CASE REPORT

A young lady with massive black pleural effusion and a yellow pleura

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SUMMARY

A young lady presented to the out-patient department with a massive right pleural effusion. The cause remained unknown despite initial investigations and pleural fluid evaluation. She underwent a medical thoracoscopy which revealed black pleural fluid and dull thickened pleura with diffuse yellow plaques. The biopsy was suggestive of xanthomatous pleuritis, but the cause remained elusive. On further evaluation, pleural fluid amylase was found to be very high and magnetic resonance cholangio-pancreaticography (MRCP) demonstrated a pancreatic pseudocyst with a pancreatico-pleural fistula (PPF). Black coloured pleural fluid and xanthomatous pleuritis are rare features seen in pleural effusion secondary to PPF. Such patients generally have no abdominal complaints at presentation and hence a high index of suspicion is essential for diagnosis.

INTRODUCTION

The cause of a pleural effusion can remain unclear in many cases despite a detailed clinical history, physical examination, and pleural fluid analysis. Invasive procedures such as medical thoracoscopy or video assisted thoracoscopic surgery (VATS) should be considered in such patients. No diagnosis is ever established for approximately 15 percent of patients despite invasive procedures.[1] Black pleural effusions are rare with only 32 cases being reported to date. The cause of such effusions include malignancy, pleuro-pancreatic fistula, fungal infection, crack cocaine induced pleural effusion, Boerhaave hydropneumothorax, bronchopulmonary fistula and thoracic endometriosis.[2] Here we present an interesting case of a young female patient with a massive right sided black pleural effusion.

CASE REPORT

A female patient in her twenties presented to our out-patient department with a one-month history of dull, non-radiating right sided chest pain, dry cough, and progressively worsening dyspnea, which was now limiting her from walking up a slope or climbing stairs. She also had loss of appetite and generalised weakness. She denied history of fever, weight loss, or hemoptysis. There was no history of trauma or history of lifting heavy weights. She denied history of tuberculosis or recent contact with a tuberculosis patient. She had no history of recurrent respiratory tract infections, bronchial asthma, diabetes mellitus or cardiac disease. She denied smoking or consuming alcohol.

She was on regular thyroxine supplementation for hypothyroidism. She was diagnosed to have an ovarian cyst two months ago when she presented with abdominal pain and for which she underwent a laparoscopic cyst excision, which was confirmed to be a simple ovarian cyst.

She was initially evaluated at a local medical center where blood investigations revealed mildly elevated leucocyte count of 12450/ mm^3 and an elevated erythrocyte sedimentation rate (ESR) of 106mm/hr. Renal and liver function tests were normal. Chest radiograph revealed a white out right hemithorax (Figure 1A) which was confirmed to be a massive right pleural effusion by ultrasonography.

She underwent a diagnostic thoracentesis and 200 ml of dark coloured fluid was aspirated (Figure 1B). Results of pleural fluid aspiration were as follows: protein of 3.4 g/dl (total serum protein: 6.0 g/dl); sugar of 138mg/dl; total white blood cell count of 160/mm^3 (80% neutrophils) and adenosine deaminase (ADA): 28 U/L (normal: 0–40 U/L). Pleural fluid cytology was negative for malignant cells. Pleural fluid bacterial culture, fungal smear and geneXpert MTB/Rif were negative. She was referred to our centre for medical thoracoscopy as she had an undiagnosed, exudative pleural effusion.

On initial examination, her vital parameters were as follows: temperature 37.2^{0}C; pulse rate 96 beats/minute; respiratory rate: 20 breaths/minute; blood pressure 108/64 mmHg; oxygen saturation 97% on room air. She had no pallor, cyanosis, icterus, or lymphadenopathy. She did not have pedal oedema or signs of increased jugular venous pressure. On respiratory system examination, percussion revealed a dull note over the entire right hemithorax. Breath sounds and vocal resonance were decreased in the entire right hemithorax. Other systems examination was normal.

Computed tomography scan (CT scan) of the chest revealed a massive right pleural effusion with collapse of the underlying lung. No evidence of pleural thickening, parenchymal lesions or mediastinal lymphadenopathy was seen.

