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Case Report

COVID 19 RELATED EFFUSION CYTOLOGY: MIMICKER OF MALIGNANCY! THREE CASE REPORT WITH LITERATURE REVIEW

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ABSTRACT

Objective: COVID-19 has emerged as the biggest challenge to the mankind. Pleural effusion is one of the common manifestations of COVID-19. We present cytological findings in two cases of pleural effusion and one case of pericardial effusion related to COVID-19. **Design:** A report of three cases. **Results:** Two cases of pleural effusion that presented 20 days after recovering from COVID-19 and one case of pericardial effusion during the course of illness. All these three cases showed cytological features such as reactive mesothelial cells which can mimic malignancy. However, lymphophagocytosis was seen in all three cases which helped us not to label these cases as malignant. **Conclusion:** These cytological findings can be a mimicker of malignancy in COVID-19 patients. Hence, detailed history and investigations are needed to confirm the diagnosis.

INTRODUCTION

Outbreak of a novel Coronavirus disease (COVID-19; previously known as 2019-nCoV)[1,2] was reported in Wuhan, China,[2]towards the end of December, 2019. This has subsequently affected 26 countries worldwide. Pneumonia is frequently seen in SARS-COV-2 which carries a mortality of 3.7% worldwide.[3] Pleural effusion was found in 5-10% of SARS-CoV-2 pneumonia as reported in three retrospective studies from China based on radiological features.[4,5,6]. Few observational studies have described that one of the late manifestations SARS-CoV-2 pneumonia is pleural effusion. This effusion is seen more than seven days after presentation with SARS-CoV-2 pneumonia[4,5,6]. Risk of development of pleural effusion is more in patients with advanced SARS-CoV-2 pneumonia.[6]We present cytological findings, which can be mimicker of malignancy in 2 cases of post COVID-19 pleural effusion and 1 case of COVID-19 pericardial effusion.COVID-19 can be a secondary cause for HLH and lymphophagocytosis seen in all 3 cases can be a feature of HLH.[7]

Case: 1

70 years old female, 30 days post COVID-19, known case of hypertension, presented with breathlessness, fever, cough and pain in right hemithorax. Blood pressure arterial: 120/70mmhg, pulse: 104bp, respiratoryrate: 24bpm, temperature: 38.5°C, oxygen saturation with finger probe was 92% on room air (RA). On physical examination, breathing sounds were decreased on the right side. In blood tests, WBC count:6.3x10^3, HB:9.2gm/dl, Haematocrit:29.6%, Platelets: 286x10^3, liver function tests, renal function tests, electrolytes and blood sugar was within normal limits.LDH:307U/L, Protein total:5.0gm, Albumin:2.8gm, ferritin:51mcg/L.

On HRCT chest, mild pleural effusion was noted on right side with sub segmental consolidation/collapse of underlying lung parenchyma. Few peripheral areas of ground glass opacities with septal thickening were noted involving bilateral lung fields with sub pleural fibrosis. These findings were suggestive of classic COVID-19 infection in resolving stage with early changes of fibrosis, CTSS-12/25(moderate grade) with mild right sided pleural effusion.

Case: 2

A 78 years old female,20 days Post COVID, known case of Iron deficiency anaemia presented with breathlessness, facial swelling, cough and chest pain. Blood pressure arterial: 130/80mmHg, pulse: 82bpm, respiratory rate: 20 bpm, fever: 38.5c, oxygen saturation with finger probe was 84% on RA. Patient received 1 PCV after admission. In blood tests, Hb: 7.1gm/dl, WBC count: 13x10^3, Platelets 183 x10^3, MCV: 68.4fl, MCH: 21.3mcg/dl, MCHC: 31.1mcg/L, protein total: 4.5gm/dl, creatinine1.6mg/dl, urea:100mg/dl, Interleukin: 642pg/ml, CPK: 10.6U/L, D-dimer: 6630ng/ml, Ferritin:

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77.4mcg/L, Anti COVID antibody total 5.59AU/ml.X-ray chest showed right upper lobe and lower lobe haziness. CT scan showed bilateral pleural effusion with collapse of upper lobe lung parenchyma.

