



Case report

A chocolate effusion – An unusual cause of elevated adenosine deaminase in the pleural fluid

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ABSTRACT

Background: Thoracic Endometriosis Syndrome (TES) is a rare diagnosis characterized by ectopic endometrial tissue in the chest. Pleural fluid adenosine deaminase (ADA) is thought to be highly specific for tuberculous pleural effusions, particularly when >40 IU/L (international units/liter).

Results: A 36-year-old woman from Cameroon (immigrated 10 years ago) with no past medical history presented to the emergency department with increasing abdominal swelling over months found to have on imaging ascites, a left adnexal lesion, a large right-sided pleural effusion and peritoneal studding. Sampling of the pleural fluid revealed dark brown fluid which on analysis was a non-specific exudate with an adenosine deaminase >100. Exploratory laparotomy by gynecology-oncology revealed a large amount of hemorrhagic ascites, multiple endometriotic implants, and a right ovarian endometrioma. Ultimately the patient was taken for video-assisted thoracoscopy (VATS) and decortication. The VATS revealed a diaphragmatic tear was seen suggesting the etiology of the pleural fluid was *trans*-diaphragmatic passage of blood through the defect. There was no evidence of malignancy or granulomas. Stains and subsequent cultures were negative on all specimens for *Mycobacterium tuberculosis*.

Discussion: Our case demonstrates a rarity of an ADA >100 IU/L due to TES rather than tuberculosis. In conclusion, ADA analysis, as with any lab test, should be interpreted within clinical context as false positives may occur. Several weeks following presentation the patient was discharged without any intrapleural catheter and near complete expansion of the lung. She was started on leuprolide and medroxyprogesterone and has no recurrent effusion or ascites in over two years since initial presentation.

1. Case presentation

A 36-year-old woman from Cameroon (immigrated 10 years ago) with no past medical history presented to the Emergency Department with increasing abdominal swelling over months. She had no respiratory symptoms, no abdominal pain, no constitutional symptoms such as fever or weight loss, and reported prior negative tuberculin skin testing.

2. Physical exam

Physical exam was notable for normal vitals. She appeared healthy. Heart exam was normal without murmurs, rubs or gallops. She had absent breath sounds on auscultation of the right lung, clear breath sounds on the left, and a distended non-tender abdomen with a fluid wave. She had no edema of her lower extremities.

3. Diagnostic studies

Complete blood count and basic metabolic profile were remarkable only for a mild anemia (hemoglobin of 11.9 g/dL). A Computed Tomography (CT) scan of the chest (Fig. 1) revealed complete opacification of the right hemithorax with right lung collapse and mediastinal shift to the left consistent with large pleural effusion. CT of the abdomen and pelvis demonstrated extensive abdominal ascites with nodularity of the peritoneum and a left adnexal cystic lesion (Fig. 2). A follow-up ultrasound of the abdomen revealed a complex cystic lesion within the left ovary concerning for a possible ovarian malignancy. Chest tube placement drained dark brown pleural fluid (Fig. 3) that was exudative and negative for bacterial and fungal cultures as well as *Mycobacterium tuberculosis*. Cell count revealed 490 nucleated cells/high-power field and 59% histiocytes and 273,000 RBCs/HPF (Fig. 4). Cytology was sent

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Fig. 1. CT of chest revealing large right pleural effusion with right lung collapse and mediastinal shift to the left.



Fig. 2. CT of abdomen and pelvis revealing abdominal ascites, nodularity of the peritoneum and left adnexal cystic lesion.

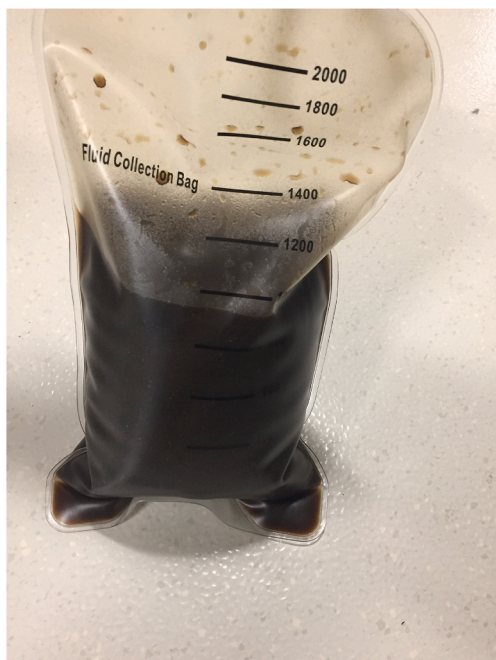


Fig. 3. Photograph of pleural fluid following chest drainage with a chest tube.

and was negative. Notably, there was a markedly elevated ADA of 102.4 IU/L. A paracentesis revealed similar dark brown fluid with comparable cellular characteristics (Fig. 4).

