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CASE REPORT OPEN ACCESS

A Foe For Lung Is A Friend For Heart: Intrapericardial Bleomycin For Malignant Pericardial Effusion – A Case Series

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A B S T R A C T

Malignant pericardial effusion is a potentially fatal problem among patients with advanced malignancies known to cause cardiac tamponade and hemodynamic instability. Pericardiocentesis and pericardial drainage are the standard initial approaches to management; however, they only offer temporary relief in most cases, due to a high rate of recurrence. The use of sclerotherapy via intrapericardial instillation of a sclerosing agent may offer a reasonable alternative. We present a case series of six patients with malignant pericardial effusion in which intrapericardial bleomycin was used to treat the effusion after pericardiocentesis was performed. Each patient received 20 mg bleomycin in 30 mL normal saline instilled into the pericardial space for two hours following image-guided pericardiocentesis, on three consecutive days. Symptoms, drainage amount, and effusion recurrence were used to measure clinical outcomes. Four of the six patients experienced significant symptomatic improvement with resolution of dyspnea and chest discomfort, decreasing subsequent amounts of pericardial drainage, and no recurrence as evaluated at their follow-up appointments. Two patients were not considered adequate treatment responders by the investigators, and experienced ongoing effusion and return of symptoms after therapy completion. There were no meaningful systemic toxicities or procedure complications. In summary, this case series indicates that intrapericardial bleomycin may be a safe and effective treatment option for malignant pericardial effusion, but some patients may not respond, demonstrating the need for tailored treatment decisions for effusions and the need for larger studies to assess reproducibility.

Keywords: Bleomycin; Malignant pericardial effusion; Cardiac tamponade; Pericardiocentesis; Intra-pericardial therapy; Case series

INTRODUCTION

Malignant pericardial effusion (MPE) is one of the worst complications in patients with advanced malignancies, ranging from cardiac tamponade to hemodynamic compromise and often death. The prevalence of pericardial effusion in cancer patients is variable, but it may occur in up to 10% of patients with advanced malignancies, with lung cancer, breast cancer, and haematologic malignancies being the predominant underlying diagnoses[1]. Of these, lung cancer is the most common, given the tendency for these tumors to metastasize to the pericardium. Patients may experience clinical symptoms including progressive dyspnea, orthopnea, chest pain, and signs of right-sided heart failure, which can significantly affect quality of life and lead to sudden death if left untreated[2].

Standard treatment options such as pericardiocentesis and catheter drainage may relieve hemodynamic effects quickly but have high rates of recurrence (up to 40%–70% recurrence within weeks), despite drainage volume[3]. Efforts to improve long-term outcomes post drain have relied on a variety of sclerosing agents to create pericardial symphysis and prevent fluid reaccumulation, including tetracycline, doxycycline, talc, and cytotoxic agents like cisplatin. These agents have their own disadvantages, including pain, fever, toxicity systemically, or efficacy that may not be sufficient for widespread adaptation[4].

Bleomycin is a cytotoxic glycopeptide antibiotic that can be both antineoplastic and sclerosing. The use of bleomycin as an agent for intrapericardial instillation has many advantages, including its ability to deliver direct cytotoxicity to malignant cells with the pericardial cavity as well as the capacity to induce local inflammation, and therefore, effective

sclerosis and obliteration of the pericardial sac[5]. Compared to other sclerosing agents, the safety profile of bleomycin is "benign" with lower systemic absorption and sclerotic effects making it feasible for patients with advanced malignancy and a reduced performance status. Phase II trial data demonstrates tolerability of treatment with the maintenance of the benefits of a reduction in recurrence rates, led to bleomycin being identified as a valid intra-pericardial agent[6].

Despite favorable data, the use of bleomycin was largely in controlled studies including phase II trials. There is scant data from clinical 'real world' or population level studies particularly where a patients have various cancers contributing to their pericardial effusion due to malignancy. Importantly, it must also be acknowledged that there have been clear treatment failures, indicating that there is value in delineating between groups of patients that responded poorly to bleomycin.

We present a case series of six patients with malignant pericardial effusion, treated with intrapericardial bleomycin from May 2023 to January 2025, with stated treatment failures as well as some successful responses to enter the discussion of the emerging evidence related to the therapeutic benefits, therapeutic failures, and clinical potential of intrapericardial bleomycin in the palliative care of cancer related pericardial effusions.

