

A Case Report on Possible Side Effect of Eteplirsen

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Disclosure

- We have no actual or potential conflict of interest in relation to this presentation

Duchenne Muscular Dystrophy (DMD)

- A fatal neuromuscular disorder affecting around one in 3,500–5,000 male births
- Characterized by progressive muscular deterioration
- Inherited in an X-linked recessive fashion
- Caused by loss-of-function mutations in the DMD gene coding for dystrophin
- Dystrophin: a cytoskeletal protein that stabilizes the plasma membrane of muscle fibers

Eteplirsen

- Also known as AVI-4658
- Designed for treatment of patients with DMD having mutation of the dystrophin gene amenable to exon 51 skipping (~13% of total cases of DMD)
- Promotes dystrophin production by restoring the translational reading frame

Eteplirsen

- Approved by the US Food and Drug Administration (FDA) in September 2016
- The first and currently only FDA-approved drug for DMD
- Granted accelerated approval on the basis of surrogate end-point results that showed increase dystrophin levels in patients

Reported Side Effects

- Procedural pain (75%)
- Proteinuria (62%)
- Vomiting (50%)
- Hypokalemia (50%)
- Back pain (50%)
- Headaches (50%)
- Balance disorder (50%)

Case Description

- 16 year old non-ambulatory Caucasian male diagnosed with Duchenne Muscular Dystrophy (DMD)
- Has exon 52 deletion
- Started treatment with Eteplirsen in March 2017

Case Description

- Tolerated the first eight infusions well
- Improvement noted in upper extremity functionality by the family
- No side effects reported

Case Description

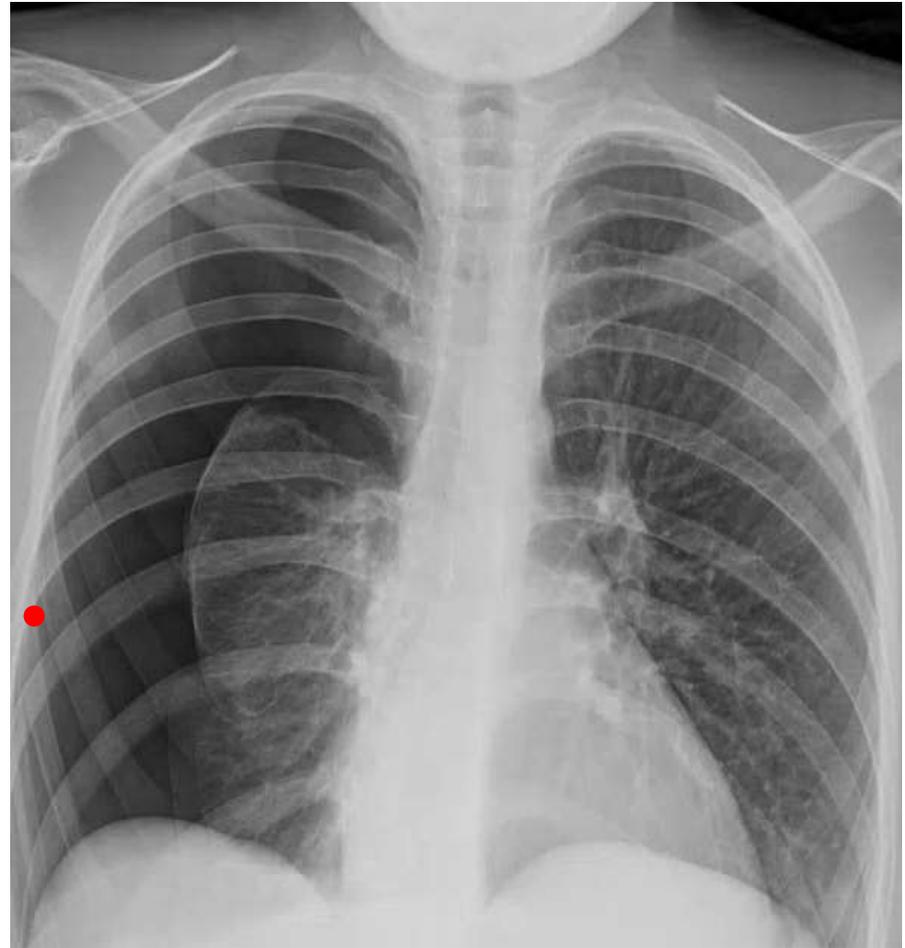
- Three days after eighth infusion, patient complained chest pain
- No fever, cough, cold, shortness of breath, nausea, vomiting
- No h/o similar complaints in the past
- No family members acutely ill
- Flu vaccination up to date

