November 2018 to September 2019. The study was approved from the Institutional Ethics Committee (PIMSRC/ EI/388A/51/2018) and written informed consent was obtained from the participants.

Inclusion criteria: All patients above 18 years of age, of either sex referred to the department as mediastinal mass to be investigated by MDCT were included.

Exclusion criteria: Patients with previous history of treatment for mediastinal masses, abnormal renal function test, contrast sensitivity and patients refusing consent to participate in the study were excluded.

Sampling method used was non-probability sampling and consecutive patients were included. Sample size was calculated as 52 cases of mediastinal masses. This was obtained using level of confidence as 95%, diagnostic accuracy (P) from previous study by Pulasani K et al., and 10% of absolute precision(d) [14].

Formula used: $n=Z^{2}_{1-\alpha/2} P(1-P) d2$

GE OPTIMA CT660 128 slice MDCT was used. Axial sections were taken from the level of thoracic inlet to the level of suprarenal glands, with sagittal and coronal reconstructions. The pre-contrast study was followed by multiphase postcontrast study. The scans were reviewed on a direct display console at multiple window settings like mediastinal window, lung window and bone window. The pre and post-contrast attenuation values, location of mass, mass effect or invasion of adjoining structures were studied. Each case suspected of mediastinal mass lesion was subjected to histopathological examination by CT-guided biopsy, transthoracic needle aspiration, endoscopic biopsy or following surgical resection.

STATISTICAL ANALYSIS

The data was analysed and the diagnostic accuracy, sensitivity, specificity and predictive values were calculated. The characteristics of patients are described as frequency and percentage for categorical variables and mean and standard deviation for continuous variables. The software used for statistical analysis with version is IBM Statistical Package for the Social Sciences (SPSS) version 20.0 for windows.

RESULTS

Majority of patients belonged to 51-70 years age group, that is 20 patients (38.5%). About 8 (15.4%) of patients were below 30 years of age [Table/Fig-1]. The study population comprised of 30 males (57.7%) and 22 females (42.3%).

Age group (Years)	Count (n)	Percent			
≤30	8	15.4			
31-50	10	19.2			
51-70	20	38.5			
71-90	14	26.9			
Mean±SD	55.5±20.5				
[Table/Fig-1]: Percentage distribution of the patients according to age. SD: Standard deviation					

Dyspnea was the most prevalent clinical symptom. Around 13 (25%) had dyspnea as presenting complaint, followed by 9 (17.3%) had neck swelling and 8 (15.4%) had chest discomfort. Presence of neck nodes were seen in 2 patients (3.8%) [Table/Fig-2].

Chief complaint	Count	Percent	
Chest discomfort	8	15.4	
Dyspnea	13	25.0	
Chest pain	4	7.7	
Tiredness and weight loss	2	3.8	
Neck swelling	9	17.3	
Cough and dyspnea	4	7.7	
Dysphagia	4	7.7	
Fever and cough	3	5.8	
Neck nodes	2	3.8	
Fever and weight loss	3	5.8	
[Table/Fig-2]: Percentage distribution of the cases according to chief complaint.			

In this sample population of 52 patients, 20 patients had mediastinal widening on chest radiography (38.5%). About 12 patients showed anterior mediastinal mass according to chest radiograph (23.1%). Bilateral hilar prominence was seen in 1 of the patients (1.9%) whereas 8 (15.4%) patients has normal chest radiograph [Table/Fig-3].

Chest radiograph	Count	Percent		
Normal	8	15.4		
Mediastinal widening	20	38.5		
Anterior mediastinal mass	12	23.1		
Right paratracheal opacity	6	11.5		
Superior mediastinal widening	5	9.6		
Bilateral hilar prominence	1	1.9		
[Table/Fig-3]: Percentage distribution of the sample population according to chest radiograph (n=52).				

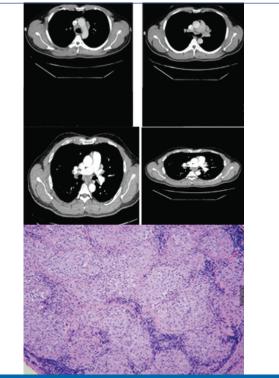
About 71.2% of the cases had their lesion in the prevascular compartment or anterior mediastinum, that is 37 out of 52 patients. 11 were found in the visceral compartment or middle mediastinum (21.1%) and 4 cases were in the paravertebral compartment or posterior mediastinum (7.7%).

