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Case Report Three cases of black pleural effusion

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ARTICLE INFO	A B S T R A C T
Keywords:	Black pleural effusions (BPE) are rare, exudative pleural effusions that produce a black fluid on
Pleural effusion	thoracentesis. While the name and definition of this pathology is undeniably simple, the etiolo-
Empyema	gies, outcomes, and treatments for BPE are incredibly complex. Currently, BPE is not well-
Pancreaticopleural fistula	demonstrated in the literature. This case series reports three patients with different etiologies.
Pancreatic pseudocyst	past medical histories, presenting symptoms, treatments, and outcomes. BPE caused by pancre-
Esophageal rupture Pleural infection Pleural disease	atic-pleural fistula and opportunistic infections are demonstrated in this case series. This report shows that early identification and treatment of the underlying cause of BPE is critical to the re-
	covery of the patients.

1. Introduction

Black pleural effusions (BPE) are extremely rare, exudative pleural effusions that have a characteristic black appearance. On presentation, BPE will resemble the symptoms of any other pleural effusion: dyspnea, cough, and pleuritic chest pain [1]. Given its striking appearance, visualization of it should immediately call to mind a handful of distinctive differential diagnoses. Herein we describe three consecutive cases of black pleural effusion managed at our institution. We subsequently describe the current literature on this entity, including a summary of all reported cases that we were able to find to date.

2. Case 1

Our first patient was a 44-year-old female who presented with a 3-month history of worsening exertional dyspnea, along with acutely worsening left-sided abdominal pain, and decreased appetite. Her only significant past medical history was an episode of acute pancreatitis 2 years prior, which was treated conservatively at an outside facility. On admission, Computed Tomography (CT) of the chest showed a large left-sided pleural effusion with complete collapse of the left lung and a pancreatic tail pseudocyst. She was placed on supplemental oxygen via nasal cannula for her dyspnea. A 14-French pigtail chest tube was placed, with a return of 300mL of black fluid (Fig. 1-A). Pleural fluid analysis revealed an exudative fluid with low pleural fluid glucose, high pleural fluid amylase, and negative gram stain and culture (Table 1).

Other significant findings included hyponatremia (121 mmol/L), hypochloremia (83 mmol/L), Lactate Dehydrogenase (LDH) of 346 U/L, lipase of 33 U/L, and otherwise normal liver function test, normal complete blood count, and negative blood cultures.

She underwent an Endoscopic Retrograde Cholangiopancreatography (ERCP) with biliary sphincterotomy followed by an Endoscopic Ultrasound (EUS)-guided cyst gastrostomy on day 3 of admission (Fig. 2). Brown fluid was aspirated from the pancreatic

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Abbreviations: BPE, Black Pleural Effusion; PPF, Pancreaticopleural Fistula.

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Fig. 1. depicts pleural fluid samples collected from all cases (Left) Case 1 from the left hemithorax, (Center) Case 2 from the right hemithorax, (Right) Case 3 from the right hemithorax.

Table 1			
Pleural fluid	analysis	of all	cases.

	Case 1	Case 2	Case 3 Right	Case 3 Left
RBC Count	20,588/uL	14,250/uL	61,806/uL	2375/uL
WBC Count	51/uL	25,000/uL	45,007/uL	2183/uL
Neutrophils	58%	96%	99%	85%
Lymphocytes	9%	2%		
Monocytes/Macrophages	28%	2%	2%	6%
Eosinophils	5%	Few		1%
Mesothelial				1%
Glucose	33mg/dL (Serum = 82mg/dL)	31 mg/dL (Serum = $117 mg/dL$)	<1 mg/dL (Serum = 66mg/dL)	107 mg/dL (Serum = $100 mg/dL$)
LDH	859U/L (Serum = 346U/L)	192U/L (Serum = 957U/L)	1000U/L (Serum = 241U/L)	1011U/L (Serum = 380U/L)
Protein	3.2 g/dL (Serum = $6.8 g/dL$)	2.0g/dL (Serum = $4.7g/dL$)	2.1g/dL (Serum = $4.7g/dL$)	1.6g/dL (Serum = $4.7g/dL$)
Amylase	6554U/L	87U/L	>6554U/L	165U/L
Gram Stain and Culture	2+ PMN	1 + PMN	4+PMN	3 + PMN
	No organisms seen	Many E. faecium	2 + E. coli	No organisms seen
		1 + C. glabrata		

