

Reactive Plasmacytosis in Effusions - Not A Rare Occurrence

Dr Gauri Naik¹, Dr Anant Kulkarni², Dr Jitendra Khedkar³, Dr Rajesh Phatale⁴,
Dr Maithili Kavathekar⁵

^{1,2,3,4,5}Department of Pathology, Sahyadri Speciality Labs, Kothrud, Pune, India

Corresponding Author: Dr Gauri Naik

DOI: <https://doi.org/10.52403/ijhsr.20231115>

ABSTRACT

Introduction: Effusions with plasma cells are uncommon. In such effusions reactive plasma cells need to be differentiated from malignant ones. In the literature we came across a single case of plasmacytic effusion in the absence of underlying malignancy.

Material and methods: A retrospective analysis of the ascitic and pleural fluid samples received for routine analysis, from Jan 2021 to Dec 2022 was done.

Result: Five cases were incidentally detected to have reactive plasmacytosis in effusions, three in pleural fluid and two in ascitic fluid. Number of plasma cells varied between 2% to 30%. In all these cases thorough clinical details were obtained and relevant investigations were studied. All the cases had ailments related to hepatobiliary system. None of these cases had any features of lymphoma or plasma cell neoplasm. In all the cases plasma cells had a reactive morphology. In one of the cases the reason for reactive plasmacytosis was viral hepatitis, in another case it was suspected to be tuberculosis. In two cases some intercurrent infection could be the cause for reactive plasmacytosis in effusion. However, in one case the patient passed away before proper investigations could be made.

Discussion: The mechanism for reactive plasmacytosis is not documented yet. Further studies in this regard are needed as the entity is not rare. In our study the incidence was 0.36% (5 cases out of a total of 1397 cases).

Keywords: Effusions, plasma cells, reactive

INTRODUCTION

EBF (extravascular body fluid) analysis can be utilised to identify particular organ involvement and help distinguish between causes that led to fluid accumulation. ^[1]

Neutrophils, eosinophils, lymphocytes, monocytes, macrophages, plasma cells, mesothelial cells and malignant cells are among the several cell types that can be detected in pleural, pericardial, and peritoneal fluids. ^[2]

Effusions with plasma cells are an uncommon condition.

Three cases of transient plasma cell infiltration in ascites and two cases of

transient plasma cell infiltration in pleural fluid are reported here.

MATERIALS & METHODS

This is a retrospective analysis of the samples of pleural fluid and ascitic fluid received in the lab for routine analysis over a period of two years from 01/01/2021 to 31/12/2022. The samples were collected in EDTA and Plain tubes.

The fluid analysis included physical examination, protein and sugar estimation and total and differential cell count, as well as gram and ZN stain. In cases of ascitic fluids, serum samples were obtained for serum albumin estimation and SAAG value

was calculated for better categorization to exudate or transudate. Fluid protein estimation was done by Biuret method and glucose estimation by Hexokinase method on Abbott Alinity ci automated biochemistry analyzer or Abbott Architect ci 4000 fully automated biochemistry analyzer.

Fluids were processed on Sysmex UF 4000 fully automated particle analyzer which works on the principle of flow cytometry and uses a blue semiconductor laser source for cell counts. For microscopy, fluids were centrifuged at 3000 rpm for 5 min, the slides were stained by Leishman stain. At least one cytocentrifuge slide was prepared and stained by Leishman stain. Total and differential cell counts given by the machine were counterchecked manually by

microscopy. The machine differentiates total nucleated cells into mononuclear and polymorphonuclear cells. On microscopic examination nucleated cells were further differentiated into lymphocytes, polymorphs, monocytes, mesothelial cells, eosinophils, plasma cells and atypical cells if any.

A total of 410 pleural and 987 ascitic fluid samples were received in the lab in two years' period.

