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DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF SCLEROSING PNEUMOCYTOMA, HAMARTOMA, LUNG CANCER AND OTHER SOLID PULMONARY NODULES

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ABSTRACT

Background: Solid pulmonary nodules are frequently encountered in thoracic imaging, and accurate differentiation between benign and malignant lesions remains challenging. Pulmonary sclerosingpneumocytoma (PSP) and pulmonary hamartoma (PH) are benign entities that may mimic lung cancer on computed tomography (CT). **Objective:** To evaluate and compare the clinical and CT imaging characteristics of PSP, PH, and lung cancer, and to identify distinguishing CT features that aid in preoperative diagnosis. **Materials and Methods:** This retrospective study included 93 patients (31 PSP, 31 PH, and 31 lung cancer) treated at Shanghai Pulmonary Hospital between September 2013 and December 2023. All diagnoses were histopathologically confirmed following surgical resection. Demographic data, clinical features, and CT characteristics were analyzed using SPSS version 23. Statistical significance was set at $p< 0.05$. **Results:** PSP predominantly affected middle-aged females (female-to-male ratio 14.5:1) and non-smokers (96.8%). PH showed a near-equal gender distribution, while lung cancer was more common in older males. PSP nodules were typically round or oval with smooth margins and higher median CT attenuation (28.9 HU), whereas PH lesions were more commonly lobulated with lower attenuation values (median 7.58 HU). Lung cancer nodules frequently demonstrated spiculation, irregular margins, and the lowest median CT values (–4.4 HU). Significant differences were observed among the three groups in age, gender, smoking status, nodule morphology, margin characteristics, and CT attenuation ($p< 0.001$). **Conclusion:** CT features—particularly nodule shape, margin, and attenuation—combined with clinical parameters such as age, gender, and smoking history, play a critical role in differentiating PSP, PH, and lung cancer. While imaging findings can guide diagnosis, histopathological examination remains the definitive diagnostic standard.

KEYWORDS: Pulmonary sclerosingpneumocytoma; Pulmonary hamartoma; Lung cancer; Computed tomography; Pulmonary nodules.

INTRODUCTION

Lung canceris the mostoften identified malignancy and the primary cause of cancer-related fatalities worldwide, with its incidence and mortality rates demonstrating a marked increase in recent years. In 2020, Global Cancer Observatory (GLOBOCAN) 2020 reported around 2.2

million new cases of lung cancer, accounting for 11.4% of all cases, and over1.8 million deaths from lung cancer, or 18.0% of all deaths.[1] PSP is a rare benign nodule which was initially thought to arise from vascular endothelial cells but later, identified as a tumor originating from the respiratory epithelium, type-2 pneumocytes. In 2015, the World Health Organization (WHO) classified it as an Adenoma.[2] The severity of symptoms depends on the size of the nodule compressing the underlying parenchyma and bronchial tubes, which manifests as a solitary, clearly defined, round, or oval nodule in a chest x-ray or computed tomography (CT) scan.Though regarded as a benign tumor, somecases have been reported as having metastasis to bone and lymph nodes, and the definite diagnosis of PSP is surgery followed by histopathological examination (HPE) and immunochemistry (IHC).[3] PH is seen in middle-aged adults, especially males between 40 and 60, and they are the most frequently observed benign lung tumors that make up around 6% of the total solitary pulmonary nodules.90% of PH is located peripherally and within parenchyma. Though they can appear in the lungs, skin, heart, chest, and other parts of the body, the lung is the site where they most occasionally occur. Due to their asymptomatic nature, most of the cases are detected incidentally during routine chest X-rays. Many times, PH has no symptoms. Those that are big enough to compress the endobronchial or nearby bronchial-vascular systems are often considered symptomatic. Hemoptysis, chest pain, shortness of breath, and coughing are the most common symptoms. While thoracic CT and chest radiography can help in diagnosis, histological analysis provides the final, definite diagnosis. Up to 50% of hamartomas include intranodular fat, which is recognized as a CT attenuation of-40 to-120 Hounsfield Units (HU). This is regarded as a trustworthy sign of a hamartoma. The main treatment modality is surgery. They seldom go through harmful transformations and have a tendency to develop slowly over a period. As a result, the choice of resection or follow-up and the surgical procedure's timing are crucial.[4]