PMN = Polymorphonuclear Cells.

pseudocyst and grew *Streptococcus viridians*, treated with 5 days of Cefpodoxime and Metronidazole. She had persistent output from the left pleural drain without re-expansion, and was referred for Video-Assisted Thoracoscopic Surgery (VATS) drainage and decortication of approximately 80% of the left lung. As part of the operative management, three 28-French chest tubes were placed. Postprocedure her chest tubes were placed to suction at $-40 \text{ cm H}_2\text{O}$ for 4 days, then transitioned to water seal. Throughout this time she maintained normal oxygen saturation on room air. She was discharged from the hospital 16 days after admission, when her left lung had re-expanded and two of the chest tubes were removed. One chest tube was maintained at home connected to a chest drain, which was later removed on one-week outpatient follow-up.

3. Case 2

The second patient was a 36-year-old female, who presented to an outside facility with a chief complaint of lower abdominal pain radiating to her back which developed acutely over the past day. She had an extensive medical history which included Marfan syndrome, metastatic neuroendocrine tumor with liver involvement, history of perforated duodenum with intra-abdominal abscesses, endocarditis, and history of polysubstance abuse.

Prior to this admission, she had a 40-day hospitalization for abdominal pain and nausea. Workup during that time was notable for imaging consistent with ulcerations or contained perforation near the gastric antrum. Subsequent upper gastrointestinal (GI) series showed no evidence of leak. General surgery was consulted during that admission and recommended no surgical intervention. Her symptoms were ultimately attributed to her metastatic neuroendocrine tumor. During this admission she received supportive management with total parenteral nutrition and pain control. Once she had been stabilized, referrals were made for outpatient oncology. Her only symptom at discharge was nausea, which had been chronic throughout this admission. The nausea was attributed to her chemotherapy and compounded by self-induced emesis. She was discharged to home but returned after 1 day to the Emergency Department for worsening abdominal pain radiating to her back.

During evaluation in the Emergency Department, the patient also complained of mid-sternal, non-radiating chest pain. Her symptoms were associated with tachycardia and hypotension. Intravenous fluid resuscitation was initiated, as well as broad-spectrum antibiotics. Chest imaging was negative for pulmonary embolism or any aortic injury. She eventually required vasopressors for persistent hypoperfusion despite fluid administration. She continued to decline thereafter, lapsing into refractory shock. She was then transferred to our facility where she remained hypotensive and symptomatic despite all the above measures.



Fig. 2. (Top) Endoscopic ultrasound and endoscopy images identifying a single $15mm \times 19mm$ cyst found in the tail of the pancreas. (Bottom) Cyst gastrostomy with contrast injection confirming placement of the scope within the cavity of the cyst. Images in Fig. 2 show placement of double pigtail stents.

CT Chest demonstrated significant effusion in the mediastinum distal to the carina, new compared to Positron Emission Tomography (PET) scan completed recently as an outpatient. Bedside echocardiography was consistent with volume depletion, prompting additional fluid resuscitation with some interval improvement in mean arterial pressure. Unfortunately, she further declined with significant acidosis and was placed on mechanical ventilation. Post-intubation, a chest tube thoracostomy was done, with return of 200mL black "ink-like" fluid (Fig. 1-B). Analysis was consistent with an exudative effusion concerning for *C. glabrata* and *E. faecium* empyema given her profound shock (Table 1).

Other significant findings were neutropenia (2800/ μ L), lactic acidosis (2.7 mmol/L), pH 7.20/HCO₃/17.3 mmol/L/PO₂ 118 mm/Hg/PCO₂ 30 mm/Hg), creatinine of 1.29 mg/dL.