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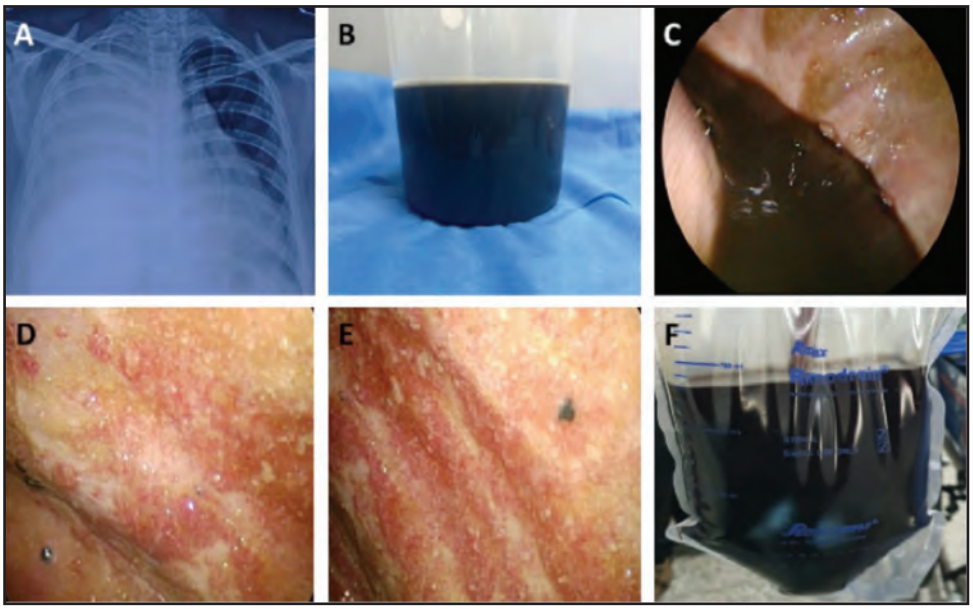

Fig. 1: A) Chest x-ray (PA view) showing complete white out right hemithorax with contralateral mediastinal shift. B) Black coloured pleural fluid obtained during diagnostic thoracocentesis. C) Black coloured pleural fluid visualised within the pleural cavity during medical thoracoscopy. D), E) Dull, thickened pleura with diffuse, yellow-coloured plaques and multiple small nodules seen on medical thoracoscopy. F) Black coloured pleural fluid collected in under water seal bag, connected to intercostal drain.

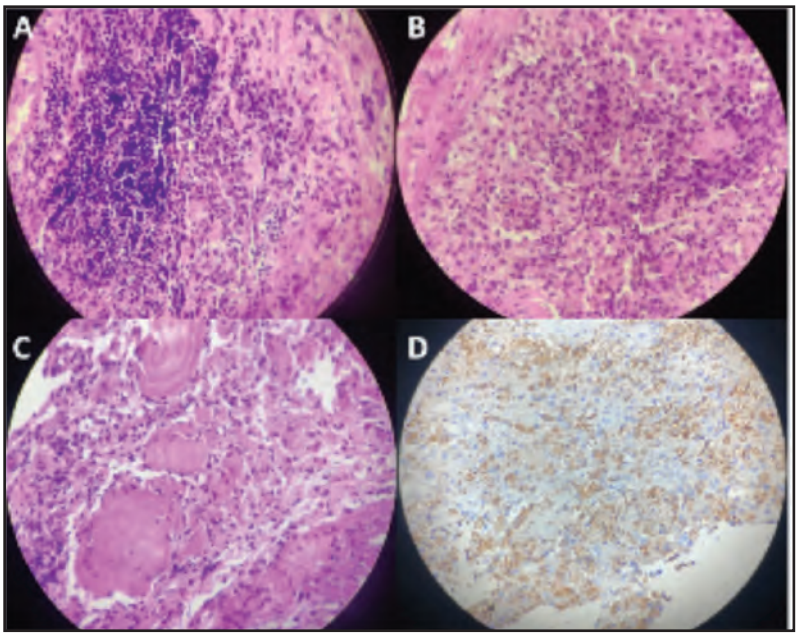

Fig. 2: A) Photomicrograph showing markedly inflamed pleural tissue with lymphocytes and plasma cells, original magnification 40X (H&E stain). B) Photomicrograph showing aggregates of foamy macrophages with lymphoplasmacytic cells, original magnification 40 X (H&E stain). C) Photomicrograph showing fibrinoid necrosis and inflammatory infiltrate within the pleural tissue, original magnification 40X (H&E stain). D) Photomicrograph shows aggregates of foamy macrophages diffusely positive for CD 68, original magnification 40 X (H&E stain).