Lung nodules are frequently discovered incidentally during routine scans or examinations for other medical conditions in clinical imaging. While the majority of these nodules are benign, it is necessary to accurately differentiate between benign and malignant lesions for appropriate therapeutic management.PSP and PH are benign lung growths seen inside these nodules. Differentiating between them can be challenging, especially when utilizing imaging methods. Found on imaging investigations, lung nodules provide a diagnostic difficulty in clinical practice because of their many causes and potential for becoming cancerous.

OBJECTIVE

1. To present a 10-year experience with PSP, PH and lung cancer from a specialized institution focusing on lung disorders. It emphasized the challenges in differential diagnosis that could result in errors, offering valuable insights into the field of pulmonarylesion diagnosis and management.
2. To identify and record the distinguishing CT characteristics between solid PSP, PH, and lung cancer.
3. To evaluate the clinical significance of the detected CT characteristics in the preoperative assessment of lung nodules.
4. To examine how these observations might improve the precision of radiological diagnosis and guide treatment approaches.

MATERIALS AND METHODS

PSP, PH and lung cancer patients, treated at the Shanghai Pulmonary Hospital, School of Medicine, were the key subjects of this study. Retrospective data between September 12, 2013 and December 30, 2023 were collected for this study, includes including all data from history to medical records. The Ethics Committee at Shanghai Pulmonary Hospital, which is affiliated with Tongji University School of Medicine, gave its permission to this research project. With surgical resection and histology, a confirmatory diagnosis of PSP, PH and lung cancer was established in each patient. The total number of patients who participated in this study was 93, 31 with PSP, 31 with PH and 31 with lung cancer.

Inclusion Criteria

I. Presence of asolid pulmonary nodule and lung cancer.
II. Histological confirmation: Requires the acquisition of a verified histological diagnosis through biopsyor surgical resection.
III. The presence of high-quality CT imaging is required.
IV. Patient demographics and clinical information: Inclusion criteria encompass instances that possess accessible demographic data (age, gender) and pertinent clinical information,such as symptoms and smoking history.
V. Presence of comprehensive data.

Exclusion Criteria

I. Non-solid or sub solid nodules.
II. Exclusion of caseswithout HPE confirmation.
III. Exclusion of cases with Inadequate CT imaging quality.
IV. Exclusion of cases with unclear diagnosis.
V. Lacking Data: Exclusion pertains to instances where data is lacking, such as missing CT features, clinical information, or histological confirmation.
VI. Exclusion of cases with insufficient follow-up data (if applicable).

The PSP, PH and lung cancer CT images were retrieved and analyzed via the Picture Archiving and Communication System (PACS). The demographic, clinical, and CT characteristics between them were investigated. Only 93 (PSP =31, PH=31, lung cancer=31) patients were eligible for our investigation.

All collected data wastabulated in Microsoft Excel 2007 and analyzed with IBM Statistical Package for Social Sciences (SPSS) version 23 software (SPSS Inc., Chicago, IL). The study data sample characteristics were assessed using descriptive statistics parameters, which include mean, median, ranges, standard deviations, and percentages. Graphical and tabular presentations were also constructed. The link between two categorical variables was described via cross-tabulation. The Fisher Exact test, Chi-square test, Mann Whitney u test, Kruskal Wallis test, ANOVA test and Independent t-test were used to compute the P-value, and a value of less than 0.05 indicated a significant difference.