She had worsening metabolic acidosis and oliguria, requiring initiation of continuous renal replacement therapy (CRRT). Gastric access was difficult to maintain, and multiple feeding tubes demonstrated coiling in the thoracic esophagus. Serial laboratory testing later revealed a newly low hemoglobin of 5.5 g/dL, raising concern for esophageal perforation. Massive transfusion protocol was initiated, and thoracic surgery was consulted. Bedside esophagogastroduodenoscopy was done and showed a severe esophageal stricture at 30 cm, precluding further passage of the scope. A second pigtail chest tube was placed for persistent pneumothorax on imaging. A CT Angiogram of the chest, abdomen, and pelvis was performed, which revealed a small pocket of free air in the abdomen concerning for perforation, an increase in intra-abdominal fluid as well as a large abdominal wall hematoma (Fig. 3). She was taken for angiography and underwent embolization of her left superior epigastric artery early on the next morning.

Despite hemostasis, she remained in shock. Intra-abdominal pressures were measured to monitor for compartment syndrome, but were not significantly elevated. Her lactate rose despite continuous renal replacement therapy. She was taken to the operating room on the evening of admission day 2 for exploratory laparotomy and abdominal washout. She was found to have duodenal perforation, as well as pancreatic necrosis. Two Abramson drains were placed, and the abdomen was closed with a Barker type temporary closure.

While she had a transient improvement in vasopressor requirement post-procedure, she ultimately continued to decline. Her family said that she would not want to continue with these extraordinary measures. Her care was transitioned to palliative intent, and she expired shortly thereafter.



Fig. 3. (Top left) Axial cut of the patient's thorax demonstrating a larger hydropneumothorax on the right with complete collapse of the right middle and lower lobes. A right-sided pigtail catheter is partially visualized. (Bottom left): Axial cut of the patient's abdomen showing a large abdominal wall hematoma, intraabdominal fluid, and a small area of free air concerning for perforation. (Right) Angiogram showing extravasation of contrast from the superior epigastric artery. Gel embolization was then performed.

4. Case 3

Our third patient was a 43-year-old female with known *ansa pancreatica* with consequent recurrent acute pancreatitis, chronic pain syndrome, chronic obstructive pulmonary disease, and gastroenteric reflux disease, who presented to an outside facility with acute onset of cough, myalgia, malaise, and progressive dyspnea and orthopnea. Upon evaluation in the emergency department, point-of-care ultrasound revealed a right-sided fluid collection. Right-sided thoracentesis was performed, yielding black pleural fluid. She was notably hypoxemic, requiring 6 L of oxygen by nasal cannula and hypotensive on vasopressors. She was transferred to our hospital for further management.

Notably, 3 weeks prior to admission, the patient had an episode of acute pancreatitis. She underwent ERCP which revealed benign biliary papillary stenosis and choledocholithiasis. Biliary and pancreatic duct stents were placed, pancreatic and biliary sphincterotomies were also done. On that admission, she was incidentally found to have transudative right-sided pleural effusion felt to be due to pancreatic pseudocyst. This was managed with a temporary chest tube placement. She was eventually discharged home with supplemental oxygen.

Upon readmission to our hospital, a right-sided pigtail chest tube was inserted. 750mL of black pleural effusion was drained (Fig. 1-C). The aspirated fluid later grew *E.coli*, consistent with empyema (Table 1).

Other significant findings include leukocytosis with left shift, normal electrolytes and renal function, hypoalbuminemia, mildly elevated alkaline phosphatase, serum amylase 284 U/L, serum lipase 85 U/L, otherwise normal liver function tests, and negative blood cultures.

CT imaging showed sequelae of prior acute pancreatitis with thin tract between a small pancreatic pseudocyst and a rimenhancing fluid collection adjacent to the esophagus. Fistulation was suspected to the pleural space, consistent with pancreaticopleural fistula. A biliary duct stent was confirmed to be in place (Fig. 4).

The patient was treated with antibiotics, and gastroenterology consultation was obtained. After multi-disciplinary discussion, it was decided to insert a left-sided pigtail chest tube. By contrast, the left-sided fluid was yellow, serous, and hazy. Fluid analysis was consistent with a simple parapneumonic effusion (Table 1).

ERCP was performed with sludge removal, pancreatic duct stent placement, and common bile duct stent placement. She completed her course of antibiotics, and chest tubes were removed. She was discharged home in a stable condition with a 4-week course of IV Ceftriaxone.