After taking informed consent, medical thoracoscopy was performed. Procedure was performed under sedation and intercostal nerve block using a Karl Storz mini-rigid thoracoscope. Thoracoscopy revealed black coloured fluid in the pleural space (Figure 1C) and dull, thickened pleural with diffuse yellow plaques and small nodules (Figure 1D,1E). During the procedure, 1800 ml of black coloured pleural fluid was drained (Figure 1F), and ten parietal pleural biopsies obtained from abnormal areas. Microscopic examination of the pleural biopsy showed markedly inflamed pleural tissue with aggregates of foamy macrophages and lympho-plasmacytic cells with few scattered eosinophils (Figure 2A, 2B). Capillaritis, microthrombi, hemosiderin laden macrophages and fibrinoid necrosis were also seen (Figure

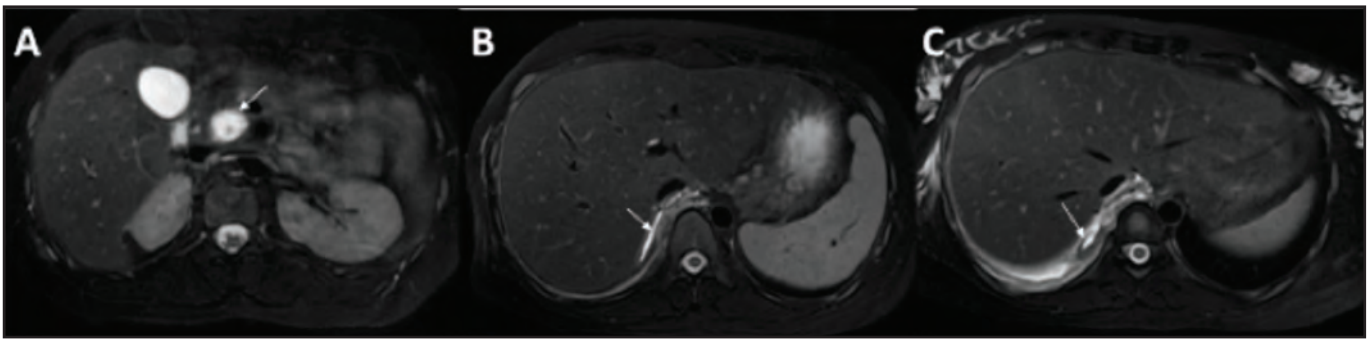

Fig. 3: A) Image of magnetic resonance cholangio-pancreaticography (MRCP) showing a pseudocyst (white arrow) in the region of uncinate process. B) Image of MRCP showing a fistulous tract (white arrow) along the crus of the diaphragm in the midline. C) Image of MRCP showing a fistulous tract opening into the right pleural cavity (white arrow).

