Value of Ultrasonography in the Diagnosis of Pleural Effusion: Analysis of 582 Cases

Ning Wang
Xi'an People's Hospital (Xi'an No.4 Hospital)
Zishuang Liu
Beijing Rehabilitation Hospital, Capital Medical University
Ting Wang
Xi'an People's Hospital (Xi'an No.4 Hospital)
Yang Bai
Xi'an People's Hospital (Xi'an No.4 Hospital)
Man Wang (wang_man1888@163.com)
Xi'an People's Hospital (Xi'an No.4 Hospital)

Research Article

Keywords: Ultrasound, exudate, transudate, separation, echo.

Posted Date: July 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-690170/v1

Abstract

Background: By comparing the different ultrasonographic manifestations in exudate and transudate, we intend to explore the value of ultrasound in auxiliary diagnosis of pleural effusion.

Methods: The ultrasonic image features, including echo, separation, light spot, pleural thickness, of 275 exudative pleural effusion (EPE) cases and 307 transudate pleural effusion (TPE) cases confirmed by laboratory examination were retrospectively analyzed.

Results: In 275 cases of EPE, the main primary diseases were pneumonia and tuberculous exudative pleurisy, the majority was unilateral (214 cases, 77.8%). Ultrasound showed 47.6% cases had septum, 58.5% cases had echo and those pleural thickness more than 3mm cases accounted for 39.6%. By contrast, in 307 patients with TPE, the major diseases were heart failure, cirrhosis and nephrotic syndrome. Most of the pleural effusions were bilateral, accounting for 97.1%. Ultrasound displayed echo in 3 cases (1.0%), separation in 8 cases (2.6%), light spot in 9 cases (2.9%), and pleural thickening (> 3mm) in 6 cases (2.0%). These positive findings in TPE were statistically less than its counterpart ($P < 0.05$).

Conclusion: Ultrasound is valuable for auxiliary diagnosis of pleural effusion. Some sonographic features of pleural effusion, like echo, septum and pleural thickening, may indicate a high possibility of EPE.

Introduction

The pleural cavity is a potential space between the lung and the chest wall, which is closed by the visceral pleura covering the lung surface and the parietal pleura covering the ribs, diaphragm and mediastinum [1]. There is a thin layer of liquid on the surface of the pleural cavity in normal people, about 5-15ml, which plays a lubricating role in the process of respiratory movement [2]. The shape and pressure of pleural cavity have great changes in each breathing cycle, so that the liquid in the pleural cavity is continuously filtered out and absorbed, and is in dynamic balance [3]. Pleural effusion can be caused by excessive or slow absorption of pleural fluid for any reason.

According to its pathogenesis, pleural effusion can be divided into two categories: exudate and transudates. The former is mostly caused by diseases that cause increased pleural permeability, such as pleural inflammation (pulmonary tuberculosis, pneumonia), rheumatic diseases (systemic lupus erythematosus (SLE), rheumatoid arthritis (RA)) [4–5]. The latter is mainly caused by diseases that increase the hydrostatic pressure or decrease the osmotic pressure of colloid in the pleural capillaries, such as congestive heart failure, liver cirrhosis, nephrotic syndrome, hypoproteinemia, etc [6–7]. The clinical diagnosis mainly depends on the biochemical examination of pleural effusion obtained by pleural puncture. The differences between transudates and exudates are mostly based on specific gravity (1.018 as the boundary), protein (30g/L as the boundary) and white blood cell ($500*10^6$/L as the boundary). Transudate is less than the above standard and exudate is greater than the above standard [8–9]. However, the above diagnosis method is invasive, which may cause complications such as intrathoracic infection and pneumothorax. The acceptance rate of patients is low, and it cannot be carried out in the elderly patients who are generally in poor condition and bedridden [10].