RESULT

Referring hospital being a renowned center for Liver transplant, the incidence of transudative Ascitic fluids received in the laboratory was the highest, i.e. 600/987 (60.79%). The distribution of the cases is shown in Tables 1 and 2.

Table 1: Distribution of ascitic fluid sample

	Ascitic Fluid 2021	Ascitic Fluid 2022	Ascitic Fluid 21-22
Hemorrhagic	72	100	172(17.42%)
Transudates	269	331	600(60.79%)
Neutrophilic exudates	51	75	126(12.76%)
Lymphocytic exudates	32	40	72(7.29%)
Mixed exudates	8	9	17(1.74%)
Total	432	555	987

Table 2: Distribution of pleural fluid samples

	Pleural Fluid 2021	Pleural Fluid 2022	Pleural Fluid 21-22
Hemorrhagic	68	87	155(37.80%)
Transudates	46	54	100(24.39%)
Neutrophilic exudates	21	24	45(10.98%)
Lymphocytic exudates	49	42	91(22.20%)
Mixed exudates	8	11	19(4.63%)
Total	192	218	410

In 22/987 (2.23%) ascitic fluid samples and 29/410 (7.07%) pleural fluid samples, abnormal cells favouring malignant aetiology were found.

The prevalence of eosinophils infiltrating the fluid was considerably higher in pleural fluid samples; just 3 (0.03%) ascitic fluid samples revealed eosinophils, compared to 16 (3.90%) pleural fluid samples.

In this study, samples that contained plasma cells were focused and elaborate analysis was carried out. Number of plasma cells varied between 2% to 30%.

Case1

A 24-year-old male, had liver failure associated with fulminant hepatitis A. He had grade 3 hepatic encephalopathy and a low-grade fever. He also suffered coagulopathy and severe renal damage. His anti-HAV IgM antibody test result was positive. He was started on wide spectrum antibiotics, osmotic diuresis, and other necessary supportive measures after being electively intubated and ventilated. He responded effectively to treatment and was gradually extubated. He began experiencing fever peaks in the interim. The antibiotics were upped since his procalcitonin level was

high. His workup for hemophagocytic lymphohistiocytosis and all cultures were negative. He had right pleural effusion which was drained. Pleural fluid was a mixed cell exudate with 30% plasma cells. The patient had persistent fever with high procalcitonin level. His X-ray chest and HRCT thorax revealed a cavitory lesion in the right lung, prompting the diagnostic bronchoscopy. *Klebsiella oxytosa* and *pneumoniae* were grown in BAL culture. It was discovered that Biofire had a mixed

polymicrobial infection. His BAL showed Galactomannan positivity. Mycobacterial culture results from the patient's BAL were negative. His hemogram revealed neutrophilic predominance with toxic granules, HB 8.7 gm/dl, TLC-7900/cumm, and a platelet count of 516000/cumm. So his medicines were changed after consulting with a specialist in infectious diseases. He responded well. His renal and liver functions got better and was discharged.