Further work-up including tumor markers (cancer antigen-125, carcinogenic embryonic antigen, and cancer antigen 19–9) were all within normal limits. Interferon gamma release assay assessing for prior exposure to tuberculosis was negative. Patient was subsequently taken for exploratory laparotomy by gynecology-oncology which revealed a large amount of hemorrhagic ascites, multiple endometriotic implants, and a right ovarian endometrioma. Pathology of biopsy specimens from the right ovary, peritoneal implants and left ovarian fossa were consistent with a diagnosis of endometriosis from all samples. The patient was sent for video-assisted thoracoscopy. Decortication was performed on the thin fibrous peel surrounding the left lung. A 2 mm defect in the R medial diaphragm was identified and closed. Pathology of the pleural peel revealed reparative and reactive changes including chronic inflammation and granulation tissue. There was no evidence of malignancy or granulomas. Smears and cultures were negative on all specimens for *Mycobacterium tuberculosis*.

4. Discussion

Given patient's new diagnosis of peritoneal endometriosis from patient's exploratory laparotomy, and the right sided diaphragmatic tear, the patient was diagnosed with a rare presentation of thoracic endometriosis syndrome.

Thoracic Endometriosis Syndrome (TES) can have a variable presentation with 73% presenting as pneumothorax, 14% as hemothorax, 7% as hemoptysis and 6% as nodules [1]. The pathophysiology of how endometrial tissue migrates into the thoracic cavity is unclear. It is thought is that endometrial tissue travels directly to the thorax via diaphragmatic fenestrations [2–4]. It is unknown whether this represents a congenital defect or direct erosion by endometrial implants [5]. Although VATS did not reveal evidence of endometrial deposits, the constellation of findings including peritoneal endometriosis and pleural fluid that mirrors the peritoneal endometrial bloody ascites, are most consistent with this diagnosis.

We find it important to highlight the elevated adenosine deaminase level in this setting. Pleural fluid ADA is typically considered highly specific for tuberculous pleural effusions, particularly when >40 IU/L. In the meta-analysis by Liang et al. mean specificity when using ADA of 40 IU/L as a cutoff is 0.9 [6]. Cell-mediated immunity and thus T-lymphocytes play an important role in the immune response to tuberculosis. It has been suggested that adenosine deaminase, an enzyme involved in purine metabolism, is in causal relationship with the T-cell response [7]. Given that physiologically that adenosine is a sign of cell-mediated immunity, it is no surprise that there are diagnoses other than tuberculosis in which elevated ADAs have been described. False positive ADAs are rare but have been demonstrated in lymphocytic predominant effusions in the setting of parapneumonic effusions and lymphoma related effusions [8]. Additionally, in the setting of non-lymphocytic predominant effusions such as our case (Fig. 4), false positive ADAs have been described in multiple diagnoses and notably in the setting of empyema [9]. To our knowledge we are reporting the first case of an elevated ADA in the setting of thoracic endometriosis syndrome.

Our case demonstrates a rarity of an ADA >100 IU/L due to TES rather than tuberculosis. In conclusion, ADA analysis, as with any lab test, should be interpreted within clinical context as false positives may occur.

5. Clinical course

Following the VATS and decortication, the lung was only partially re-inflated. Patient's hospital course was complicated by pleural space infection. Several weeks following presentation the patient was discharged without any intrapleural catheter and near complete expansion

	Pleural Fluid	Peritoneal Fluid
Color	Dark Brown	Dark brown
LDH fluid/serum (U/L)	1083/231	--
Protein fluid/serum (G/DL)	6.4/6.6	--
RBCs	273,000	312,000
Total Nucleated Cells	460 (59% histiocytes, 10% lymph, 25% mono, 3% poly)	681 (60% histiocytes, 27% lymph, 9% mono, 1% poly)
Culture/Gram stain	Negative	Negative
Adenosine Deaminase (U/L)	102.4	--

Fig. 4. Pleural fluid and peritoneal fluid characteristics.

of the lung. She was started on leuprolide and medroxyprogesterone and has no recurrent effusion or ascites two years since initial presentation.

Grant

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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