MATERIALS AND METHODS

Study Design and Duration

This work was conducted as a prospective case series spanning from May 2023 to January 2025. A total of six patients with malignant pericardial effusion were included. The design aimed to evaluate the clinical outcomes of intrapericardial bleomycin therapy following pericardiocentesis, with specific attention to both treatment responders and non-responders.

Patient Selection

Eligible participants were adult patients with a confirmed diagnosis of malignancy complicated by symptomatic pericardial effusion. Diagnosis of malignant effusion was established on the basis of cytological confirmation of malignant cells in the pericardial fluid and/or radiological evidence strongly suggestive of neoplastic infiltration. Patients presenting with cardiac tamponade physiology or recurrent pericardial effusion requiring drainage were included. Exclusion criteria comprised hemodynamic instability precluding catheter-based therapy, severe coagulopathy, active infection, and prior intrapericardial sclerotherapy.

Intervention Protocol

All patients underwent pericardiocentesis under echocardiographic guidance, followed by placement of a pericardial catheter for continuous drainage. After initial stabilization and confirmation of adequate catheter position, intrapericardial bleomycin was administered.

- **Dosage and Schedule**: A standard regimen of 20 mg bleomycin diluted in 30 mL of normal saline was instilled intrapericardially once daily for three consecutive days (Day 1–Day 3).
- **Dwell Time**: After each instillation, the catheter was clamped for two hours to maximize local drug contact and cytotoxic effect.
- **Monitoring**: Patients were closely monitored for hemodynamic parameters, electrocardiographic changes, drainage volumes, and systemic adverse effects.

Outcome Measures

The primary endpoints were:

1. **Symptomatic relief** – improvement in dyspnea, orthopnea, and chest pain.
2. **Drainage dynamics** – progressive reduction in daily pericardial drainage volumes until reaching ≤20 mL/day, at which point catheter removal was performed.
3. **Recurrence rate** – absence or reaccumulation of pericardial fluid on follow-up echocardiography within three months.

Secondary endpoints included adverse events related to intrapericardial bleomycin and all-cause mortality during the study period.

Response Categorization

- **Responders**: Patients demonstrating progressive drainage reduction, symptom relief, and no recurrence on follow-up.
- **Non-responders**: Patients with persistent or recurrent pericardial effusion despite intrapericardial bleomycin therapy.

Among the six cases, four patients achieved favorable outcomes, while two patients failed to respond adequately, representing non-responders within this series.

Follow-up
All patients were followed longitudinally with serial clinical evaluations and echocardiography at 2 weeks, 1 month, and 3 months post-therapy. Long-term monitoring continued alongside oncological management.

Case Presentations
Case 1 (Responder)
A 36-year-old female with synovial sarcoma of the lung on palliative chemotherapy presented with worsening dyspnea, orthopnea, and chest pain of three weeks' duration. ECG revealed low voltage QRS complexes with electrical alternans, while echocardiography confirmed a large pericardial effusion with right atrial and right ventricular diastolic collapse, consistent with cardiac tamponade. Pericardiocentesis with catheter placement was performed, and intrapericardial bleomycin was administered as per protocol (20 mg daily for three days). Drainage volumes progressively reduced (150 mL on Day 1, 80 mL on Day 2, 40 mL on Day 3, and 20 mL on Day 4), after which the catheter was removed. The patient experienced marked symptomatic relief and remained free of recurrence on serial follow-up while continuing palliative chemotherapy.

Case 2 (Responder)
A 58-year-old male with advanced non-small cell lung carcinoma (NSCLC) presented with acute dyspnea and hypotension. Echocardiography demonstrated a large pericardial effusion causing tamponade physiology. Following pericardiocentesis, intrapericardial bleomycin was instilled. The patient tolerated therapy well with a gradual decline in drainage output, achieving <20 mL/day by Day 5. At three-month follow-up, the patient remained asymptomatic with no recurrence of pericardial effusion and stable oncological status.

Case 3 (Responder)
A 45-year-old female with metastatic breast carcinoma presented with pleuritic chest pain, palpitations, and progressive shortness of breath. Echocardiography revealed a circumferential pericardial effusion with signs of tamponade. She underwent catheter drainage followed by three consecutive instillations of intrapericardial bleomycin. The patient's dyspnea resolved and pericardial drainage ceased by Day 4. She remained recurrence-free on echocardiographic surveillance for three months.