Case Description

- Was evaluated in ER for c/o chest pain
- Described as anterior chest wall pain, sharp, moderate to severe in intensity, non-radiating
- Vitals signs stable
- Exam revealed severely reduced breath sounds over the right lung fields

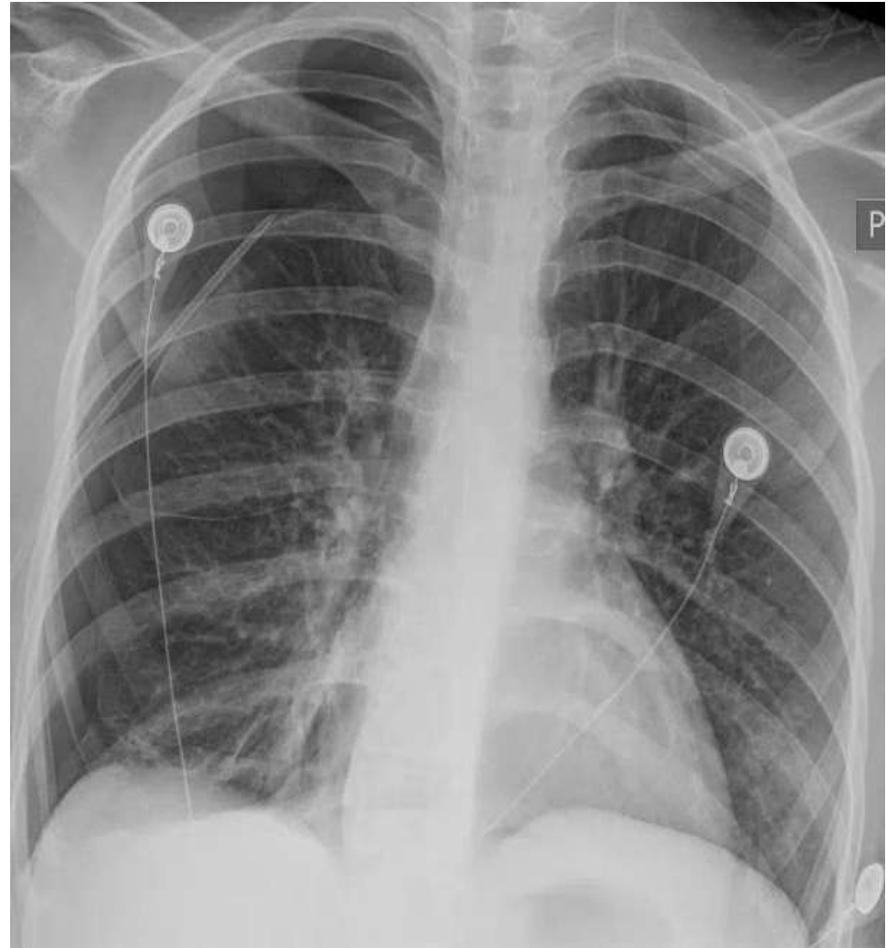
On ER presentation

Chest X-ray (CXR)
revealed 70%
pneumothorax on
right side



After chest tube placement (Day 1)

- Chest tube placed in ER
- Repeat x-ray after chest tube placement showed improvement in pneumothorax by only about 10%