Case: 3

A 40 years old female, presented with fever and chest pain, no comorbidities. Pulse rate: 86bpm, SpO2: 97% using finger probe on RA, BP: 120/80mmHg, RR: 22/min. In blood tests, WBCcount:17x10^3,Hb8.6gm/dl,platelets:100x10^3,Urea:83mg/dl,Creatinine:1.3mg/dl,SGPT:58U/L,SGOT:159U/L,LDH:459 U/L, Proteintotal: 5.0gm/dl, Albumin: 3.0gm/dl, Bilirubin total: 1.19mg/l, Alkpo4:396IU/L, Ferritin: 445ng/ml. Nasopharyngeal swab for COVID 19 was negative, however X ray chest showed ground glass opacities in lower lobes of both the lungs with increased cardiac silhouette (pericardial effusion). HRCT chest too showed ground glass opacities in both the lungs. Probable diagnosis of COVID 19 was made and patient received treatment for the same.

Pleural fluid analysis (Case 1 &2): Appearance and color: slightly turbid and yellowish in both cases, protein: 2.6gm% (case 1), 3.0gm %(case 2). On cytological examination, centrifuged smear studied from both cases were cellular, it showed lymphocytes and many reactive mesothelial cells with high N:C ratio, nuclear atypia mimicking malignancy, however lymphophagocytosis was noticed in both the fluids as shown in figure 1.

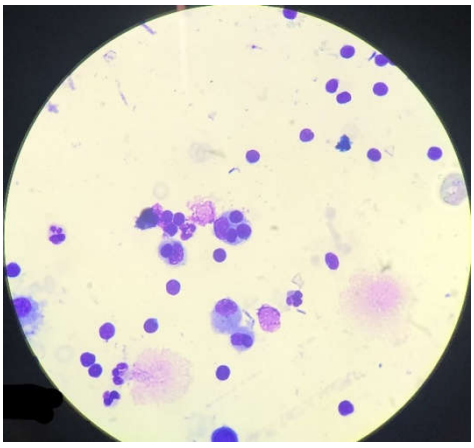

Figure 1 Lymphophagocytosis in pleural fluid

Pericardial fluid analysis (Case 3): Appearance and color: turbid, reddish, protein: 2.824gm%. On cytological examination, centrifuged smear studied were highly cellular, predominantly showing singly scattered population of reactive mesothelial cells showing anisonucleosis and nucleomegaly, along with binucleation and multinucleation mimicking malignancy. Lymphophagocytosis was seen along with inflammatory cells comprising mainly of lymphocytes in a haemorrhagic background. The patient succumbed to her disease while in hospital and further investigations could not be carried out.

DISCUSSION

Case 1 and Case 2 were diagnosed patients of COVID-19 and presented approximately 20 days after testing positive while Case 3 was RTPCR negative but still was diagnosed as COVID-19based on CT and X Ray findings.[8,9,10] Both case 1 and case 2 developed pleural effusion late in the course of disease however case 3 developed pericardial effusion early in disease course. Both Case 1 and Case 2 pleural fluid and case 3 pericardial fluid revealed exudate type of effusion, using Lights criteria.[11] Centrifuged smear prepared show many reactive mesothelial cells with reactive atypia mimicking malignancy. However, lymphophagocytosis was noted in all 3 cases. An association between COVID-19 and HLH-like syndrome has been reported.[3,12] One interesting feature of the disease is the hemophagocytosis. Characteristics of hemophagocytosis includes presence of red blood cells, platelets, or white blood cells within the cytoplasm of macrophages.[7]Lymphophagocytosis seen in our 3 cases is a known feature of HLH along with other features. However only 1 case of pericardial effusion showed raised ferritin. The other 2 patients of pleural effusion came late as post COVID-19, so previous investigations were not available and bone marrow was not done in all these patients. Hence, we could not confirm the diagnosis of HLH.

CONCLUSION

We are presenting this case report of 3 patients to highlight reactive changes in mesothelial cells on cytological examination of pleural/pericardial fluid in COVID-19 patients. These features can be a mimicker for malignancy especially when RTPCR report for COVID-19 is negative in a patient or patient presenting late in disease course after a negative report and there is a clinical suspicion of malignancy. So, here with this case report, we emphasize on the fact that history of COVID-19 is important in such cases. As with the evolution of pandemic, patients are presenting late in disease course with new symptoms after initial improvement.

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