Out of 52 cases in this study, only 7 (13.5%) had no involvement of adjacent organs. About 9 cases (17.3%) had abutment of main pulmonary artery, arch of aorta and right pulmonary artery. About 7 (13.5%) patients had caused compression of trachea [Table/Fig-4].

Adjacent organ involvement	Count	Percent			
Absent	7	13.5			
Mass effect on Brachiocephalic vein	1	1.9			
Encases superior vena, pericardial effusion, indents lung	1	1.9			
Encases lower trachea, left pulmonary artery	1	1.9			
Displacement of right CCA, SCA, IJV	1	1.9			
Abutment of trachea and RMB	7	13.5			
Encases arch, AA, loss of fat plane with MPA	1	1.9			
Compresses trachea	7	13.5			
Encases SVC	1	1.9			
Abutment of MPA, Arch of aorta, RPA	9	17.3			
Collapse of right lung with pleural effusion	2	3.8			
Abutment of oesophagus and vertebral bodies	1	1.9			
Erodes xiphisternum	1	1.9			
Abutment of Abuts LA	4	7.7			
Abutment of trachea, MPA, Arch, oesophagus	2	3.8			
Abutment of RA	1	1.9			
Infiltrates lung, pleura with pericardial effusion	1	1.9			
Infiltrates lung with multiple hepatic metastases	1	1.9			
Abutment of vertebral column, heart and right lung	2	3.8			
Abutment of lung with pleural and pericardial effusion	1	1.9			
[Table/Fig-4]: Percentage distribution of the cases according to adjacent organ involvement. CCA: Common carotid artery; SCA: Subclavian artery; IJV: Internal jugular vein; RMB: Right main					

bonchus; AA: Ascending artey, oca, Subukararatey, iov, internarjogua veir, nivib, night main bonchus; AA: Ascending aorta; IMA: Main pulmonary artery; SVC: Superior vena cava; RPA: Right pulmonary artery; LA: Left atrium; RA: Right atrium

In this study, according to diagnosis by CT, 15 patients (28.8%) had lymphoma, 9 patients (17.3%) had multinodular goitre with retrosternal extension. About 5 patients (9.6%) had mediastinal teratoma, 2 patients (3.8%) had sarcoidosis [Table/Fig-5] and 1 patient (1.9%) had nonseminomatous germ cell tumour [Table/Fig-6].

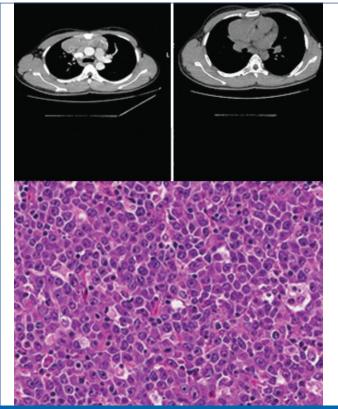


[Table/Fig-5]: A 39-year-old man presented with bilateral diminutive vision. CXR showed bilateral hilar prominence. CECT chest showing right paratracheal, subcarinal and hilar lymphadenopathy. Corresponding histopathology shows non-caseating granuloma of sarcoidosis. Haematoxylin and Eosin stain. Magnification 10X.

Mangalanandan Sreenivasan et al., Diagnostic Accuracy of MDCT in Evaluation of Mediastinal Masses

Computed tomography report	Count	Percent			
Lymphoma	15	28.8			
Thymoma	3	5.8			
Invasive thymoma	2	3.8			
Thymic cyst	1	1.9			
Multinodular goiter with retrosternal extension	9	17.3			
Bronchogenic cyst	2	3.8			
Sarcoidosis	2	3.8			
Malignant neoplasm of oesophagus	3	5.8			
Nonseminomatous germ cell tumour	1	1.9			
Thymic carcinoma	5	9.6			
Thymolipoma	1	1.9			
Oesophageal duplication cyst	1	1.9			
Mediastinal teratoma	5	9.6			
Pericardial cyst	1	1.9			
Neuroblastoma	1	1.9			
[Table/Fig-6]: Percentage distribution of the mediastinal masses according to CT report.					

In this study, CECT shows multiple conglomerate lymph nodes in prevascular, para-tracheal and hilar region; CT diagnosis of lymphoma, [Table/Fig-7]. Colloid nodules with degeneration constituted 17.3% [Table/Fig-8].



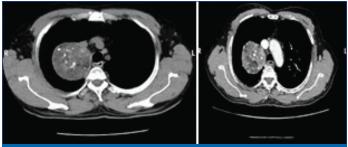
[Table/Fig-7]: A 20-year-old male presented with right supraclavicular lymph node enlargement of one month duration. CECT shows multiple conglomerate lymph nodes in pre-vascular, para-tracheal and hilar region CT diagnosis of lymphoma and CT-guided biopsy revealed large B cell lymphoma. Haematoxylin and Eosin stain. Magnification 40X.