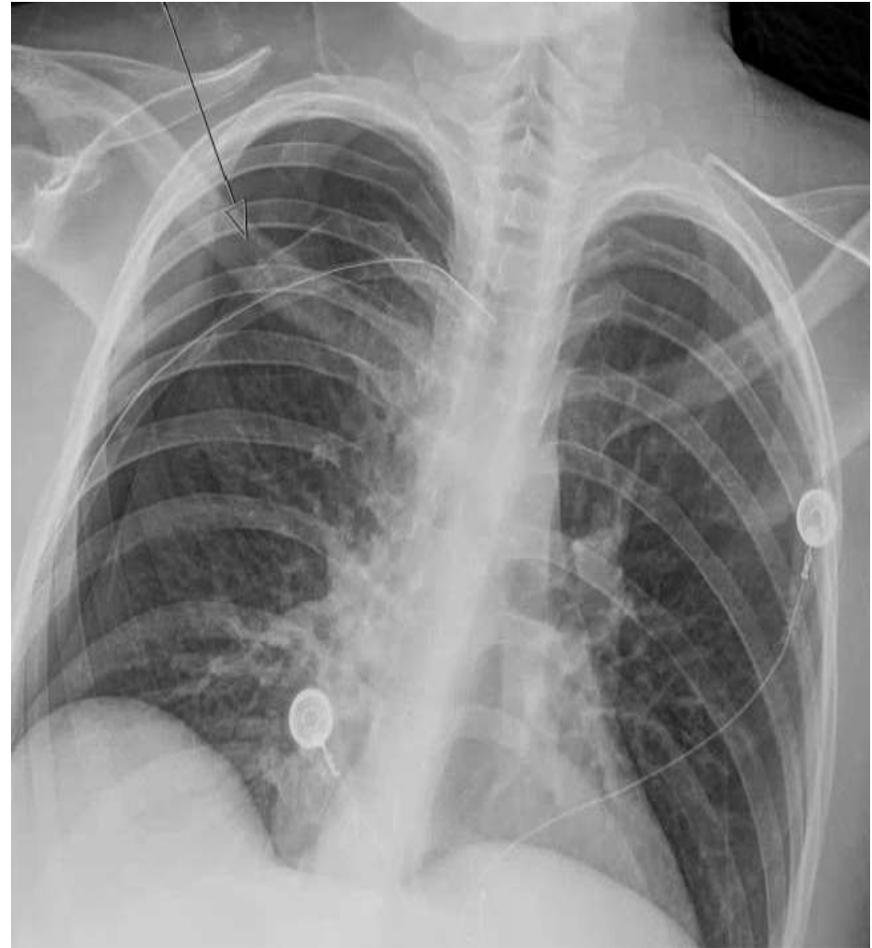


Case Description

- Chest tube changed due to inability to keep the lungs expanded
- Continued to have significant air leak
- Slight worsening of the pneumothorax even after one week of non-operative management

Pre-surgical CXR (Day 8)