Ultrasound has the characteristics of high sensitivity and accurate localization. Because of its non-invasive, simple and easy to be accepted by patients, it has been widely used in the localization and quantification of pleural effusion [11]. The purpose of this study is to evaluate the value of ultrasound in the diagnosis of pleural effusion by

comparing the imaging characteristics of different pleural effusion (with or without separation, echo intensity, pleural thickening or not).

Materials And Methods

Subjects

Two groups of patients were inpatients in our hospital from January 2016 to October 2020. 275 patients with exudative pleural effusion were included in the experimental group, and 307 patients with pleural effusion were included in the control group. The ultrasonic imaging characteristics of patients before treatment were retrospectively analyzed. All the Patients in two groups were treated with thoracentesis after ultrasound examination. The postoperative pleural effusion was determined by routine biochemical test, and the qualitative standard was Light standard. If one of the following criteria was met, it could be diagnosed as exudate: pleural effusion/serum protein ratio>0.5, pleural effusion/serum lactate dehydrogenase (LDH) ratio > 0.6, pleural effusion LDH level was higher than 2/3 of the high limit of serum normal value. General information, including age, gender, smoking history, was collected from inpatient medical records. All procedures performed in studies involving human participant were in accordance with the ethical standards of the institutional research committee and Informed consent was obtained from the participant included in the study. Written consent to publish the clinical or possible personal information was obtained from the participant included in the study.

Ultrasonic instrument

Mindray M9 ultrasonoscope with convex array and linear array probes was used, and the probe frequency was 3.5MHz.

Ultrasonography

The patient was seated with his back facing the examinee, his or her upper body lying on the back of the chair, with hands holding his head to move the scapula upward and widen the intercostal space. The ultrasonic probe explored the 7th rib to 8th rib of the posterior axillary line, and made a cross-sectional observation. If the anechoic dark area was observed, the probe would make an oblique sectional observation one by one along the intercostals from the upper edge of the area, to determine the range of effusion, internal echo, whether there was separation and whether there was any echo. After the measurement on one side, the same method was used to measure the thoracic cavity on the other side. After the measurement, the puncture fluid was aspirated under ultrasound positioning, and the pleural effusion was sent for routine biochemical examination.

Statistical Analysis

Excel was used to record the data and SPSS 22.0 was used to analyze the data. The measurement data were expressed as mean ± standard deviation, and the comparison was performed by t-test. The count data were expressed as cases and percentage (%), and the comparison was performed by chi square test. $P < 0.05$ was regarded as statistical difference.

Results

The general information of experimental group and control group is listed in Table 1. There were 152 males and 123 females in the experimental group, with the age range of 17–83 years. 148 males and 159 females were studied as

controls, their age ranged from 19 to 84 years. In the experimental group, 214 cases (77.8%) had unilateral effusion and 61 cases (22.2%) had bilateral effusion. On contrary, in controls, unilateral effusion cases were 9, accounting for only 2.9%, and most of the patients had bilateral pleural effusion (298 cases, 97.1%), the difference was statistically significant ($P < 0.05$). In the group of exudative pleural effusion patients, a great majority of cases were initial treatment, accounting for 76.0%, while, in the control group, only 18.9% of the patients were newly treated, with a $P < 0.05$. The main primary diseases in the experimental group were complicated parapneumonic pleural effusion (24.7%), empyema (14.9%), tuberculous exudative pleurisy (31.3%), pleural metastasis/primary malignant tumor (25.1%) and rheumatic disease (4%); the primary diseases in the control group were heart failure (71.0%), liver cirrhosis (16.9%) and nephrotic syndrome (12.0%).