Case 4 (Responder)
A 62-year-old male with esophageal carcinoma and liver metastases developed acute orthopnea and jugular venous distension. Echocardiography confirmed a large pericardial effusion with hemodynamic compromise. After pericardiocentesis, intrapericardial bleomycin was administered. Daily drainage declined steadily, and the catheter was removed on Day 5. At subsequent visits, the patient reported sustained relief in respiratory symptoms with no recurrence of effusion until last follow-up.

Case 5 (Non-Responder)
A 49-year-old male with small-cell lung carcinoma presented with severe breathlessness and chest tightness. Initial pericardiocentesis drained 400 mL of hemorrhagic fluid. Despite intrapericardial bleomycin instillation for three consecutive days, the drainage volume remained persistently high (>150 mL/day), and dyspnea persisted. Echocardiography at one-week follow-up revealed re-accumulation of effusion. This case was categorized as a **treatment failure**, and the patient required repeat pericardial drainage.

Case 6 (Non-Responder)
A 55-year-old female with metastatic ovarian carcinoma presented with recurrent pericardial effusion after prior pericardiocentesis. Following catheter placement, she received intrapericardial bleomycin according to the standard regimen. However, there was no significant reduction in daily drainage, and echocardiography at two weeks demonstrated persistent moderate effusion. The patient's clinical status deteriorated due to progressive systemic disease, and this case was considered a **non-responder** to intrapericardial bleomycin therapy.

RESULTS
A total of six patients with malignant pericardial effusion were included in this case series. The cohort comprised individuals with diverse underlying malignancies, including lung, breast, esophageal, and ovarian cancers. Four patients responded favorably to intrapericardial bleomycin therapy, with resolution of symptoms, progressive reduction in drainage, and no recurrence on follow-up. Two patients were classified as non-responders, with persistent effusion despite standard therapy. No major systemic toxicity or serious adverse events were observed in any case.

Table 1. Baseline demographics and underlying malignancy of patients

Case	Age (years)	Sex	Primary Malignancy	Disease Status
1	36	F	Synovial sarcoma (lung)	Metastatic
2	58	M	Non-small cell lung carcinoma	Advanced
3	45	F	Breast carcinoma	Metastatic
4	62	M	Esophageal carcinoma	Metastatic
5	49	M	Small-cell lung carcinoma	Advanced
6	55	F	Ovarian carcinoma	Metastatic

Table 1 summarizes the demographic distribution and underlying malignancies of the six patients included in the series.

The study population represented a heterogeneous oncological background, with lung cancers being predominant (three cases), followed by breast, esophageal, and ovarian malignancies. Both genders were represented equally. All patients were in advanced or metastatic stages of their respective cancers.

Table 2. Clinical presentation and diagnostic findings

Case	Symptoms at Presentation	ECG Findings	Echocardiography Findings
1	Dyspnea, chest pain, orthopnea	Low voltage QRS, electrical alternans	Large effusion, RA/RV diastolic collapse
2	Acute dyspnea, hypotension	Sinus tachycardia, low voltage	Large effusion, tamponade physiology
3	Dyspnea, chest pain, palpitations	Low voltage complexes	Circumferential effusion, tamponade signs
4	Orthopnea, JVD, respiratory distress	Sinus tachycardia	Large effusion with hemodynamic compromise
5	Severe breathlessness, chest tightness	Low voltage QRS	Large hemorrhagic effusion, tamponade physiology
6	Recurrent effusion, dyspnea	Sinus tachycardia	Moderate to large effusion, persistent fluid

Table 2 outlines presenting symptoms and key diagnostic findings for all patients.

Dyspnea was the most consistent symptom, present in all six patients, often accompanied by chest pain, orthopnea, or hypotension. Echocardiography confirmed tamponade physiology in most cases, validating the urgency for intervention.

Table 3. Treatment details and pericardial drainage dynamics

Case	IP Bleomycin Regimen (20 mg/day × 3)	Drainage Volume Day 1 (mL)	Day 2 (mL)	Day 3 (mL)	Day 4 (mL)	Catheter Removal (Day)
1	Completed	150	80	40	20	4
2	Completed	200	100	50	25	5
3	Completed	180	90	40	15	4
4	Completed	220	120	60	30	5
5	Completed	400	250	180	160	Not achieved (failure)
6	Completed	300	200	170	150	Not achieved (failure)

Table 3 depicts intrapericardial bleomycin treatment regimens, daily drainage dynamics, and catheter outcomes.

Four patients demonstrated a steady reduction in pericardial drainage, allowing catheter removal within 4–5 days. In contrast, two patients (Cases 5 and 6) continued to exhibit persistently high drainage volumes without meaningful reduction, classifying them as non-responders.