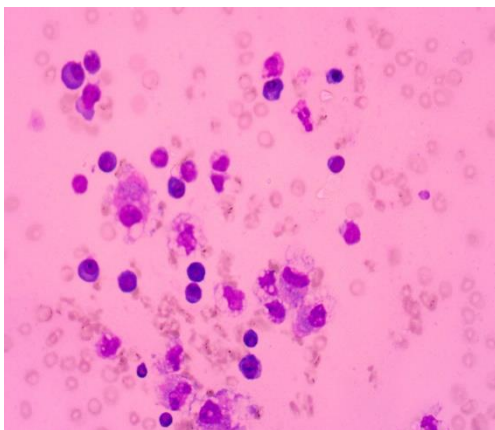


Figure 1 Low Power

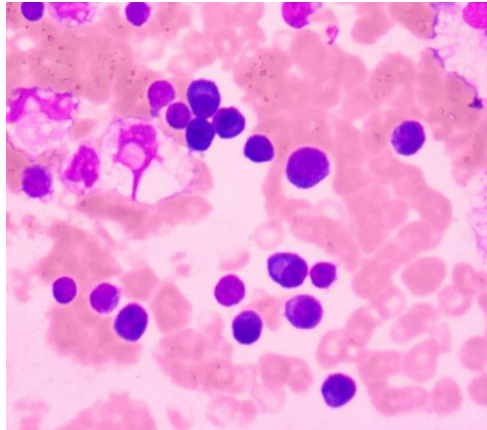


Figure 2: High Power

Figure 1 and 2: Leishman-stained cytospin preparation of pleural fluid from Case 1 displaying lymphocytes, a few neutrophils, macrophages, and a few plasma cells.

Case 2

A liver transplant for Wilson's disease was performed on a 8-year-old boy, around one and a half months ago. Around 20 days after surgery, he had also had pigtail insertion for posttransplant subhepatic collection. This time, the patient was admitted with high grade fever. After being investigated, the immunosuppressants were changed, and antibiotics and other supportive care were started. Fever abated, cultures were sterile. He had tachycardia, tachypnoea, and acidosis with conserved lactates over the course of the following two to three days. Antibiotics were upgraded. Repeat chest x-ray revealed right pleural effusion (hepatic hydrothorax) that required controlled drainage. Fluid ADA & Gene expert were negative, despite fluid analysis showing lymphocytic exudate and 15% plasma cells. His CBC revealed moderate thrombocytopenia, microcytic hypochromic

anaemia, and neutrophilia with a TLC of 9000/cmm, a platelet count of 127000/cmm, and a Hb of 8.9 gm/dl. He was given empirical treatment for pseudomembranous colitis because of his numerous loose motions. He gave a good response and gradually settled. But he again started having fever spikes due to which he was shifted over to Ceftazidime to which he responded well. He has improved clinically.

Case 3

A 30-year-old man had noncirrhotic portal fibrosis leading to DCLD with ascites. On regular investigation, the ascitic fluid tap revealed a transudate with 60% lymphocytes and 10% plasma cells. His peripheral blood revealed a neutrophilic preponderance, TLC of 6200/cumm, a Hb of 8.4 gm/dl, and a platelet count of 50000/cumm. His liver transplant was planned. After conducting necessary

investigations in view of transplant surgery, he was discharged. But after 15 days, he was brought with huge G. I bleed with acute renal failure and hypovolemic shock. Even after proper emergency care, he could not be survived.

Case 4

A 51-year-old man had ascites and DCLD. He was advised liver transplant. All investigations were done in view of transplant surgery. On routine examination upon initial admission, his ascitic fluid was haemorrhagic with 2% plasma cells. His corresponding CBC revealed a platelet count of 51000/cumm, TLC of 5500/cumm, and Hb of 10.2 gm/dl. The patient's ICT was 3+ positive and he was reactive for HbsAg. Additionally, he tested positive for IgG antibodies against CMV, EBV, and varicella zoster. He had a positive interferon gamma release assay. His X-ray chest was unremarkable, but the CT scan of his thorax revealed a slight left pleural effusion and subsegmental atelectasis in the left lower lobe. The patient was hospitalised for DCLD, HRS, coagulopathy, hydrothorax, and SBP on two or three occasions. With the exception of an increase in effusion, a further CT thorax taken after two months revealed the same changes. The patient's ascitic fluid was tapped three or four times over the course of the following two to three months, and on regular analysis, it revealed neutrophilic exudate consistent with SBP but no plasma cells. After 3 months, the patient finally passed away due to septic shock with multiorgan failure secondary to DCLD.