RESULT

The mean age in PSP was observed at 53.5 ± 9.5 S. D. (range: 29-67), with the 50– 69 agegroup mainlyaffected (70.96%). However, inPH it was 52.3 ± 11.4 S. D (range: 28– 68). Most PH was aged 40– 69 years (87.08%). Based on the sample data, there was no statistically significant age difference between them, with a p-value of .657. For gender, PSP had a 14.5:1 female-to-male ratio [f: 29(93.5%), m: 6.5%)], whereas PH had a 1.21:1 ratio (f: 17(54.8%), m: 14(45.2%)]. The test shows a strong correlation between gender and pulmonary lesion type ($p < 0.001$). In PSP, only 1 (3.2%) smoker, with 30(96.8%) non-smokers. 9 (29%) of PH patients smoked, whereas 22 (71%) donot. Smoking status and pulmonary lesion type are significantly associated, with a p-value of 0.006. PSP had more non-smokers (96.8%) than PH (71.0%). Bothgroups were asymptomatic: PSP (77.4%) and PH(74.2%), and most patients were discovered accidentally during the physical examination. The p-value between themis 0.052. 31 PSP cases, of which 17 (54.83%) were peripherally and 14 (45.16%) were centrally located. In PH, 19(61.30%) were peripherally and 12 (38.70%) were centrally located. The mean nodule diameter for PSP was 14.4 mm±4.6S. D(range: 7– 27 mm), and for PH, it had 13.0± 4.0 S. D (range: 7– 23.6 mm). In PSP, 4(12.9%) of nodules were between 1– 9 mm, 23(74.19%) of nodules at 10– 19 mm and 4(12.9%) of nodules at 20– 29 mm, with the highest majority of nodules (83.87%) lying between 10– 19 mm. In PH, 3 (9.67%) nodules were between 1- 9 mm, 26 (83.87%) nodules were between 10-19 mm, and 2 (6.45%) nodules were between 20-29mm. The most significant number of PH nodules was between 10-19 mm. The p-value between the nodule sizes is 0.196. In terms of nodule distribution, In PSP, 16 were located in the right lung [RUL (=1)(3.2%),the RML(=7)(22.6%),and theRLL (=8)(25.6%), and15 were located in the left lung [LUL (=5)(16.1%)and LLL (=10) (32.3%). The lower lobe is affected mainly in both lobes, n=18(58.1%). Whereas in PH, 16 were located in the right lung [RUL (=8)(25.8%),RML(=2) (19.4%)] and RLL (=6) (32.3%)]. 15 nodules in the left lung, [LUL (=5)(16.1%), and LLL (=10 (32.3%)]. The p-value of 0.019 suggests a significant association between nodule location and the type of pulmonary lesion. Regarding PSP morphological CT features, 12 (38.7%) had oval with smooth edges, 10(32.3%) had a round with an explicit edge, 7 (22.6%) had lobulated, and 2(6.5%) had irregular shapes. In PH, nodules were mostly lobulated 21 (67.7%), followed by 7 (22.6%) round with a clear margin, 2 (6.5%) ovals with a smooth border (6.5%), and 1 (3.2%) irregular shape. P-value 0.001 showed a significant association between nodule shape and pulmonary lesion type in PSP and PH. Between the PSP and PH, calcification were was seen in only 3 out of 31 cases and is absent in PH. Calcification, especially punctate, is seen in 3 PSP. The p-value obtained was.238. The CT values of both PSP and PHwere variable in both conditions. In PSP, the observed CT value (Hounsfield units) ranges from 6.34 to 87.96 H. U, with a median CT value of 28.9 and anInterquartile range(IQR) (Q1, Q3) of 20.8, 40.4. The IQR range between them is 19.6. Meanwhile, in PH, the CT value ranges from-15.11 to 41.7 HU, with amedianCTvalueof 7.58,and theIQR (Q1,Q3) is 0.87, 23.6. We conducted another comparison between PSP, PH, and malignant lung nodules, The Fisher exact test was used to compare the differences. The average age of individuals with PSP was were 53.5 years (S.D = 9.5), while those with PH was 52.3 years (S.D = 11.4). The average age of individuals with lung cancer is 62.9 years (SD = 8.2). There were substantial variations in age between both groups ($p < 0.001$). However, individuals with PSP and PH were similar ages. Gender distribution: In the case of PSP, 93.5% of the cases were female, while in the case of PH, 54.8% were female. In contrast, 58.1% of lung cancer cases were male. These differences were statistically significant ($p< 0.001$). PSP were was predominantly found in females, while PH had a more equal distribution between genders. On the other hand, lung cancer is more prevalent in males. There were significant variations in smoking rates between the groups ($p=0.025$). Among the participants with PSP, 96.8% were non-smokers, while among those with PH, 71.0% were non-smokers. In the case of lung cancer, 80.6% of the participants were non-smokers. CT Scans: There was a notable difference ($p =0.002$) in the use of PSP and PH for physical evaluation, with a higher proportion of lung cancer cases being detected through the physical examinations. Symptoms: The differences observed were not statistically significant. It is important to do imaging and histology tests. There were significant variations ($p< 0.001$) in nodule shape and margin between PSP, PH, and lung cancer. In lung cancer nodules, irregular shape constituted (6.5%), lobulated (25.8%), oval, clear (16.1%), round clear (3.2%),lobutaed,spiculated (32.3%) and spiculated (16.1%).Nodule Size: There were no statistically significant changesobserved ($p = 0.062$). Nodule Location: There were no statistically significant changes observed ($p = 0.065$).CT Values: There were significant differences observed ($p< 0.001$), with a median of 28.9 for PSP, 7.58 forPH, and-4.4 forlung cancer.