Table 4. Clinical outcomes and follow-up

Case	Symptomatic Relief	Recurrence on Follow-up	Response Category
1	Yes	No	Responder
2	Yes	No	Responder
3	Yes	No	Responder
4	Yes	No	Responder
5	No	Yes	Non-responder
6	No	Yes	Non-responder

Table 4 summarizes patient-level clinical outcomes and response categories.

Among the six patients, four were classified as responders, achieving complete symptomatic relief, drainage reduction, and no recurrence on follow-up. Two patients were non-responders, exhibiting persistence or recurrence of effusion despite therapy.

DISCUSSION

Malignant pericardial effusion (MPE) is a severe clinical event seen in advanced malignancies, often resulting in life-threatening cardiac tamponade. The management of MPE is a recurring dilemma, especially in patients with short life-expectancy and poor performance status[7]. Although pericardiocentesis has remained the mainstay of acute management, the frequent recurrence of effusion following pericardiocentesis has led to evaluation of additional modalities, including intrapericardial instillation of sclerosing or cytotoxic agents. In this regard, bleomycin has been increasingly equally effective for both local tumor control and to induce pericardial sclerosis preventing future recurrence and perhaps improving quality of life[8].

In this case series, we provide real world data on six patients with MPE treated with intrapericardial bleomycin between 2023 and 2025. Four patients had a favorable response, achieving dyspnea relief, significant reduction in pericardial drainage and no recurrent effusion noted before death during follow-up[9]. However, two patients did not have a positive outcome with good intrapericardial bleomycin therapy. This highlights the unpredictable nature of disease biology and treatment responses in this patient population.

Efficacy of Intrapericardial Bleomycin

Our results are similar to previous studies demonstrating the efficacy of bleomycin as a sclerosing agent. Yane et al. (1994) were the first published report to use intrapericardial bleomycin in malignant pleural effusions (MPE) with effective fluid control and minimal systemic toxicity. Previous study in a randomized comparison of intrapericardial bleomycin to drainage alone in lung cancer patients, found a significantly lower recurrence rate for those in the bleomycin group, and, more importantly, established its benefits over conventional drainage. Likewise, a trial demonstrated the use of bleomycin for pericardial sclerosis and longer effusion-free survival[10]. Our case series provides similar results, with most patients achieving durable control and improvement in symptoms at the follow up.

Treatment Failures and Possible Explanations

Importantly, two patients in our series had no response to bleomycin therapy. One had small-cell lung carcinoma, a tumor type demonstrating aggressive biology and rapid progression. The second had metastatic ovarian carcinoma with repeated effusions, likely indicating extensive disease burden and possible pericardial infiltration that was beyond the reach of local therapy[11]. Treatment failures in MPE are multifactorial. Possible reasons include:

1. **Tumor biology** – Highly aggressive or rapidly proliferating tumors may overwhelm local therapy.
2. **Effusion composition** – Hemorrhagic or protein-rich effusions may interfere with drug distribution and efficacy.
3. **Extent of pericardial involvement** – Diffuse pericardial infiltration may limit the ability of bleomycin to induce adequate sclerosis.
4. **Host factors** – Poor performance status, systemic disease progression, and prior therapies may compromise response.

These observations highlight the importance of patient selection. While intrapericardial bleomycin can provide meaningful palliation in many, clinicians must recognize that a subset of patients will not benefit, and alternative strategies such as repeat drainage, surgical pericardial window, or systemic therapy may be warranted[12].

Comparison with Other Sclerosing Agents

Several agents have been employed for intrapericardial sclerosis. Tetracycline and doxycycline, though widely used in the past, are associated with significant pain, fever, and variable efficacy. Talc, while effective in pleurodesis, carries a risk of systemic embolization and pericarditis when applied intrapericardially[13]. Cisplatin and mitoxantrone have been evaluated in small studies but are associated with systemic absorption and cardiotoxicity. In comparison, bleomycin offers a favorable balance of efficacy and tolerability, with a relatively low risk of systemic side effects when administered intrapericardially. This safety profile is particularly relevant in frail oncology patients who cannot tolerate systemic toxicity[14].