Table 1
Baseline demographic and clinical characteristics

Characteristics	Exudates (n = 275)		Transudates (n = 307)		P value
	No. %		No.	%	
Gender					> 0.05
Male	152	55.3	148	48.2	
Female	123	44.7	159	51.8	
Age (years)					> 0.05
< 60	109	39.6	126	41.0	
≥ 60	166	60.4	181	59.0	
First-time treatment					< 0.05*
Yes	209	76.0	58	18.9	
No	66	24.0	249	81.1	
Location of PE					< 0.05*
Unilateral	214	77.8	9	2.9	
Bilateral	61	22.2	298	97.1	
Primary disease					
CPPE	68	24.7	0	0	
Empyema	41	14.9	0	0	
Tuberculous exudative pleurisy	86	31.3	0	0	
Pleural carcinomatosis	69	25.1	0	0	
Rheumatic diseases	11	4.0	0	0	
Heart failure	0	0	218	71.0	
Cirrhosis	0	0	52	16.9	
Nephrotic syndrome	0	0	37	12.0	
PE = Pleural effusion; CPPE = Complicated parapneumonic effusion.					

As shown in Table 2, compared with the ultrasonic imaging characteristics of the experimental group and the control group, there were differences in the presence or absence of light spots, separation, echo and pleural thickening between the two groups. The experimental group, namely the exudate group, compared with the leakage group, the ratio of positive ultrasonic performances, such as light spots, separation, echo, pleural thickening, was high (Fig. 1), the difference was statistically significant ($P < 0.05$).

Table 2
Characteristics of the ultrasonograph in two groups

Characteristics	Exudates	Transudates	P value
Echo			< 0.05*
No	114	304	
Yes	161	3	
Separation			< 0.05*
No	144	299	
Yes	131	8	
Light spot			< 0.05*
No	135	295	
Weak	109	9	
Strong	31	0	
Pleural thickness			< 0.05*
≤ 3mm	166	301	
>3mm	109	6	

Ultrasound findings of different diseases, including complex parapneumonic pleural effusion (CPPE), empyema, tuberculous exudative pleurisy, pleural metastatic tumor/mesothelioma, are listed in Table 3. It can be seen that in the subpopulations of empyema, the proportion of light spots, separation, echo and pleural thickening was the largest, which were 36/41, 41/41, 34/41 and 30/41 respectively. By comparison, in the subgroup of liver cirrhosis patients with transudate, the proportion of light spot, separation, echo and pleural thickening was the lowest, which were 0/52, 0/52, 0/52 and 0/52 respectively.

Table 3
Ultrasonographic features of different primary diseases in patients with exudates

	No light spot	Weak light spot	Strong light spot	No separation	Separation	No echo	Echo	Pleural thickness (≤ 3mm)	Pleural thickness (> 3mm)
CPPE	5	56	7	27	41	19	49	41	27
Empyema	5	22	14	0	41	7	34	11	30
Tuberculous exudative pleurisy	55	25	6	57	29	46	40	45	41
Pleural carcinomatosis	61	6	2	53	16	39	30	58	11
Rheumatic diseases	10	0	1	7	4	3	8	11	0
Heart failure	218	9	0	224	3	226	1	226	1
Cirrhosis	52	0	0	52	0	52	0	52	0
Nephrotic syndrome	37	0	0	37	4	37	0	37	0

CPPE = Complicated parapneumonic effusion.

Discussion

In our study, 275 cases of exudative pleural effusion and 307 cases of exudative pleural effusion were included. The ultrasonic imaging characteristics of every case were analyzed retrospectively. The results showed that: in 275 cases of exudative pleural effusion, 140 cases had light spots (50.9%), 131 cases had septa (47.6%), 161 cases had low echo (58.5%) The pleural thickening was more than 3 mm in 109 cases (39.6%). There was a difference in the proportion of patients with the above manifestations between the two groups ($P < 0.05$). According to the etiology of exudative pleural effusion, the results showed that compared with other diseases, the proportion of pleural effusion in empyema patients with light spots, separation, low echo and pleural thickening was higher, which were 87.8%, 100%, 82.9% and 73.2% respectively.