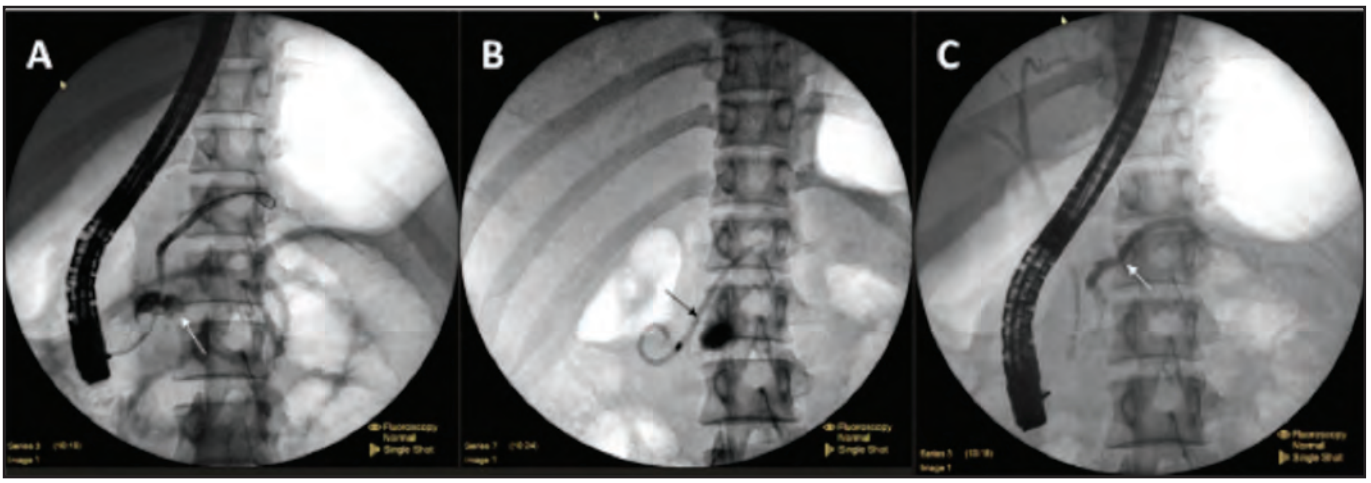

Fig. 4: A) Fluoroscopy image of endoscopic retrograde cholangio-pancreaticography (ERCP) showing a pancreatic duct communicating with the pseudocyst (white arrow). B) Fluoroscopy image of ERCP showing the stent in situ in the pancreatic duct (Black arrow). C) Fluoroscopy image of ERCP showing normal pancreatic duct (white arrow) and resolution of the pseudocyst.

2C). There were no granulomas or atypical cells. Immunohistochemistry revealed CD68 positive foamy macrophages (Figure 2D). A histopathological diagnosis of xanthomatous pleuritis was made. Post-procedure a 24 Fr intercostal chest was placed, and her daily pleural fluid drain output ranged from 500 ml to 700 ml. The cause of her pleural effusion remained unclear.

In view of the history of abdominal pain and black coloured pleural effusion, the possibility of pleural effusion secondary to pancreatitis was entertained. Pleural fluid amylase was performed and found to be very high (103420 U/L). Serum amylase and lipase were mildly elevated at 157 U/L and 511 U/L, respectively. Serum calcium and serum triglycerides levels were within normal limits. In view of her very high pleural fluid amylase levels (>50,000 U/L), a possibility of pancreatico-pleural fistula (PPF) was considered.

To confirm PPF, magnetic resonance cholangio-pancreaticography (MRCP) was performed. It demonstrated a well-defined collection measuring 3.6 x 2.1 cm with internal debris in the region of the uncinate process, which was likely to be a pseudocyst (Figure 3A). A linear tract was seen extending posteriorly from this pseudocyst and coursing along the crus of the diaphragm in the midline and communicating with the right pleural cavity (Figure 3B, 3C). There was no evidence of calculi or sludge in the gall bladder and biliary tree. In view of the above findings a diagnosis of xanthomatous pleuritis secondary to a pancreatico-pleural fistula caused by idiopathic pancreatitis was made.

Patient underwent an endoscopic retrograde cholangio-pancreaticography (ERCP) which showed the pancreatic duct communicating with the pseudocyst (Figure 4A). Sphincterotomy was performed and a 5fr, 7cm pigtail stent was placed in the pancreatic duct (Figure 4B). Soon after the pancreatic duct stenting the daily quantity of pleural fluid drained, started to decrease. Intercostal drain was removed after 10 days when pleural fluid drain decreased to less than 50ml/day for 3 consecutive days and after ultrasonography of the chest showed no residual pleural effusion.

Patient is currently under regular follow up with no recurrence of abdominal pain or pleural effusion. The pancreatic duct stent was removed after 3 months when repeat pancreaticogram showed resolution of the pseudocyst (Figure 4C).