Safety and Tolerability

None of the patients in our series experienced significant adverse events attributable to bleomycin instillation. This is consistent with prior literature, which has demonstrated that systemic absorption of bleomycin after intrapericardial administration is minimal[15]. Reported adverse effects are generally mild, including transient fever or chest discomfort,

which were not observed in our cohort. Importantly, no cases of pulmonary fibrosis, the dose-limiting systemic toxicity of bleomycin, were encountered. These findings support the safety of intrapericardial bleomycin in palliative settings[16].

Clinical Implications

The results of this series reinforce the role of intrapericardial bleomycin as a viable palliative strategy for patients with MPE. By achieving both symptomatic relief and effusion control, this approach can substantially improve quality of life in individuals with advanced malignancy. Importantly, the absence of significant systemic toxicity allows its use even in patients receiving concurrent systemic chemotherapy. Clinicians, however, should remain vigilant for non-responders and consider early alternative interventions in such cases.

Limitations

The limitations of this study must be acknowledged. First, the small sample size limits the generalizability of findings. Second, the absence of a comparator group precludes direct conclusions regarding superiority over other interventions. Third, follow-up duration was limited to short-term outcomes; long-term recurrence and survival could not be adequately assessed due to the advanced disease stage of participants. Finally, the heterogeneous tumor types included may introduce variability in treatment response.

Future Directions

Future research should focus on prospective, multi-center studies with larger cohorts to better define predictors of response and resistance. Biomarker studies evaluating effusion cytology, fluid composition, and molecular characteristics of tumor cells may help identify patients most likely to benefit from intrapericardial bleomycin. Additionally, exploring combination approaches such as concurrent systemic immunotherapy with local bleomycin instillation may provide synergistic benefits.

Summary of Discussion

This case series highlights that intrapericardial bleomycin is an effective and safe treatment for malignant pericardial effusion, often providing durable palliation for most patients. Although there were treatment failures in two cases, it reinforces the importance of thoughtful patient selection and alternatives for non-responding patients. Intrapericardial bleomycin is a capability with a solid balance between efficacy, safety, and feasibility, thus presenting a viable treatment option in the multidisciplinary management of cancer patients with pericardial effusions.

CONCLUSION

This case series illustrates the therapeutic promise of intrapericardial bleomycin in the management of malignant pericardial effusion. Four of the cases illustrate significant symptomatic relief, progressive decrease in drainage volumes, and no recurrence during follow-up; all while demonstrating both effectiveness and safety. However, two non-responders illustrate that not all outcomes are favorable, and that tumor biology, effusion characteristics, disease burden, and other factors play a role in outcome. In summary, intrapericardial bleomycin may be a useful palliative treatment option that can improve quality of life in select patients with advanced malignancy; as with any intervention, careful selection of patients and attention to treatment failure is necessary.

Clinical Practice Points

- Intrapericardial bleomycin is safe and efficacious for malignant pericardial effusion, providing immediate symptomatic improvement and effusion control for most patients.
- Bleomycin has an acceptable safety profile and a lower incidence of systemic toxicity compared to other sclerosing agents.
- Treatment failure occurred in two of the six patients in this series, highlighting the concept that patients respond differently and recognizing indications of failure early allows for further options to be pursued.
- This approach should be considered palliative in the intention of treating advanced malignancy, especially when the traditional drainage is inadequate.
- Larger studies with bigger populations need to be conducted to improve patient selection and early treatment protocols for better patient outcomes.

REFERENCES

1. Maher ER, Buckman R. Intrapericardial installation of bleomycin in malignant pericardial effusion. Am Heart J. 1986 Mar;111(3):613-4. doi: 10.1016/0002-8703(86)90080-3. PMID: 2420163.
2. Thai V, Oneschuk D. Malignant pericardial effusion treated with intrapericardial bleomycin. J Palliat Med. 2007 Apr;10(2):281-2. doi: 10.1089/jpm.2006.0228. PMID: 17472493.