Exudative pleural effusion is mostly caused by diseases that increase pleural permeability, such as tuberculosis, pneumonia, rheumatic diseases, pleural metastasis of lung cancer, mesothelioma. The main diseases included in this study include pneumonia, tuberculosis, lung cancer and rheumatic diseases. Parapneumonic pleural effusion is a common complication of community-acquired pneumonia, mainly due to inflammation involving the pleura [12]. According to laboratory examination and clinical characteristics, parapneumonic pleural effusion (PPE) can be divided into uncomplicated parapneumonic pleural effusion (UPPE), CPPE and empyema [13]. The patients included in this study were CPPE and empyema. The former accounted for 62.4% and the latter 37.6%. Compared with UPPE, CPPE had higher protein, LDH and CRP, but lower glucose and PH [14]. The progress of PPE can be divided into three stages: stage I is the exudative stage, with low content of inflammatory cells and good fluidity; stage II is the fibrous purulent stage, with deposition of fibrin and fibrous septum; stage III (tissue organization stage) with fibrous cell proliferation and pleural thickening [15–16]. This study also confirmed the characteristics of CPPE and empyema from the ultrasound images: the probability of light spot, separation, low echo and pleural thickening is high, and

these features are more obvious in empyema. Tuberculous exudative pleurisy is an extrapulmonary disease caused by the entry of Mycobacterium tuberculosis into the pleural cavity [17]. Due to the high reaction of the pleura to the tuberculous toxin, it is easy to form exudate, and the effusion is characterized by high lymph component and high protein content (> 3g/10ml) [18]. Tuberculous pleural effusion has high fluidity in the early stage, but because of its high protein content, the viscosity of pleural effusion increases and tissue adheres with time, then reticular separation will form. After pleural effusion is gradually absorbed, the cell composition increases relatively, which will be shown as strong light spots on ultrasound [19–20]. In an analytical study on the ultrasonic manifestations of 18 patients with tuberculous pleurisy, 100% of the patients with pleural effusion showed separation, and pleural thickening was demonstrated in 6 cases [21]. In our study, 86 cases of tuberculous exudative pleurisy were obtained, 36% of the patients' ultrasound performances showed light spots, and 33.7% of the patients' ultrasound performances showed separation, the ratios were lower than the previous study.

Lung adenocarcinoma is an important cause of pleural effusion [22]. 90% of the patients with cancer included in our experimental group are lung adenocarcinoma, 65.2% of them are primary diagnosis and treatment (45 cases), 34.8% are pleural effusion after chemotherapy (24 cases). Because of the extensive invasion of malignant tumor cells, the pleura adjacent to pleural effusion was damaged in a large area, thus the malignant pleural effusion is rich in plasma protein, inflammatory cells, epithelial cells and tumor cells secreted proteins [23]. Compared with the patients with primary malignant pleural effusion, the malignant pleural effusion in patients receiving treatment will be gradually absorbed with the progress of chemotherapy, and the component of protein will be relatively increased, then separation and wrapping will be formed [24–25]. Ultrasonic images will be reflected accordingly. From our statistical results, 45 patients were initially diagnosed, only 2 cases showed signs of separation, while 66.7% of patients with pleural effusion after chemotherapy showed a separation, compared with the former, there was an upward trend. The pulmonary diseases caused by rheumatism mainly include interstitial lung disease, alveolar disease, pulmonary artery disease, etc. Main rheumatisms that cause pleura disease are SLE and RA [26]. Pleural effusion occurs in about 24% of SLE patients. This be related to lupus pleurisy, the biochemical examination of which shows multi-nuclear cells are dominant in acute stage, while monocytes are the main ones in chronic stage. Pleural effusion absorption can be repeated, and finally left pleural thickening [27].

The incidence rate of pleural effusion caused by RA is as high as 38–73% [28]. Pleural effusion in RA patients has high LDH and protein content, and the content of sugar is obviously reduced. Monocytes and multinucleated cells are the main in pleural effusion. Pleural effusion can be repeatedly produced and encapsulated, forming parcels and adhesion eventually [29]. 11 patients with rheumatic diseases were included in this study, of which 4 cases had separation in the pleural effusion and 8 had echo, which was in line with the characteristics of rheumatic pleural effusion.