5. Discussion

Pleural effusions are common with an estimated incidence of greater than 1.5 million cases per year. The most common etiologies are congestive heart failure, pneumonia, and cancer. Determining the underlying cause is imperative for appropriate treatment of the effusion, ensuring appropriate resolution and/or management of the fluid [2]. BPE is infrequently reported in the literature. Etiologies identified in literature to date include infections, pancreatic pseudocysts with pancreaticopleural fistula, metastatic melanoma, hemorrhage due to lung cancer, charcoal aspiration, teratomas, autoimmune conditions, and crack cocaine use [Table 2].

When encountering BPE in practice, the provider should combine thorough history-taking with pleural fluid analysis to determine the etiology. While BPE is a rare discovery, there are a limited number of etiologies in the differential diagnosis. The European Respi-



Fig. 4. (Top left and right) Axial and sagittal cut of CT chest with contrast showing a rim-enhancing fluid collection in the right lower lobe with a chest tube in the space. There is an adjacent rim-enhancing fluid collection along the medial aspect of the pleura adjacent to and running along the posterior mediastinum and esophagus, which terminates at the level of the diaphragmatic hiatus. This is suspected to be a fistula. (Bottom left) ERCP with cannulation of the pancreatic duct. After contrast injection, extravasation of contrast is seen from the pancreatic tail.

ratory Society published an interactive case highlighting the sequential thought process and management of a patient with BPE [3]. When the history is non-specific or multiple causes of the dark effusion are plausible, diagnostic tests are necessary. Beyond the usual studies included in Light criteria [5], black pleural fluid should be tested for pancreatic enzyme levels, amylase, cytopathology, and bacterial and fungal cultures.

A prior case series proposed mechanisms for the formation of black pleural effusion; these mechanisms can be broadly categorized into two major groups [4]. The first is the presence of black-pigmented material in the effusion, such as in *A. niger* empyema where the spores are known to be black in color, cytoplasmic melanin in melanoma cells, and aspiration of charcoal slurry. The second group is local inflammation, usually due to irritating substances such as pancreatic enzymes or blood with consequent liquefactive necrosis.

All three of our patients likely fall into the latter category. Case 2 had a viscus perforation with infiltration of intestinal material and blood into the abdomen and then into the mediastinum. The presence of *Candida* and bacteria in the pleural fluid supports this assumption [6]. *C. glabrata* is known to be part of normal endogenous flora. Where it was previously thought to be a nonpathogenic entity, it has since been documented to be associated with high rates of mortality when seen in immunocompromised patients [7]. *Candida* empyema in general is relatively rare but has been reported in cases of esophageal or gastric rupture [6]. There are presently no randomized trials to guide the optimal approach to treating *Candida* empyema, and mortality can be as high as 54% despite appropriate therapy [6].

Case 1 and 3 both suffered from chronic pancreatitis, complicated by pancreatic pseudocysts with spillage of peripancreatic fluid and enzymes into the pleural space, which represent the most reported cause for BPE. Of patients with chronic pancreatitis, 4.5% go on to develop pleural effusion [8]. Pleural effusion-formation in the setting of pseudocysts has been proposed by Saraya et al. [4] to form through anterior or posterior extension of the pseudocyst. Anterior disruption into the peritoneal cavity results in pancreatic ascites; posterior disruption causes a retroperitoneal fistula into the pelvis or superiorly through the esophageal or aortic hiatus. Finally, there may also be direct penetration through the dome of the diaphragm, such as in our case.

Endoscopic treatment of pancreatic pseudocysts is effective, with a 94% initial success rate and 90% cyst resolution rate. Approximately 16% of cases have cyst recurrence. Alternative strategies include surgery or percutaneous drainage [9].

In our review of the literature, 38 unique cases were found and are summarized (Table 2). The most common etiology was related to pancreaticopleural fistula or pancreatitis-related effusions (n = 15), followed very closely by neoplasia (n = 12). Using the approach to the cases as described by Saraya, as discussed above, most reported cases were within the second group of black effusion caused by liquefaction and necrosis (n = 30), with the remainder falling under the first group and consisting of a variety of black-pigmented materials (eg, crack cocaine-related charcoal pigment, charcoal slurry, *A. niger* spores). Most cases required additional interventions including surgery, endoscopic intervention, and medical management. While BPE tended to respond favorably to intervention, 9 cases resulted in mortality or transition to hospice care. All but 2 of these cases were related to metastatic malignancy.