According to this study, lymphoma had accuracy of 91.5%. Thymoma had accuracy of 97.9%. Thymic carcinoma showed accuracy of 95.7% while mediastinal teratoma [Table/Fig-9] had accuracy of 89.4%. Thymic cyst, bronchogenic cyst [Table/Fig-10], goitre with retrosternal extension, thymolipoma, pericardial cyst and oesophageal duplication cyst could be diagnosed with 100 percent accuracy compared to the gold standard test of histopathological examination [Table/Fig-11]. According to this study, predictive power of CT in detecting Malignancy when biopsy is gold standard is almost in perfect agreement with kappa value of 0.92. In this

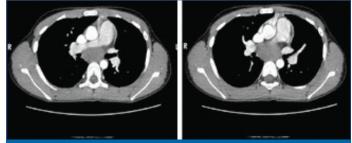
study, sensitivity of detecting malignancy is 100% and specificity is 92.6%. The study had accuracy of 96.2% in differentiating malignant mediastinal masses from benign lesions [Table/Fig-12].

Biopsy report	Count	Percent		
Lymphoma	14	26.9		
Thymoma	2	3.8		
Small round cell tumour	1	1.9		
Thymic cyst	1	1.9		
Colloid nodules with degeneration	9	17.3		
Bronchogenic cyst	2	3.8		
Sarcoidosis	3	5.8		
Malignant oesophageal neoplasm	3	5.8		
Ganglioneuroma	1	1.9		
Thymic carcinoma	4	7.7		
Thymolipoma	1	1.9		
Oesophageal duplication cyst	1	1.9		
Mature cystic teratoma	6	11.5		
Pericardial cyst	1	1.9		
Infiltration by adenocarcinoma	1	1.9		
Plasmacytoma	1	1.9		
Tuberculosis	1	1.9		
[Table/Fig-8]: Percentage distribution of mediastinal masses according to biopsy				

[Table/Fig-8]: Percentage distribution of mediastinal masses according to biopsy report.



[Table/Fig-9]: A 28-year-old man with dyspnea. MDCT reveals anterior mediastinal mass showing fat, soft tissue and calcifications, proved to be mature cystic teratoma on biopsy.



[Table/Fig-10]: A 19-year-old male presented with dyspnea of one month duration. CECT chest showed a well-defined cystic lesion of size 4.8×3.7×3.8 cm in the subcarinal region suggestive of bronchogenic cyst.

DISCUSSION

Mediastinum is a complex anatomical segment in the chest having an intricate anatomy making it prone to various pathologies ranging from benign cysts to aggressive malignancies. MDCT is employed to diagnose various causes of mediastinal widening and often correct diagnosis is obtained using CT alone. It also helps to delineate the extent and nature of lesions and their relation with adjacent organs [12,13]. Odev K et al., concluded MDCT has greater accuracy for detecting mediastinal lesions with better resolution and more consistent contrast enhancement with a single bolus of contrast [12]. Pulasani K et al., concluded that anterior mediastinal masses represent the majority of mediastinal lesions with thymic lesions being the most common [14]. In this study, also 37 cases out of 52 (71%) are in the prevascular region (anterior mediastinum) which is in concordance with the previous study.

Predictive power	Lymphoma	Thymoma	Thymic cyst	Multinodular goiter	Bronchogenic cyst	Sarcoidosis	Malignant neoplasm of oesophagus
Sensitivity	85.7	100.0	100.0	100.0	100.0	66.7	100.0
Specificity	93.9	97.8	100.0	100.0	100.0	100.0	97.2
False Negative	14.3	0.0	0.0	0.0	0.0	33.3	0.0
False positive	6.1	2.2	0.0	0.0	0.0	0.0	2.9
Positive Predictive value	85.7	66.7	100.0	100.0	100.0	100.0	93.4
Negative Predictive value	93.9	100.0	100.0	100.0	100.0	97.8	93.6
Positive Likelihood ratio	14.14	45.00	-	-	-	48.2	44.0
Negative Likelihood ratio	0.15	0.00	0.00	0.00	0.00	0.33	1.00
Accuracy	91.5	97.9	100.0	100.0	100.0	97.9	93.6
[Table/Fig-11a]: Predictive power of CT report and Biopsy report							