Table 1: Results showing the Demographic characteristicsdifferences in between PSP andPH, mean age,gender andsmokinghistorywere compared.

	PSP(n=31)	PH(n=31)	p-value
Mean Age	53.5±9.5S.D(29-68)	52.3±11.4S.D(28-67)	.657 *
Gender			
Male	2(6.5%)	14 (45.2%)	<0.001 **
Female	29 (93.5%)	17(54.8)	
Smoking History			
Yes	1(3.2%)	9(29%)	0.006 **
No	30(96.8%)	22(71%)	

* Independent t test, ** Chi square test
PSP (Pulmonary sclerosing pneumocytoma), PH (Pulmonary hamartoma)

Table 2: Results showing the CT characteristics between the PSP and PH, Nodule laterality, nodule size, nodule location, nodule shape and margin, calcification and median CT values were compared.

	PSP	PH	p-value
Nodule laterality			
Central	14	12	.797 **
peripheral	17	19	
Mean Nodule size (mm)	14.4± 4.6S.D (Range: 7-27mm)	13± 4.0S.D(Range: 7– 23.6 mm)	.196 *
Nodule location in lungs	1(3.2%)	8(25.8	
RUL	7(22.6	%)	
RML	%)	2(6.5%)	0.019
RLL	8(25.8	6(19.4	***
LUL	%)	%)	
LLL	5(16.1	10(32.3	
	%)	%)	
	10(32.3	5(16.1	
	%)	%)	
Shape and Margin			
Oval, clear	12(38.7	2(6.5%)	
Round, clear	%)	7(22.6	0.001
Lobulated	10(32.3	%)	***
Irregular	%)	21(67.7	
Calcification	7(22.6	%)	.
Median CT value(HU)	%)	1(3.2%)	238 **
	2(6.5%)	No	<0.001
	3	7.58,Q1	****
	28,9,Q1, Q3	,Q3 0.87,23.	
	20.8,40. 4	6	

* Independent t test, ** Chi square test, *** Fisher exact test, **** Mann Whitney U test

Table 3: Results between the 3 nodule types (PSP, PH and lung cancer).

	PSP	PH	Lung cancer	p-value
Age	53.5±9.5	52.3±11.4	62.9±8.2	<0.001 *
Gender	F: 2993.5	17(54.8%)	13(41.9%)	<0.001 **
Smoking	M: 26.5	14(45.2%)	18(58.1%)	
No				
Yes				
	30(96.8%)	22(71.0%)	25(80.6%)	0.025¹
Reason for CT	1(3.2%)	9(29.0%)	6(19.4%)	
Accident				
Physical examination				
Clinical symptoms				
Pre-operative examination	1(3.2%)			0.002¹ *
	22(71.0%)	1(3.2%)	1(3.2%)	
Clinical symptoms	6(19.4%)	29(93.5%)	18(58.1%)	
Cough		1(3.2%)	12(38.7%)	
Chest pain	2(6.5%)	0		1**
Fever				0.319¹ **
Sputum	7(22.6%)	7(22.6%)	8(25.8%)	1***
	0	1(3.2%)	2(6.5%)	0.656¹ *
	1(3.2%)	3(9.7%)	4(12.9%)	
	3(9.7%)	1(3.2%)	6(19.4%)	

ANOVA*, Chi square test **, Fisher exact test***

Table 4: Resultof CT characteristics of PSP, PH and lung cancer patients including nodule size, location, shape, margin, and CT value.