Table 2

Black pleural effusions cases (A-LL).

Author	Age/Sex	Diagnosis	Management	Outcome
Watanabe et al.	57/M	Pancreaticopleural fistula; Acute on chronic	Tube thoracostomy	Effusion resolved
Ye, J. et al. [11]	64/M	Pancreaticopleural fistula; Suspected IgG4	Thoracentesis; Endoscopic pancreatic duct	Effusion resolved
Arumairaj, A.J. et	48/M	Pancreatic pleural effusion	Tube thoracostomy	Effusion resolved
ai. [12] Miyadera, K. et al. [13]	59/F	Pancreaticopleural fistula/Autoimmune pancreatitis	Endoscopic pancreatic sphincterotomy and pancreatic duct stent placement/Systemic steroids	Effusion resolved
Nikiforov et al.	27/M	Severe acute pancreatitis	Tube thoracostomy	Effusion resolved
Tanaka, T. et al.	55/M	Boerhaave syndrome	Thoracentesis; Surgical repair	Effusion resolved
Jagganath et al.	24/M	Pancreaticopleural fistula; Pancreatic pseudocyst	Tube thoracostomy, somatostatin analogue; Open cystogastrostomy	Effusion resolved
Newman et al.	34/M	Crack cocaine	Thoracentesis	Unknown
Ng, Z. et al. [18]	80/F	Metastatic adenocarcinoma with indeterminate primary; Complicated by intrapleural hemorrhage	Thoracentesis	Effusion resolved
Yousaf, Z. et al.	71/M	Metastatic adenocarcinoma with indeterminate	Thoracentesis; Tube thoracostomy; Wedge resection	Death
Ishigaki, S. et al.	54/F	Pancreaticopleural fistula/Pancreatic pleural effusion	Thoracic and endoscopic pancreatic duct drainage	Effusion resolved
Sumalani et al.	49/M	Metastatic melanoma	Thoracentesis	Death
Fernandez et al.	86/M	Metastatic adenocarcinoma of the lung	Thoracentesis	Death
Hirsche et al. [23]	65/F	Boerhaave Syndrome	Tube thoracostomy; Operative repair of esophageal rupture	Effusion resolved
Mansour et al. [24]	38/F	Thoracic endometriosis	Thoracentesis; VATS with pleurectomy; Hormonal therapy	Effusion resolved
Mitra et al. [25]	35/F	Mediastinal cystic teratoma	Exploratory thoracotomy; Surgical excision of mediastinal teratoma	Effusion resolved
Guo, F. et al. [26]	14/F	Pancreatic pseudocyst	Thoracentesis; Surgical internal jejunal drainage	Effusion resolved
Patel, G. et al.	63/M	Metastatic melanoma	Tube thoracostomy; Chemical pleurodesis	Effusion resolved; Transitioned to palliative care
Hirosawa et al.	58/M	Pancreaticopleural fistula; Pancreatic pseudocyst	Tube thoracostomy; ERCP; Endoscopic nasopancreatic drainage	Effusion resolved; Death due to unrelated cause
Mishe'el, S. et al.	77/M	Metastatic melanoma	Thoracentesis	Death
Thampy, E. et al. [30]	58/F	Metastatic mucinous adenocarcinoma of the lung complicated by intrapleural hemorrhage	Thoracentesis; Palliative chemotherapy	Persistent pleural effusion; Indwelling pleural catheter placement
Chhabra, A. et al. [31]	74/M	Metastatic melanoma	Bedside ultrasound-guided thoracentesis	Effusion resolved
Jayakrishnan, B. et al. [32]	56/M	Metastatic pulmonary adenocarcinoma complicated by massive pleural bleeding	Thoracentesis; Medical treatment for lung and prostate cancer	Persistent pleural effusion
George et al. [33] Kaur et al. [34]	38/M 37/F	Rheumatoid pleurisy Pancreaticopleural fistula: Pancreatic pseudocyst	Thoracentesis; Low dose prednisone therapy	Effusion resolved
Mookheriee et al	37/F	Pancreaticopleural fistula: Pancreatic pseudocyst	duct stent placement Tube thoracostomy: ERCP with pancreatic	Effusion resolved
[35] Huang et al. [36]	47/M	Panereation laural fictula: Panereatio pseudocyst	dust stenting Thoracenteeis	Death
Makino et al. [37]	39/M	Pancreaticopleural fistula; Pancreatic pseudocyst	Tube thoracostomy; Endoscopic	Effusion resolved
Koide et al. [38]	54/M	Pancreaticopleural fistula	Thoracentesis	Effusion resolved
Liao, W–C. et al. [39]	71/M	Metastatic melanoma	Tube thoracostomy	Effusion resolved; Further treatment declined
Mohan, K.M. et al. [40]	35/M	Metastatic melanoma	Tube thoracostomy followed by chemical pleurodesis	Recurrence of fluid; Lost to follow-up
Pantanowitz et al. [41]	88/M	Postoperative sympathetic pleural effusion; Crack cocaine	Thoracentesis	Unknown
_	46/M	Parapneumonic pleural effusion; Crack cocaine	Thoracentesis	Unknown