Predictive power	Nonseminomatous germ cell tumour	Thymic carcinoma	Thymolipoma	Oesophageal duplication cyst	Mediastinal teratoma	Pericardial cyst
Sensitivity	-	75.0	100.0	100.0	100	100.0
Specificity	97.9	97.7	100.0	100.0	89.4	100.0
False negative	0	25.0	0.0	0.0	0	0.0
False positive	2.1	2.3	0.0	0.0	10.6	0.0
Positive predictive value	0.0	75.0	100.0	100.0	99	100.0
Negative predictive value	100.0	97.7	100.0	100.0	100.0	100.0
Positive likelihood ratio	0	32.25	-	-	9	-
Negative likelihood ratio	1,03	0.26	0.00	0.00	0	0.00
Accuracy	97.9	95.7	100.0	100.0	89.4	100.0

[Table/Fig-11b]: Predictive power of CT report and Biopsy report.

	Biopsy report			
CT report	Malignant	Benign	Total	
Malignant	25	2	27	
Benign	0	25	25	
Total	25	27	52	

[Table/Fig-12a]: Predictive power of CT in detecting Malignancy when Biopsy is Gold standard. Kappa=0.92**; Almost perfect agreement

Predictive power	
Sensitivity	100.0
Specificity	92.6
False negative	0.0
False positive	7.4
Positive predictive value	92.6
Negative predictive value	100.0
Positive likelihood ratio	13.5
Negative likelihood ratio	0.0
Accuracy	96.2
Accuracy	90.2

[Table/Fig-12b]: Predictive power of CT in detecting malignancy when biopsy is gold standard. Kappa (<0: Poor agreement; 0.0-0.2: Slight agreement; 0.2-0.4: Fair agreement; 0.4-0.6: Moderate

Agreement; 0.6-0.8: Substantial agreement; 0.8-1.0: Almost perfect agreement)

The study population comprised of 52 patients. The most common age group to present with mediastinal mass according to this study is 51-70 age group which involves 20 patients. Hattiholi VV et al., concluded that most of the patients with mediastinal mass is in the age group of 61-70 [15]. In this study, 71% of the mediastinal mass are in the prevascular region (anterior mediastinum) which is in concordance with the previous studies of Takeda S et al in Japan [11] and Hattiholi VV et al., in Karnataka, India [15]. According to Pandey S et al., sensitivity of MDCT in detecting malignancy came out to be 94%, specificity is 90% [13], positive predictive value of 94%, negative predictive value of 90% with diagnostic accuracy of 93%. The present study has a sensitivity of 100%, specificity of 92.6% with a positive predictive value 92.6% and negative predictive value100% with diagnostic accuracy of 96.2%. About 92% of accuracy was reported by Pulasani K et al., in their study in 2015 for mediastinal masses studied by MDCT evaluation and histopathological correlation [14]. Accuracy in this study is 96.2%. In their study thymic lesions, constituted 14% of the total, while present study shows 11.5%. In a study by Chen J et al., on 34 patients with CT diagnosis of thymic mass [16], thymic lesions constituted 44.9% and 19% of the mass in the study by Pulasani K et al., was lymph nodes while present study shows 28% of lymph nodes [14].

In this study, there were nine cases (17%) of multinodular goiter presenting as mediastinal lesion. In this study, all the 9 cases were predicted correctly on CT. CT diagnosis of multinodular goiter had 100% sensitivity, 100% specificity and 100% accuracy. In each of the cases, the mediastinal thyroid was in direct continuity with tissue originating from the cervical thyroid. The present study had three cases of oesophageal carcinoma which were diagnosed with 93.6% accuracy. In this study, oesophageal carcinoma, all showed heterogeneous enhancement (100%). Among the 3 cases of oesophageal carcinoma, none showed mediastinal invasion. This is 5.8% of the total patients. According to the study by Pulasani K et al., oesophageal mass is 4% [14]. Percentage of oesophageal mass in the study of Hattiholi VV et al., is 4.4% [15]. The main purpose of CT in patients with oesophageal carcinoma is to stage the disease as accurately as possible, in order to determine which patients may be suitable for surgical resection.

Limitation(s)

The study had limitation of having less number of cases as sample population.

CONCLUSION(S)

MDCT is useful in evaluating the distribution of mediastinal masses and their relationship to adjacent structures and differentiating between malignant mediastinal masses from benign lesions. In this study 43 out of 52 cases (83%) where correctly predicted by MDCT evaluation with histopathological examination as gold standard. Sensitivity of detecting malignancy is 100% and specificity is 92.6%. The present study had accuracy of 96.2% in differentiating malignant mediastinal masses from benign lesions.