	PSP	PH	Lung cancer	p-value
Nodule size (mm)	14.4±4.6	13.0±4.0	15.4±3.4	0.062*
Nodule location				
RUL	1(3.2%)	8(25.8%)	9(29%)	
RML	7(22.6%)	2(6.5%)	3(9.7%)	0.065**
RLL	8(25.8%)	6(19.4%)	6(19.4%)	
LUL	5(16.1%)	10(32.3%)	7(22.6%)	
LLL	10(32.3%)	5(16.1%)	6(19.4%)	
Shape and margin				
Irregular	2(6.5%)	1(3.2%)	2(6.5%)	
Lobulated	7(22.6%)	21(67.7%)	8(25.8%)	
Oval, circular	12(38.7%)	2(6.5%)	5(16.1%)	<0.001**
Round, circular	10(32.3%	7(22.6%)	1(3.2%)	
Lobulated, spiculated			10(32.3%)	
spiculated			5(16.1%)	
Median CT Value (HU)	28.9, Q1, Q3 20.8 40.4	7.58, Q1, Q3 0.87, 23.6	-4.4,Q1,Q3 -30.7,19.5	<0.001***
Total	31	31	31	

ANOVA, Fisher exact test**, Kruskal Wallis test****

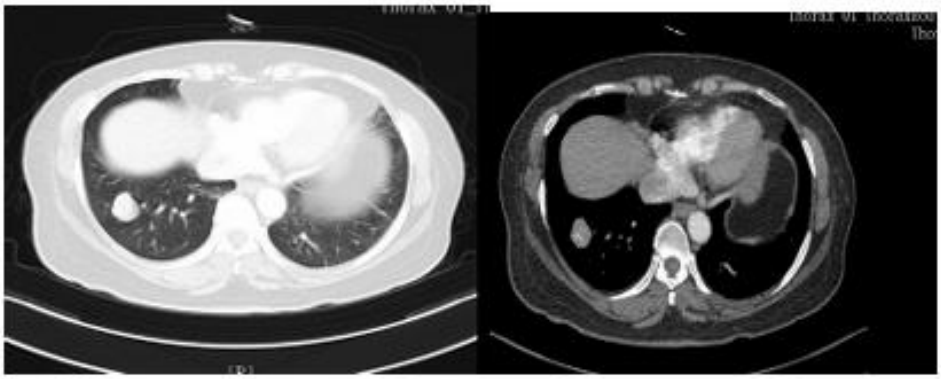

Fig.1: The above figure showsthe axial and mediastinal CT viewof 58 years oldfemale showing 27 mmlarge, lobulated PSP nodules inright lower lobe, with punctate calcification.

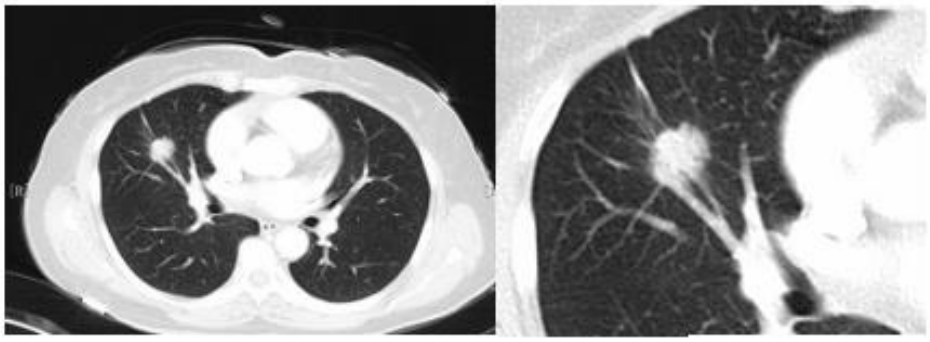

Fig.2: 63 years oldfemale axial CTwithenlarge view had history of fever showing a soft tissue density nodule with a diameter of 2 cminmiddle lobe of right lobe,with rough edge, lobulations and spiculations.The density of lesion is uneven.