Table I: Clinical details of published cases with black pleural effusion due to pancreatico-pleural fistula

	Author/Year	Age/Sex	Symptoms at presentation	Side of effusion	Pleural fluid Amylase	Mode of Diagnosis	Treatment
1	Koide *et al*/2012	54/M	Dyspnoea	Left	5292 IU/L	CT scan	Conservative
2	Huang *et al*/2013	47/F	Dyspnoea	Left	53600 IU/L	CT Scan	Conservative
3	Kaur *et al*/2014	37/F	Dyspnoea/Chest Pain	Right	23000 U/L	CT Scan	ERCP-Pancreatic Duct Stenting
4	Mookherjee *et al*/ 2014	37/F	Right Chest pain/ Dyspnoea	Right	26673 IU/L	MRCP	ERCP-Pancreatic Duct Stenting
5	Hirosawa *et al*-2016	58/M	Left Chest pain/ Dyspnoea	Left	10649 IU/L	CT Scan/ERCP	ERCP-Pancreatic duct stenting
6	Guo e*et al*/2017	14/F	Cough, Right Chest Pain	Bilateral Right>Left	NA	MRCP	Surgery
7	Ishigaki *et al*/2018	54/M	Asymptomatic	Right	4752U/L	CT Scan/ERCP	NA
8	Index case	26/F	Dyspnea, dry cough and dull chest pain	Right	103420 U/L	MRCP	ERCP-Pancreatic duct stenting

CT: Computed tomography; ERCP: Endoscopic retrograde cholangio-pancreaticography; IU/L : International units per litre; MRCP: Magnetic resonance cholangio-pancreaticography; NA: Not available.

Table II: Clinicoradiologic details, diagnosis and outcomes of reported cases of xanthomatous pleuritis.

Sl. No	Author/year	Age (Years)/ Sex	Symptoms at presentation	Radiology	Pleuroscopic appearance	Final Diagnosis	Treatment received/ Recurrence at follow up
1	McGuire et al/ 2009	69/Female	Pleuritic chest pain, dyspnea	Massive Left PE	Two plaques with petechial hemorrhage	Unclear	Steroids/ No recurrence at 18 months
2	Singh et al/ 2018	21/Male	Dyspnea, chest pain	Moderate Left PE	Greyish pigmented pleura	Unclear Unclear	Oral amoxicillin 6 weeks/ No recurrence at 3 months
3	Bateman et al/ 2020	54/Male	Dry cough, dyspnea, joint pains	Moderate Left PE	Diaphragmatic mass with yellow pleural plaques	Unclear	Oral steroids/ Recurrence at 10 months
4	Nakashima et al/ 2022	62/Male	Dyspnea	Left PE	Diffuse yellow plaques	Pancreatico-Pleural Fistula	Distal pancreatectomy/ Follow up details NA
5	Augustine et al/ 2022	27/Female	Dyspnea, Chest Pain, Fever	Moderate Left PE	Xanthomatous Pleuritis	Tubercular Pleural Effusion	Anti-Tubercular Treatment/ No recurrence at 1 year
6	Present report	24/Female	Dyspnea, dry cough and dull chest pain	Massive Right PE	Diffuse yellow plaques	Pancreatico-Pleural Fistula	ERCP pancreatic duct stenting/ No recurrence at 6 months

ERCP: Endoscopic retrograde cholangio-pancreatiography; NA: Not available

DISCUSSION

Pleural effusions are a common complication of pancreatic disease with the latest reports suggesting that they occur in nearly 50% of the patients with acute pancreatitis. Various mechanisms have been described for the development of pleural effusion which includes transdiaphragmatic lymphatic blockage, exudation of fluid into the pleural cavity from the subpleural diaphragmatic vessels and formation of pleuro-pancreatic fistula.[3]

Black pleural effusion or soy sauce pleural effusion has been reported in only 32 cases to date. The causes of black pleural effusion range from malignancy (14 patients), pleuro-pancreatic fistula (8 patients), acute pancreatitis (1 patient), fungal infections (3 patients), crack cocaine induced pleural effusion (2 patients) Boerhaave hydropneumothorax, bronchopulmonary fistula and thoracic endometriosis (1 patient each).[2] Clinical details of cases of PPF leading to black pleural effusion are shown in Table I.