Leakage of pleural effusion is mainly caused by body circulation or low colloid osmotic pressure in the pulmonary circulation, retention of water and sodium, obstruction of venous return, pleural membrane itself has no pathological changes [30]. The leakage liquid is mostly clear and transparent liquid, colorless or light yellow, low protein quantity, low cell count and no bacterial infection [31]. With the progress of the disease, the routine and biochemical changes of the leakage liquid will not be obvious. In our study, the ultrasound images of the control group showed that most of the cases had no adhesion, wrapping, light spot, pleural pathological hypertrophy and other characteristics. It should be pointed out that in the control group of heart failure cases, ultrasound showed that 9 patients had weak light spots in pleural effusion, 3 patients had a small amount of separation, 1 patient had low echo, 1 patient had pleural thickening, which may be related to patients with long-term recurrent heart failure, pulmonary congestion, concurrent infection, and a small amount of exudative components in pleural effusion.

In general, through the collection and collation of large sample information, we found that ultrasound has auxiliary diagnostic value in exudative pleural effusion. If there are light spots, separation, pleural thickening and other signs in pleural effusion, pleural effusion is likely to be exudative.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participant were in accordance with the ethical standards of the Xi'an People's hospital (Xi'an No.4 hospital) research committee and Informed consent was obtained from the participant included in the study.

Availability of data and material

The datasets used during the current study are available from the corresponding author on reasonable request.

Authors Contributions

N W wrote the manuscript, ZS L performed the data analysis, T W contributed to the conception of the study, Y B collected the data, M W collected the data and helped perform the analysis with constructive discussions. All authors have read and approved the manuscript.

Consent for publication

Not applicable.

Competing interests

No.

Funding

No.

Acknowledgments

No.

References

1. McGrath EE, Anderson PB. Diagnosis of pleural effusion: a systematic approach. Am J Crit Care. 2011, 20(2):119-127.
2. Ferreiro L, Toubes ME, San José ME, *et al*. Advances in pleural effusion diagnostics. Expert Rev Respir Med. 2020,14(1):51-66.
3. Allama AM, Abou-Elela DH, Ibrahim IM. Pleural and serum markers for diagnosis of malignant pleural effusion. Asian Cardiovasc Thorac Ann. 2020,28(9):560-565.
4. Bielsa S, Acosta C, Pardina M, *et al*. Tuberculous Pleural Effusion: Clinical Characteristics of 320 Patients. Arch Bronconeumol (Engl Ed). 2019,55(1):17-22.