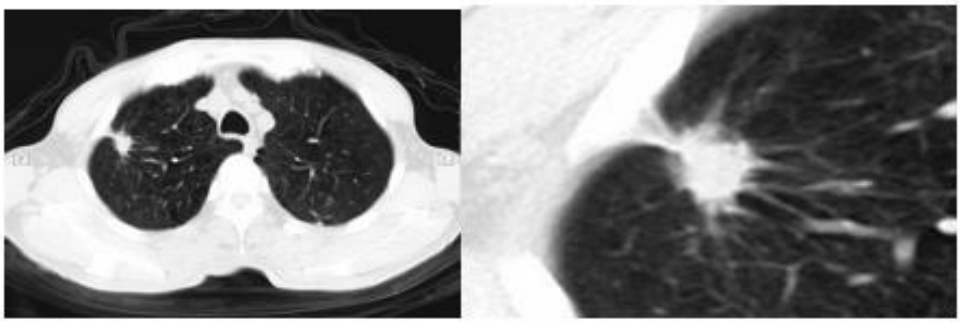

Fig. 3: 70 years old male axial and enlarge CT showing over inflation like changes in both lungs field. A nodular shadow with a diameter of about 1.4 cm, with rough edges and spiculated and lobulated margin can be seenin the upperlobe of rightlung.

DISCUSSION

In our study the mean age for PSP was 53.5 years, patients' age ranged (29-68), and the most affected gender was female (93.5%). With a female-to-male ratio of 14.5:1, this high ratio disparity indicates that PSP tends to appear more commonly in the female population. Our result was consistent with previous research. The incidence of smokers and nonsmokers with confirmed PSP varied in other papers that are currently accessible. However, none of the studies identified smoking as a risk factor or its influence on neoplasm development. In this study, 30 patients (96.8%) in PSP did not have any history of smoking habits. Only 1 (3.2%) had a history of smoking. Another study found (62.5%) patients were nonsmokers.[5] This study showed there were a more significant number of cases among nonsmokers; this proved there was no direct association between smoking habits and the appearance of PSP lesions. In PSP, mostpatients did not have anyclinical symptoms, and most caseswere discovered during the routine chest x-ray as a soft tissue mass[6], only a few patients suffer from clinical symptoms.InourStudy, PSP showed the distinct morphological features on unenhanced C.T. scans, appearing as a round or oval

shape, smooth border, and calcification in 30% of cases, 71% were oval and round shapes with soft and clear margins, 10 were round shapes with clear margins (32.3%), 22.6% were lobulated shapes, and 6.5% were irregular shapes (6.5%). Though solid nodules don't have any internal characteristics, on three PSP cases (9.67%) presented punctual calcification on the internal surface. These morphologic characteristics were distinctive enough to distinguish malignant nodules from PSP, as the former had a lobulated border, spiculated, and occasionally calcified.[7] In our study, 29% patient with a history of smoking, and 71% without a history of smoking. Although the association between the smoking developments of lung hamartoma had not been fully explained in previous research, a previous study showed that 52.4% of patients had a history of smoking and 47.6%had nohistory.[8] Calcification, particularly popcorn-like, high-fat content (up to 50%), moderate development, peripheral location, and absence of invasion indicate hamartoma on thoracic C.T scan.[9] Approximately 10-30% exhibit calcification, and 50% exhibit fat, which is pathognomonic.[10] In our study, 67.7% with lobulated shapes, (22.6%) round shapes, (6.5%) oval shapes with clearmargins, and 3.25 % irregularmargins. A Chi-square test performed to see if there is a significant relationship between smoking status and the kind of lung lesion. The p-value is 0.006. The findings indicate a notable correlation between smoking status and the probability of developing either PSP or P.H. The noted correlation suggeststhat smoking status may influence the development or manifestation of various lung diseases. The statistical significance is influenced by the more significant proportion of nonsmokers in the PSP group (96.8%) compared to the PH group (71.0%). The average ages of PSP and PH patients were similar, while lung cancer patients were older and had a higher degree of age variability. In the study conducted by JS Brown et al,563 cases of lung cancer diagnosed,240(43%)were aged over 75 years.[11] The mean age was 71 years(range 31-95),However our results was little less in overall comparison to PSP and PH but it' s almost near to other study conducted. This observation highlights the significance of taking into account age differences while making decisions and developing treatment plans for lung nodules. The groups had distinct smoking patterns, since the majority of PSP and PH patientswere non-smokers, whereas a significant proportion of lung cancer patients had a smoking history. This highlights the significance of smoking as a contributing factor to the development of lung cancer and emphasizes the necessity for personalized treatments that are dependent on an individual's smoking habits.