Case 5

A 46-year-old man with recently diagnosed diabetes was hospitalised with acute necrotizing pancreatitis. His serum lipase level was 1354/uL, while serum amylase level was 1107/uL. Corresponding CBC showed Hb 11.4gm/dl, TLC 13900/cumm with neutrophilic predominance, and platelet count 233000/cumm. On CT scan, there was practically complete pancreatic

necrosis with partial splenic vein thrombosis. Hepatomegaly and a bilateral pleural effusion were seen. A number of the peripancreatic, paraaortic, paracaval, and aortic lymph nodes were enlarged. The patient responded well to treatment and was discharged. He was readmitted after 3–4 days, with complaints of breathing difficulties, generalised weakness, and abdominal pain. A huge collection of air and fluid was seen in place of the pancreatic necrosis on CT scan. The size of previously swollen lymph nodes was also enhanced, as was the thrombosis in the splenic vein. On admission, the CBC revealed Hb -11.6 gm/dl, TLC 25900/cumm with neutrophilic predominance and reactive thrombocytosis with a platelet count of 704000/cumm. His PT and PTT were deranged but stabilised after vitamin K supplement. His CBC returned to normal with antibiotics and adequate hydration. Pancreatic necrosectomy via laparoscopy was performed. But on the third postoperative day, the patient's fever spiked. He once again had marked neutrophilic leucocytosis, with a TLC of 37700/cumm and 93% neutrophils. Despite a negative blood culture, *Klebsiella pneumoniae* was detected in the pancreatic fluid. Higher antibiotics and all supportive care were given to the patient. His pleural fluid was tapped during his recovery period. Pleural fluid was haemorrhagic upon normal testing, with 80% lymphocytes and 2% plasma cells. Patient tolerated the treatment well. The TLC improved to normal and was discharged.

DISCUSSION

Plasma cells were identified incidentally in each of the five situations mentioned above. In Case 1, there were 30% plasma cells in the patient's pleural fluid but no atypia. (Fig 1 and 2) His BAL culture for M. TB was negative, but he had a positive serology for Hepatitis A. He had a cavitary lesion in his right lung on his chest X-ray and HRCT, which was most likely caused by *Klebsiella pneumoniae* and *Klebsiella oxytosa*. His

biofire revealed mixed polymicrobial illness as well. A serum protein electrophoresis was carried out in light of the increased plasma cell content of the pleural fluid. Electrophoresis of the serum protein failed to reveal any monoclonal bands. (Fig. 3) The patient responded favourably to the

therapy. The presence of plasma cells in his pleural fluid could only be explained by a viral infection, given his overall clinical characteristics and laboratory results. As far as we are aware, there hasn't yet been an instance like this published in the literature.