In patients with pancreatico-pleural fistula, necrotic pancreatic and ascitic fluid traverse the fistulous connection to reach the pleural cavity resulting in a black coloured pleural effusion.[4,5] The most common presenting symptom in these patients was dyspnoea followed by chest pain, cough, fever, and abdominal pain. Seven patients had exudative effusion while one had transudative effusion. Recurrence was seen in four patients and one patient died.[2]

Pancreatic fistulas are rare and usually seen as a complication of alcoholic pancreatitis.[6] They are seen in 0.4% to 7% of chronic pancreatitis patients and in 6% to 14% of patients with pancreatic pseudocyst.[7] Pancreatico-pleural fistulas develop either as a consequence of pseudocyst rupture or disruption of posterior wall of the pancreatic duct.[8] It is usually seen in middle aged men, and they present with pulmonary symptoms. Up to half of them have no history of pancreatitis. Our patient was a young female with no addictions. While she had a history of abdominal pain

attributed to an ovarian cyst previously, she had no abdominal complaints at presentation.

Pancreatico-pleural fistulae related pleural effusions are usually moderate to massive and predominantly left sided. Right and bilateral pleural effusions are seen in 19% and 14% of the patients, respectively. Pleural fluid analysis usually reveals an exudative pleural effusion with extremely elevated pleural fluid amylase levels.[9] While high amylase can be seen in many conditions such as acute pancreatitis, oesophageal rupture, lymphoma and other malignancies, levels above 50,000U/L are seen only in PPF. MRCP is the diagnostic modality of choice as it is non-invasive and demonstrates the fistulous connection, pancreatic parenchymal and ductal structural changes, and the presence of intra or extra pancreatic pseudocysts.[10]

Xanthomatous inflammation is a rare, benign type of chronic inflammation which has generally been reported from organs such as the kidney, gall bladder, appendix, prostrate etc. It is characterised by the presence of foamy macrophages admixed with lymphocytes, plasma cells, neutrophils, and multinucleated giant cells.[11] Xanthomatous inflammation of the pleura is extremely rare with only five cases[12-15] being reported till date (Table II) of which only one was secondary to PPF. Like in the previous case report, our patient had diffuse yellow plaques over the pleural surface.[15] Chronic inflammation secondary to presence of pancreatic enzymes in the pleural cavity and the overwhelming of the lysosomal system of the macrophages due to the ingestion of erythrocytes and platelets from the haemorrhagic effusion causing deposition of phospholipids, are likely to be the mechanisms of xanthomatous inflammation of the pleura secondary to PPF.[18 -23] Ours is the first case to be reported of a black pleural effusion with xanthomatous pleuritis, secondary to PPF.

PPF can be managed medically, endoscopically, and surgically. Medical management consists of pleural fluid drainage and reducing pancreatic exocrine secretions using a combination of octreotide and total parenteral nutrition. The success rate of medical management is moderate, and failure leads to higher rate of complications and prolonged treatment. ERCP with pancreatic duct stenting is the current treatment of choice and can be combined with octreotide administration. It aims to restore the anatomic continuity of the pancreatic duct to provide a path of lower resistance for the pancreatic secretions to flow into the duodenum allowing time for the fistulous connection to heal. Surgery is used as a last resort, only if medical and endoscopic management fails.[9,10] Our patient was successfully managed with pleural fluid drainage using intercostal drain and pancreatic duct stenting.

CONCLUSION

Black pleural effusion is a rare presentation of PPF. It can present as a right sided pleural effusion with no abdominal complaints. Having a high index of suspicion is essential. Presence of black coloured pleural effusion, a very high amylase level (>50,000 U/L) and/or yellow plaques on pleura should raise the suspicion of a PPF, and it should be evaluated accordingly. MRCP is the diagnostic modality of choice, and PPF can be successfully managed with minimally invasive endoscopic techniques.

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DECLARATION

All the authors of this manuscript declare no competing interest or any financial support being received. Informed consent has been obtained from the patient.

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