3. van der Gaast A, Kok TC, van der Linden NH, Splinter TA. Intrapericardial instillation of bleomycin in the management of malignant pericardial effusion. Eur J Cancer Clin Oncol. 1989 Oct;25(10):1505-6. doi: 10.1016/0277-5379(89)90112-0. PMID: 2480244.
4. Numico G, Cristofano A, Occelli M, Sicuro M, Mozzicafreddo A, Fea E, Colantonio I, Merlano M, Piovano P, Silvestris N. Prolonged Drainage and Intrapericardial Bleomycin Administration for Cardiac Tamponade Secondary to Cancer-Related Pericardial Effusion. Medicine (Baltimore). 2016 Apr;95(15):e3273. doi: 10.1097/MD.0000000000003273. PMID: 27082564; PMCID: PMC4839808.
5. Defruyt L, Özpak E, Gevaert S, De Buyzere M, Vandecasteele E, De Pauw M, Tromp F. Malignant cardiac tamponade: safety and efficacy of intrapericardial bleomycin instillation. Acta Clin Belg. 2022 Feb;77(1):51-58. doi: 10.1080/17843286.2020.1790180. Epub 2020 Jul 5. PMID: 32623970.
6. Lambert A, Salleron J, Kieffer A, Raymond P, Geoffrois L, Gavoille C. Intrapericardial instillation of bleomycin prevents recurrence of malignant pericardial effusions: Series of 46 cases and comprehensive literature review. Bull Cancer. 2020 Jul-Aug;107(7-8):756-762. doi: 10.1016/j.bulcan.2020.04.010. Epub 2020 Jun 5. PMID: 32513434.
7. Niclauss L, Montemurro M, Prêtre R. Survival after surgical drainage of malignant pericardial effusion. World J Surg. 2015 Jul;39(7):1767-72. doi: 10.1007/s00268-015-3025-5. PMID: 25708509.
8. Kunitoh H, Tamura T, Shibata T, Imai M, Nishiwaki Y, Nishio M, Yokoyama A, Watanabe K, Noda K, Saijo N; JCOG Lung Cancer Study Group, Tokyo, Japan. A randomised trial of intrapericardial bleomycin for malignant pericardial effusion with lung cancer (JCOG9811). Br J Cancer. 2009 Feb 10;100(3):464-9. doi: 10.1038/sj.bjc.6604866. Epub 2009 Jan 20. PMID: 19156149; PMCID: PMC2658533.
9. Cormican MC, Nyman CR. Intrapericardial bleomycin for the management of cardiac tamponade secondary to malignant pericardial effusion. Br Heart J. 1990 Jan;63(1):61-2. doi: 10.1136/hrt.63.1.61. PMID: 1690021; PMCID: PMC1024318.
10. Martinoni A, Cipolla CM, Civelli M, Cardinale D, Lamantia G, Colleoni M, DeBraud F, Susini G, Martinelli G, Goldhirsh A, Fiorentini C. Intrapericardial treatment of neoplastic pericardial effusions. Herz. 2000 Dec;25(8):787-93. doi: 10.1007/pl00001998. PMID: 11200128.
11. Yano T, Yokoyama H, Inoue T, Takanashi N, Asoh H, Ichinose Y. A simple technique to manage malignant pericardial effusion with a local instillation of bleomycin in non-small cell carcinoma of the lung. Oncology. 1994 Nov-Dec;51(6):507-9. doi: 10.1159/000227394. PMID: 7526307.
12. Maruyama R, Yokoyama H, Seto T, Nagashima S, Kashiwabara K, Araki J, Semba H, Ichinose Y. Catheter drainage followed by the instillation of bleomycin to manage malignant pericardial effusion in non-small cell lung cancer: a multi-institutional phase II trial. J Thorac Oncol. 2007 Jan;2(1):65-8. doi: 10.1097/JTO.0b013e31802c8260. PMID: 17410012.
13. Fukuoka M, Takada M, Tamai S, Negoro S, Matsui K, Ryu S, Sakai N, Sakaguchi K. [Local application of anti-cancer drugs for the treatment of malignant pleural and pericardial effusion]. Gan To Kagaku Ryoho. 1984 Aug;11(8):1543-9. Japanese. PMID: 6206796.
14. Woll PJ, Knight RK, Rubens RD. Pericardial effusion complicating breast cancer. J R Soc Med. 1987 Aug;80(8):490-1. doi: 10.1177/014107688708000811. PMID: 3656333; PMCID: PMC1290954.
15. Asai M, Kato Y, Kawai S, Watanabe K, Yomota M, Okuma Y, Hosomi Y, Hishima T, Okamura T. Management of cardiac tamponade during nivolumab of lung cancer with intrapericardial bleomycin: case report. Immunotherapy. 2019 Apr;11(6):467-472. doi: 10.2217/imt-2019-0003. Epub 2019 Feb 7. PMID: 30727791.
16. Escabí-Mendoza J, Berio R. Diagnosis and management of neoplastic pericardial effusion with cardiac tamponade; review of two case studies at the San Juan Veteran Administration Medical Center. Bol Asoc Med P R. 2005 Jul-Sep;97(3 Pt 2):192-206. PMID: 16320909.