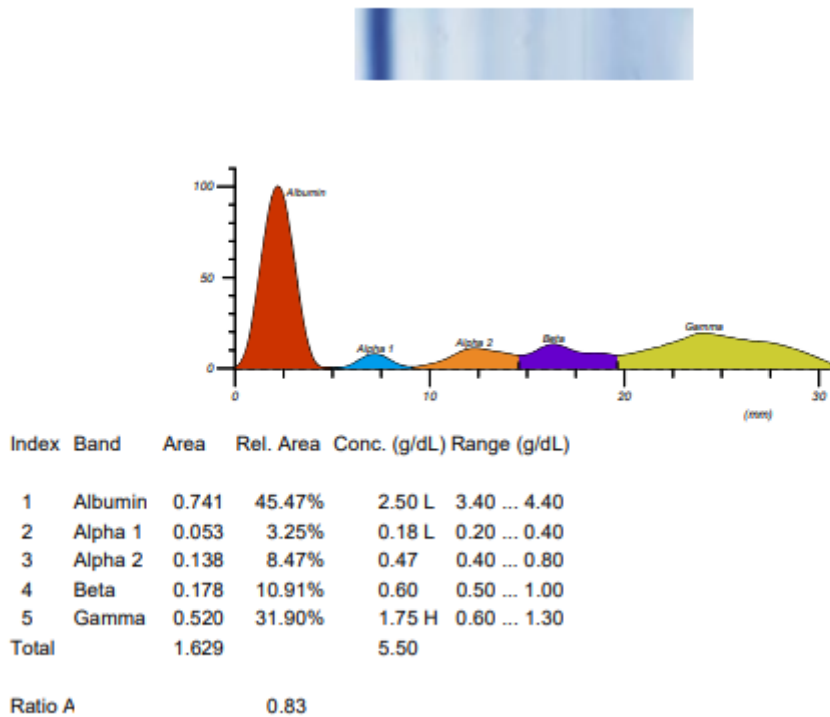


Figure 3 shows the results of Case 1 Sr protein Electrophoresis using agarose gel electrophoresis

In Case 2, an 8-year-old kid with Wilson's disease underwent liver transplant and was on immunosuppressants. After surgery, he developed infectious complications. He developed a right-sided pleural effusion, which was composed of lymphocytic exudate and 15% plasma cells. Pleural fluid ADA and gene expert tests were negative for M Tuberculosis and Non tubercular mycobacteria. Patient improved under the cover of antibiotics. The precise reason why plasma cells were found in the pleural effusion is yet unknown. Neoplasia and tuberculosis were, however, ruled out after taking into account the clinical course and the findings of the tests because the clinical course was fairly acute and reacted effectively to antibiotics. Therefore, it indicates that there is an ongoing infection.

Case 3 was a DCLD patient who developed ascites as a result of noncirrhotic portal fibrosis. He had transudative ascitic fluid that contained 10% plasma cells. His investigations done in view of transplant surgery didn't figure out the reason for the presence of plasma cells in the ascitic fluid. And it was not possible to conduct any further investigations or follow-up since the patient passed away within 15 days as a result of a significant GI bleed.

Case 4 involved a DCLD patient with ascites who was a liver transplant candidate. His ascitic fluid was haemorrhagic and contained 2% plasma cells during initial admission. His accompanying hemogram lacked plasma cells. The patient's ICT was 3+ positive, and he tested positive for HBs Ag. The patient's IGRA positive status,

which denotes latent or active tuberculosis, was the most intriguing finding. His CT scan of the chest revealed subsegmental atelectasis in the left lower lobe and a minor left pleural effusion. These results raise the possibility of TB. However, the patient was taken to the hospital twice more for SBP, coagulopathy, hydrothorax, and DCLD after this episode. Additionally, three to four taps of his ascitic fluid revealed neutrophilic exudate typical of SBP but no plasma cells. After three months, the patient passed away from multiorgan failure brought on by DCLD and septic shock.

Case 5 had an acute necrotizing pancreatitis with abdominal lymphadenopathy and coagulopathy caused by vitamin K deficiency. He had haemorrhagic pleural fluid with 2% plasma cells when it was tapped during the recovery phase. *Klebsiella pneumoniae* was detected in his pancreatic fluid. Although it may be due to an infectious disease, the precise cause of plasma cells in the pleural fluid in this instance remains unknown.

Although a relationship between TB and polyclonal gammaglobulinemia is well known, one with MGUS is less well documented in the literature. Following a study of the literature, Cheung et al. reported a case of MGUS in a patient with disseminated TB. Another case report showed how MGUS and TB coexisted in a patient with penile TB.^[3] In these cases, serum protein Electrophoresis is predicted to reveal a unique monoclonal band against a background of diffuse hypergammaglobulinemia.

Only one example of abnormal-looking clonal plasma cells infiltrating pleural fluid together with active pulmonary tuberculosis and a parapneumonic effusion in a patient with a history of acute myeloid leukaemia has been reported in the literature. Although the patient's IGRA results and CT Thorax findings suggested tuberculosis in case 4, the diagnosis of tuberculosis was not confirmed by culture, ZN stain, or histology. Additionally, the mystery remained unresolved because there were

only 2% of plasma cells in the ascitic fluid and none in the subsequent ascitic taps.