REFERENCES

- Carter BW, Benveniste MF, Madam R. ITMIG classification of mediastinal compartments and multidisciplinary approach to mediastinal masses. RadioGraphics. 2017;37:413-36.
- [2] Nasseri F, Eftekhari F. Clinical and radiologic review of the normal and abnormal thymus: Pearls and pitfalls. RadioGraphics. 2010;30(2):413-28.
- [3] Davis RD, Oldham NH, Sabiston DC. Primary cysts and neoplasms of the mediastinum: Recent changes in clinical presentations, methods of diagnosis, management and results. Annals of Thoracic Surgery.1987;44:229-37.
- [4] Tian L, Liu LZ, Cui CY, Zhang WD, Kuang YL. CT findings of primary nonteratomatous germ cell tumours of the mediastinum-A report of 15 cases. Eur J Radiol. 2012;81(5):1057-61. doi: 10.1016/j.ejrad.2011.02.005. Epub 2011 Feb 25. PMID: 21353416.
- [5] Aggarwal B, Aggarwal A, Gothi R, Doda SS, Aggarwal SK. Clinical applications of multi-detector row(multi-slice) CT. Indian J Radiol Imaging. 2002;12:473-82.
- [6] Webb WR. Advances in computed tomography of the thorax. Radiol Clin North Am. 1983;21(4):723-29.
- [7] Sones PJ, Torres WE, Colvin RS. Effectiveness of CT in evaluating intrathoracic masses. AJR Am J Roentgenol. 1982;139:469-75.
- [8] Morgenthaler TI, Brown LR, Colby TV, Harper CM, Coles DT. Thymoma. Mayo Clin Proc. 1993;68:1110-23.

- [9] Strollo DC, Rosado de Christenson ML, Jett JR. Primary mediastinal tumours: Part II, Tumours of the middle and posterior mediastinum. Chest. 1997;112:1344-57.
 [10] Kim JH, Goo JM, Lee HJ, Chung MJ, Jung SI, Lim KY, et al. Cystic tumours
- in the anterior mediastinum-Radiologic pathologic correlation. J Comput Assist Tomogr. 2003;27(5):714-23.
- [11] Takeda S, Miyoshi S, Akashi A, Ohta M, Minami M, Okumura M, et al. Clinical spectrum of primary mediastinal tumours: a comparison of adult and pediatric populations at a single Japanese institution. Journal of Surgical Oncology. 2003;83:24-30.
- [12] Odev K, Arbaş BK, Nayman A, Arıbaş OK, Altınok T, Küçükapan A. Imaging of cystic and cyst-like lesions of the mediastinum with pathologic correlation. J Clin Imaging Sci. 2012;2:33. doi:10.4103/2156-7514.97750.
- [13] Pandey S, Jaipal U, Mannan N, Yadav R. Diagnostic accuracy of multidetector computed tomography scan in mediastinal masses assuming histopathological findings as gold standard. Polish Journal of Radiology. 2018;83:234-42. doi:10.5114/pjr.2018.76709.
- [14] Pulasani K, Narayanaswamy I, Ramprakash HV. Evaluation of mediastinal mass lesions using multi-detector row computed tomography and correlation with histopathological diagnosis. Int J Sci Stud. 2015;3(6):156-63.
- [15] Hattiholi W, Gupta P, Hattiholi J. Role of Multidetector computed tomography in the evaluation of mediastinal mass lesions. International Journal of Anatomy, Radiology and Surgery. 2018;7(4):RO40-45.
- [16] Chen J, Weisbrod GL, Herman SJ. Computed tomography and pathologic correlations of thymic lesion. J Thoracic Imaging. 1988;3:61-65.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Radiology, Pushpagiri Institute of Medical Science, Thiruvalla, Pathanamthitta, Kerala, India.

- 2. Resident, Department of Radiology, Pushpagiri Institute of Medical Science, Thiruvalla, Pathanamthitta, Kerala, India.
- 3. Professor, Department of Radiology, Pushpagiri Institute of Medical Science, Thiruvalla, Pathanamthitta, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Mangalanandan Sreenivasan,

Pushpagiri Institute of Medical Science, Thiruvalla, Pathanamthitta, Kerala, India. E-mail: anand.mangal443@gmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: May 11, 2020
- Manual Googling: Oct 01, 2020
- iThenticate Software: Dec 23, 2020 (12%)

Date of Submission: May 10, 2020 Date of Peer Review: Jun 17, 2020 Date of Acceptance: Oct 01, 2020 Date of Publishing: Jan 01, 2021

ETYMOLOGY: Author Origin