The nodules exhibited considerable variations in their morphological characteristics between the different groups, displaying clearly distinguishable forms and borders. These findings offer useful information in interpreting imaging results and differentiating between various forms of lung nodules. Thepresence of lobulated, spiculated and Irregular margin indicates the malignancy of nodules though lobulated shape were also found in PH.The presence of spiculated,lobulated and Irregular shapes were proved by the previous study. In the study by conducted by Miayamata et al, malignant lung nodule were characterized by lobulations and spiculations,this showed our result consistent with the previousstudy.[12] In comparison to both PH and lung cancer, the PSP typically has higher median CT values and a broader range of CT values, indicating the denser tissue characteristics. The PH exhibits median CT values that are in the middle range and a modestrange of CT values. Lung cancerhas the lowestmedianCTvalues and smaller IQR suggesting the presence of less dense lesion characteristic of malignancies. CT values exhibit substantial variation among PH, PSP, and lung cancer. This highlights the usefulness of CT readings in differentiating between various formsof lung nodules and informing clinical decision-making.

To summarize, this study offers detailed understanding of the clinical features of PSP, PH and lung cancer nodules. It emphasizes the significance of taking in to account factors such as age, gender, smoking status, imaging characteristics, and CT values when making a differential diagnosis and planning treatment. In this study between the comparisons of three nodule types, prominent change in nodule shape and margin and CT value noted in contrast to PSP and PH, Making the diagnosis easier. Additional study using bigger sample sizes and long-term follow-up is necessary to confirm these findings and improve diagnostic and therapeutic approaches for patients with lung nodule.

CONCLUSION

A comparative study of two nodules revealed their differences. Gender, smoking history, nodule form, and CT value varied significantly, having a high female-to-male ratio of 14.5:1 and PH has an equal gender distribution. The PSP group is mostly non-smokers, suggesting a link. The distribution of lung nodules shows that PSP prefers the lower lobe and PH the higher, which is noteworthy. Morphological CT characteristics show that nodule morphology and margin distinguish PSP from PH. PSP nodules are oval or round with smooth margins, while PH nodules are lobulated. A strong association exists between nodule form and illness type. The considerable variation in CT results shows that lesions of the two categories have different density characteristics (measured in Hounsfield units). Though some differences were observed between the two benign tumors in our study, they are not specific to the confirmatory diagnosis. The definite diagnosis is surgery, followed by histopathology diagnosis. In another study comparison between the PSP, PH, and malignant lung nodules. This study highlights the key differences and similarities among PSP, PH, and lung cancer nodules. Age, gender, smoking history, and CT features all play crucial roles in differential diagnosis and treatment planning. CT value, nodule shape, margin, and nodule morphology are the most important and striking

features to diagnose the malignant nodule in the early stages, and understanding these factors can improve clinical decision-making and patient outcomes.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical Approval

The Ethics Committee at Shanghai Pulmonary Hospital, which is affiliated with Tongji University School of Medicine, gave its permission to this research project.

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None available

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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N/A

Provenance and peer review

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