5. Ferreiro L, Porcel JM, Bielsa S, *et al*. Management of pleural infections. Expert Rev Respir Med. 2018,12(6):521-535.
6. Cartin-Ceba R, Krowka MJ. Pulmonary Complications of Portal Hypertension. Clin Liver Dis. 2019 Nov,23(4): 683-711.
7. Ferreiro L, Porcel JM, Valdés L. Diagnosis and Management of Pleural Transudates. Arch Bronconeumol. 2017,53(11): 629-636.
8. Light RW, Macgregor MI, Luchsinger PC, *et al*. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972,77(4): 507-513.
9. Cornes MP, Chadburn AJ, Thomas C, *et al*. The impact of between analytical platform variability on the classification of pleural effusions into exudate or transudate using Light's criteria. J Clin Pathol. 2017,70(7): 607-609.
10. Charach G, Karniel E, Grosskopf I, *et al*. Monitoring Pleural Effusion in Elderly Patients Using Internal Thoracic Impedance. Isr Med Assoc J. 2020, 2(2): 94-99.
11. Hansell L, Milross M, Delaney A, *et al*. Lung ultrasound has greater accuracy than conventional respiratory assessment tools for the diagnosis of pleural effusion, lung consolidation and collapse: a systematic review. J Physiother. 2021,67(1): 41-48.
12. Ferreiro L, San José ME, Valdés L. Management of Parapneumonic Pleural Effusion in Adults. Arch Bronconeumol. 2015,51(12): 637-646.
13. Bueno Fischer G, Teresinha Mocelin H, Feijó Andrade C, *et al*. When should parapneumonic pleural effusions be drained in children? Paediatr Respir Rev. 2018,26: 27-30.
14. Pereira RR, Alvim CG, Andrade CR, Ibiapina CDC. Parapneumonic pleural effusion: early versus late thoracoscopy. J Bras Pneumol. 2017,43(5):344-350.
15. Yang W, Zhang B, Zhang ZM. Infectious pleural effusion status and treatment progress. J Thorac Dis. 2017 Nov,9(11):4690-4699.
16. Freitas S, Fraga JC, Canani F. Thoracoscopy in children with complicated parapneumonic pleural effusion at the fibrinopurulent stage: a multi-institutional study. J Bras Pneumol. 2009,35(7): 660-668.
17. Shaw JA, Irusen EM, Diacon AH, *et al*. Pleural tuberculosis: A concise clinical review. Clin Respir J. 2018,12(5): 1779-1786.
18. Han M, Xiao H, Yan L. Diagnostic performance of nucleic acid tests in tuberculous pleurisy. BMC Infect Dis. 2020,20(1): 242.
19. Petborom P, Dechates B, Muangnoi P. Differentiating tuberculous pleuritis from other exudative lymphocytic pleural effusions. Ann Palliat Med. 2020,9(5): 2508-2515.
20. Skouras VS, Kalomenidis I. Pleural fluid tests to diagnose tuberculous pleuritis. Curr Opin Pulm Med. 2016,22(4): 367-377.
21. Akhan O, Demirkazik FB, Ozmen MN, *et al*. Tuberculous pleural effusions: ultrasonic diagnosis. J Clin Ultrasound. 1992,20(7): 461-465.
22. DeMaio A, Clarke JM, Dash R, *et al*. Yield of Malignant Pleural Effusion for Detection of Oncogenic Driver Mutations in Lung Adenocarcinoma. J Bronchology Interv Pulmonol. 2019,26(2): 96-101.
23. Wang S, Chen H, Zhong J, *et al*. Comparative study of EGFR mutations detected in malignant pleural effusion, plasma and tumor tissue in patients with adenocarcinoma of the lung. Lung Cancer. 2019,135: 116-122.

24. Tao H, Meng Q, Li M, *et al*. Outcomes of bevacizumab combined with chemotherapy in lung adenocarcinoma-induced malignant pleural effusion. Thorac Cancer. 2018,9(2): 298-304.
25. Yang Z, Song Z, Chen Z, *et al*. Metabolic and lipidomic characterization of malignant pleural effusion in human lung cancer. J Pharm Biomed Anal. 2020,180: 113069.
26. Leslie KO, Trahan S, Gruden J. Pulmonary pathology of the rheumatic diseases. Semin Respir Crit Care Med. 2007,28(4): 369-378.
27. Hannah JR, D'Cruz DP. Pulmonary Complications of Systemic Lupus Erythematosus. Semin Respir Crit Care Med. 2019,40(2): 227-234.
28. Rodríguez-Zarco E, Vallejo-Benítez A, Otal-Salaverri C. Pleural Effusion Associate with Rheumatoid Arthritis: Diagnostic Clues. J Cytol. 2019,36(4): 222-223.
29. Yunt ZX, Solomon JJ. Lung disease in rheumatoid arthritis. Rheum Dis Clin North Am. 2015,41(2): 225-236.
30. Lew SQ. Hydrothorax: pleural effusion associated with peritoneal dialysis. Perit Dial Int. 2010 Jan-Feb,30(1):13-8.
31. Chaaban T, Kanj N, Bou Akl I. Hepatic Hydrothorax: An Updated Review on a Challenging Disease. Lung. 2019,197(4):399-405.