Decision made to proceed with surgical management

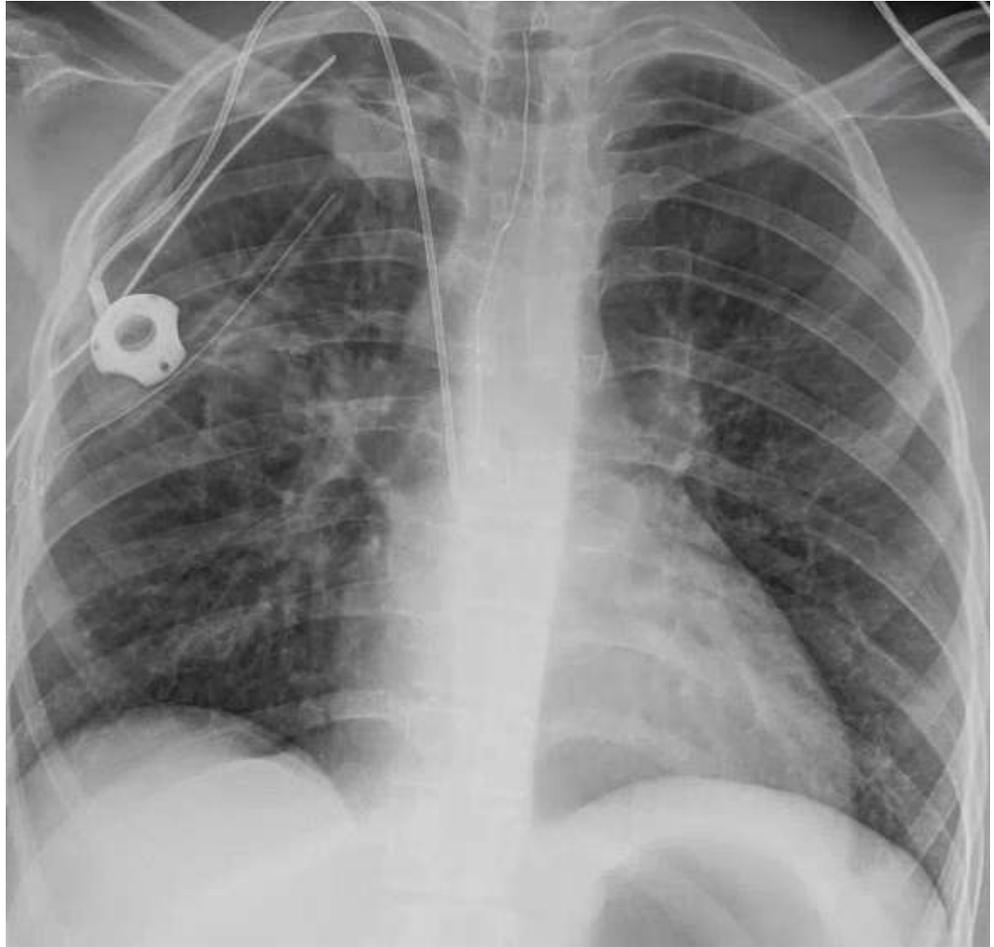


Case Description

- Patient underwent Video Assisted Thoracoscopic Surgery (VATS) on Day 8
- Found to have blebs at the right lung apex as well as at the anterior portion of the superior lobe
- Underwent wedge resection
- Pleurodesis was done over 80% of the thorax

Post-surgical CXR (Day 8)

Only 10-15%
pneumothorax
present post
procedure



Case Description

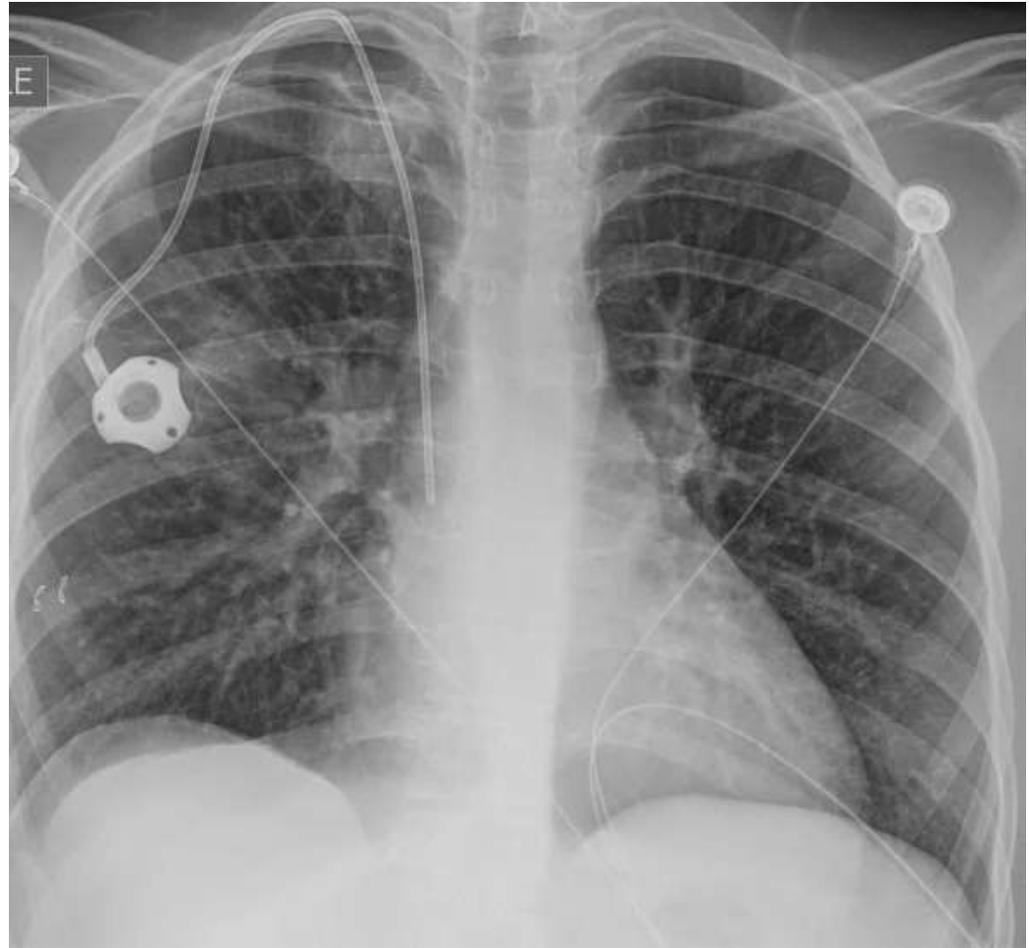
- Pathology report on the resected portion of lung tissue:
 - Subpleural blebs
 - Pleuritis with chronic inflammation, eosinophils and giant cell reaction
 - Alveolar hemorrhage, edema, vascular congestion, chronic inflammation and focal emphysematous change
 - No evidence of granulomas or malignancy