(continued on next page)

Table 2 (continued)

Author	Age/Sex	Diagnosis	Management	Outcome
Rojas-Solano, J.F.	89/M	Metastatic adenocarcinoma of the lung	Thoracentesis; Pleural biopsy	Effusion resolved; Transitioned
Lai, C–C. et al. [43]	46/M	<i>Rhizopus oryzae</i> empyema; History of acute myelogenous leukemia s/p allogeneic bone marrow transplant	Thoracentesis, antibiotics	Death
Singh, B. et al. [44]	34/M	Crack cocaine	Thoracentesis, pleural biopsy	Unknown
	45/M	Crack cocaine	Thoracentesis	Unknown
	Unknown	Crack and tobacco smokers; Primary pulmonary adenocarcinoma	Thoracentesis	Unknown
	Unknown	Crack and tobacco smokers; Metastatic melanoma	Thoracentesis	Unknown
Kimmerling, E.A. et al. [45]	64/M	Invasive Aspergillosis secondary to A. niger infection	Intravenous antibiotics; bronchoscopically guided intracavitary antibiotics	Death
Justiniani, F. et al.	25/M	Activated charcoal aspiration; Esophageal rupture	Tube thoracostomy; Antibiotics	Effusion resolved
Metzger. et al. [47]	63/M	Aspergillus niger infection; bacterial superinfection	Tube thoracostomy; Antibiotics; Right upper lobe lobectomy	Effusion resolved

Other types of black effusions exist within the human body. Most commonly, black ascites is associated with similar etiologies as described above for black pleural effusions with additional causes of ovarian cancer and leakage of fecal matter [48,49]. Black or very dark colored urine is uncommon, but the differential includes metastatic melanoma, alkaptonuria, porphyria and rhabdomyolysis [50]. Melanuria, or melanoma present in the urine, turns black after it has been exposed to the air due to oxidization and can be useful for diagnosing metastatic melanoma [51]. Rarely, black fluid has been associated with post operative fungal infections [52]. Black fluid from bronchoalveolar lavage samples during bronchoscopy of the lungs has also been reported; the causes are vast including copious carbon-laden macrophages from cigarette and synthetic marijuana [53,54]. There have also been case reports of black joint effusions from onchronosis secondary to alkaptonuria and melanosis from metal-on-metal joint replacements causing dark synovial fluid and synovium [55,56]. Overall, these effusions follow a similar suspected pathway to that of black pleural effusion with most caused by necrosis or pigment related effusions.

6. Conclusion

Black pigmentation is a highly unusual but distinctive finding in patients with effusions, and the distinctive color helps to narrow the differential. There are multiple causes for BPE, including pancreatic pseudocyst-formation with resulting fistulation into the pleura, and esophageal rupture as we have described in this case series and review of the literature. Recognition of potential differentials will aid in directing further investigations and therapy towards the underlying cause. Overall outcomes are favorable for BPE when related to pancreatic pseudocyst (often requiring a significant number of interventions) but are poor when associated with metastatic melanoma.

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Declaration of competing interest

None.

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