Looking at a glance, none of the five cases had any skeletal lesions or other signs of plasma cell neoplasms like multiple myeloma or lymphoma. Regardless of the plasma cell percentage, the morphology of the plasma cells was always reactive. In Case 1, the viral aetiology can explain the origin of the plasma cell effusion. It can be guessed that Case 4 was caused by tuberculosis. In cases 2 and 5 a concurrent infection may have been the cause, whereas in case 3, the patient passed away before thorough examination.

Only seven of the 80 patients with multiple myeloma who had pleural effusions were having myelomatous effusion, according to research by Ja Min Byun et al.^[4] Rarely, Hodgkin lymphoma, viral infections, and tuberculosis (TB) can exhibit a little increase in plasma cells in effusion cytology.^[5]

Only 6% of myeloma patients will experience pleural effusion.^[3,6] and is usually brought on by nephrotic syndrome, pulmonary embolism, congestive heart failure due to amyloidosis, and infection.^[3,7] Less than 1% of instances of myelomatous pleural effusion are recorded.^[3,6,7] Myelomatous effusion's pathophysiology is still a mystery. There are several proposed pathways for myelomatous pleural effusion. Infiltration of the pleural fluid by malignant plasma cells (which is associated with a worse prognosis), direct infiltration of the pleural fluid from adjacent tissues, pulmonary embolism, congestive heart failure brought on by amyloidosis, chronic renal failure, and mediastinal lymph node infiltration with lymphatic obstruction are all potential mechanisms. Nephrotic syndrome (caused by renal tubular infiltration with paraprotein and the development of glomerular damage) is another.^[7] Cardiac failure has been the most frequent cause of effusion in PCM among these several etiological causes.^[6,7]

The pleural fluid profile in the majority of MPE cases is exudate (97.4%) and lymphocytic (78.6%).^[3]

Peritoneal involvement with ascites is one of the extramedullary involvements of MM that is highly uncommon, and only a few numbers of instances have been documented.^[8]

Patients with myeloma typically develop ascites as a result of severe plasma cell invasion of the liver. Ascites can also develop as a result of additional concomitant conditions such as heart failure, kidney injury, and infectious peritonitis. Myelomatous ascites, on the other hand, are relatively uncommon in MM patients and are brought on by peritoneal infiltration of tumour cells.^[8] They could appear at the time of presentation or, more often, grow as the disease progresses.

In contrast to myelomatous ascites, pleural plasmacytic effusions are more frequently documented and occasionally described as an early symptom of illness.^[8]

In lymphoma patients, pleural effusions are not an uncommon problem. However, patients with plasma cell dyscrasia or infectious disorders like tuberculosis do not frequently experience pleural effusions that are abundant in plasma cells.^[4]

Rodriguez et al. reported the first incidence of (MPE) in 1994.^[5,6]

Pleural effusion is a rare sign of PCM that typically appears later in the course of the disease and is typically brought on by another disease process. The identification of atypical plasma cells in pleural fluid cytology, the demonstration of the monoclonal protein in pleural fluid electrophoresis, and histologic confirmation with biopsy are the diagnostic criteria to confirm the myelomatous aetiology.^[3,6,7]

It is always important to distinguish between the reactive plasma cells and the malignant plasma cells. Neoplastic lesions have more plasma cells in the effusion than reactive processes. Further evidence of plasma cell neoplasia is the existence of immature plasma cells with noticeable nucleoli. A thorough clinical history should

always be taken in unsure cases of plasma cell rich effusion, coupled with the use of auxiliary procedures. Examples include any history of plasma cell neoplasm in other parts of the body, complaints of back discomfort, or lytic lesions in the skull.^[5]

It might be beneficial to use ancillary methods like flow cytometric immunophenotyping for plasma cells. A useful diagnostic indicator of plasma cell neoplasm in effusion fluid is the presence of a larger percentage of CD 38 and CD 138 positive cells in the sample. The cells also exhibit restriction of the light chain. This information may also be obtained using immunocytochemistry on cell block preparation of the effusion sample. However, these auxiliary techniques may have limitations, such as poorly preserved fluid samples and fewer plasma cells in a given sample. Other biochemical, radiological findings and information about monoclonal bands in blood and urine are also useful aspects.^[5]