Figures

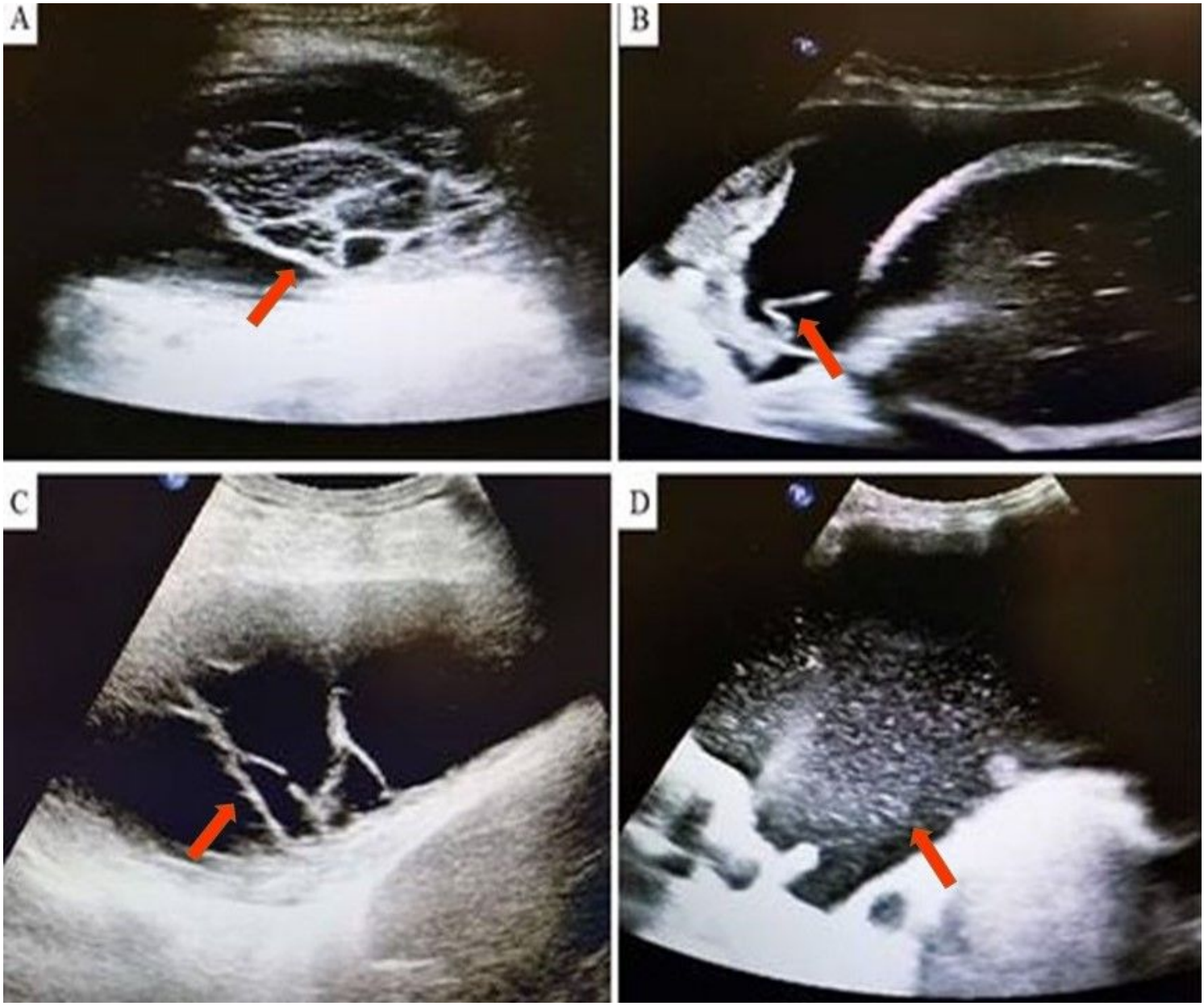

Figure 1

(A) 44 years old, male, right empyema, with more septation, (B) 28 years old, female, left complicated parapneumonic pleural effusion, with a small amount of septation, (C) 56 years old, female, SLE with left pleural effusion, with a small amount of septation, (D) 46 years old, male, left empyema, with more intense spots.