Case Description

- Chest tube removed 5 days after surgery (Day 13)
- Complete resolution of pneumothorax noted on the follow up CXR

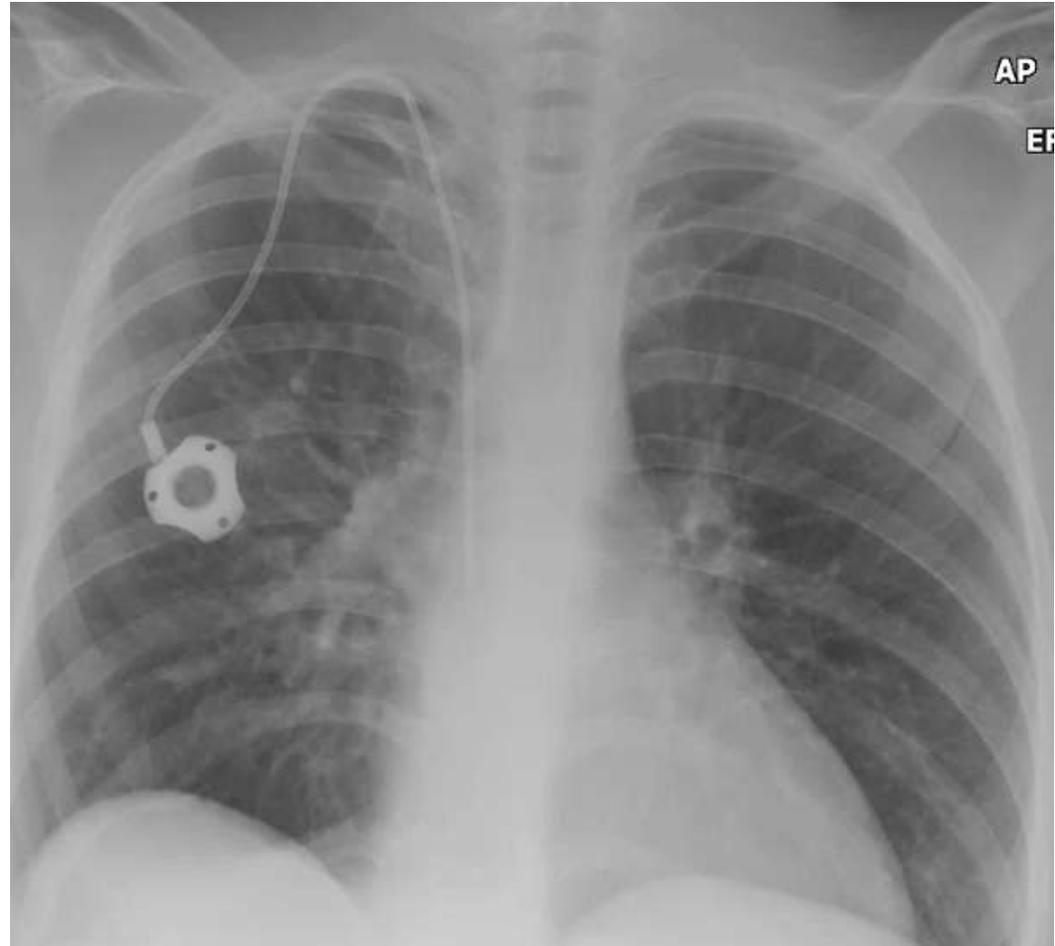
Day of discharge (Day 14)

Patient
discharged
home in stable
condition



Outpatient follow up CXR (Day 19)

Follow up CXR showed no acute cardiopulmonary process



- About 150 patients had been treated with eteplirsen by this time
- Pneumothorax was yet to be reported
- No other possible cause of pneumothorax could be found
- Family chose to continue treatment with eteplirsen
- Patient doing well on follow up with neurology, cardiology, pulmonology

Discussion

- Need for post-marketing surveillance
- Pharmacovigilance becomes more important

Thank you