CONCLUSION

Plasma cell infiltration in body fluids without underlying plasma cell neoplasm or lymphoma or diagnosed tuberculosis have never been reported in the literature. The mechanisms of effusion plasmacytosis have never been studied earlier due to the rarity of plasmacytic effusions.^[4] It is most likely related to the elevated cytokines in effusions. A patient with polyclonal hyperimmunoglobulinemia and idiopathic plasmacytic lymphadenopathy exhibited elevated IL-6 in his PE, but his blood IL-6 was normal, according to T Mori et al.^[4] This theory needs to be verified by additional study.

Limitation of the study:

Flow cytometry of the fluids could not be done either due to improperly preserved fluids or a smaller number of plasma cells in the fluid.

Declaration by Authors

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Clinical and Laboratory Standards Institute (CLSI). Analysis of body fluids in clinical chemistry. Approved guideline. Document C49-A. CLSI, Wayne, USA: 2007.
2. Strasinger S K, De Lorenzo M S. Serous fluids. F A Devis. Urinalysis and body fluids, 5th ed. Philadelphia F A Devis company; 2008. p. 225
3. Sameh Soliman D, Ali M, Akikki S, et al. Transient Pleural Fluid Infiltration by Clonal Plasma Cells Associated with Pulmonary Tuberculosis. *Case Rep Oncol.* 2020;13(2):883-891. Published 2020 Jul 29. doi:10.1159/000507984
4. Li B, Nong L, Zhang J, Wang W, Wang Q, Zhang Y, Ren S, Wang M. Plasmacytic Pleural Effusion as a Major Presentation of Angioimmunoblastic T-Cell Lymphoma: A Case Report. *Curr Oncol.* 2022 Oct 13;29(10):7637-7644. doi: 10.3390/curroncol29100603. PMID: 36290880; PMCID: PMC9600574.
5. Gochhait D, Dey P, Verma N. Cytology of plasma cell rich effusion in cases of plasma cell neoplasm. *J Cytol.* 2016 Jul-Sep;33(3):150-153. doi: 10.4103/0970-9371.177147. PMID: 27756988; PMCID: PMC4995873.
6. Arunsurat I, Reechaipichitkul W, So-Ngern A, Ungareevittaya P, Chaisuriya N, Teawtrakul N, Ratanawatkul P, Chumpangern W. Massive pleural effusion due to IgG-Kappa subtype multiple myeloma: A case report. *Respir Med Case Rep.* 2019 Dec 12; 29:100984. doi: 10.1016/j.rmcr.2019.100984. PMID: 31886127; PMCID: PMC6921219.
7. Babu KA, Sundararajan L, Prabu P, Parameswaran A. Disseminated plasma cell myeloma presenting as massive pleural effusion. *Eur Clin Respir J.* 2015 Nov 24;2. doi: 10.3402/ecrj.v2.27028. PMID: 26664659; PMCID: PMC4660938.
8. Choi SY, Hae Young Lee, Boem Ha Yi, Min Goo Lee, Hee Jin Kim, Seong Ho Park. Myelomatous Ascites as an Initial Manifestation of Extramedullary Involvement of Multiple Myeloma. 2017;76(3):187-187. doi: <https://doi.org/10.3348/jksr.2017.76.3.187>

How to cite this article: Gauri Naik, Anant Kulkarni, Jitendra Khedkar, Rajesh Phatale, Maithili Kavathekar. Reactive plasmacytosis in effusions - not a rare occurrence. *Int J Health Sci Res.* 2023; 13(11):122-129. DOI: <https://doi.org/10.52403/ijhsr.20231115>
