Peer Review File

Article information: https://dx.doi.org/10.21037/vats-23-17

Reviewer A

Anterior mediastinal AVMs are rare, and I believe this case report has a certain value. The main issue with this report is the inadequate presentation and explanation of contrast-enhanced CT images, as AVMs are often diagnosed by contrast-enhanced CT scans.

1) AVMs can occur anywhere in the body and are defined by an abnormal connection between arteries and veins. Therefore, it is important to describe which artery is the feeding artery and which vein is the draining vein. In the two cases presented here, were the feeding arteries and draining veins identified? If so, please add this information. In addition, the authors state that in Case 1, the AVM infiltrated the superior vena cava, but can a non-tumorous AVM cause infiltration? Or was it simply that the draining vein of the AVM was connected to the superior vena cava? Please address this point.

Reply 1: Added vasculature details to case 1

Changes in the text: After a multidisciplinary meeting discussion, the patient was referred to thoracic surgery and underwent a median sternotomy and resection of the anterior mediastinal mass with repair of Superior Vena Cava (SVC) tear and right hemidiaphragmatic plication. The solid mass was found in the anterosuperior mediastinum overlying the SVC. The mass was attached to the confluence of the right and left brachiocephalic vein where it becomes the SVC. The right phrenic nerve was also involved in the tumour with no prospect of preserving it and was therefore divided. A small portion of the right upper lung was wedge resected out to free it from the mass. A portion of the pericardium overlying the right atrium was resected en bloc with the tumour. Upon mobilisation, it became clear that the mass was directly connected to the vasculature. A Satinsky clamp was placed across the base of the tumour as it was cut free from the SVC, necessarily taking a portion of the vasculature. A 2cm defect in the SVC was closed with 4/0 running prolene with good effect. After resection of the mass, the right hemidiaphragm was plicated (Line 131-134)

2) For contrast-enhanced CT images of AVM, it is essential to present non-contrast and contrast-enhanced CT (both early and delayed phases, if available) at the same level. Also, Figure 2A in Case 1 is presented in lung window settings but should be presented in mediastinal window settings. Please consult with a radiologist at your institution and reattach appropriate contrast-enhanced CT images with appropriate settings. Please also consult with a radiologist regarding the description of these CT images.

Reply 2: I have changed figure 2A to mediastinal view

Changes in the text: View changed on figure 2a

3) In Case 1, a CT-guided biopsy was performed, but I think that a CT-guided biopsy for AVMs carries a high risk of bleeding complications. Although it was unavoidable in this case because the diagnosis was not made, please add a literature-based discussion in the Discussion section on whether CT-guided biopsy for AVMs is safe or not.
Reply 3: Discussion of endovascular embolisation as a possible management option.
Changes in the text: To obtain tissue, a variety of techniques have been described, including CT-guided transthoracic needle biopsy, video-assisted thoracoscopic surgery, mediastinoscopy, and open surgical biopsy (5). CT guided biopsy of AVMs carry a risk of bleeding complications (17). In both of the reported cases the potential neoplastic diagnosis was the emphasis rather than a vascular anomaly and therefore a CT guided biopsy was performed in Case 1. (Line 244-247)

4) In the Discussion, please add a literature-based review on what typical imaging findings of AVMs outside the anterior mediastinum are on CT and PET-CT. Also, please describe whether those imaging characteristics were present in these cases.
Reply 4: Discussion of both common CT findings in AVM and how they reflect on our case.
Changes in the text: Although AVMs can be isolated, many of them are associated with a number of syndromes, most commonly hereditary haemorrhagic telangiectasia.
Traditionally, computer tomography with intravenous contrast has been the imaging modality of choice when approaching mediastinal masses (7). On non-contrast CT, diagnosis of AVMs may be difficult however following contrast administration the feeding arteries and draining veins are typically present. The intervening nidus can be demonstrated with a "bag of worms" appearance. In our cases, despite undergoing CT Thorax with contrast the differential diagnosis did not include AVMs. Both radiology reports suggested thymic mass or teratoma as possible diagnosis. (Line 234-239)_

5) AVM treatments include not only surgical resection but also endovascular embolization as a representative treatment method. A literature-based discussion on this point is also necessary.
Reply 5: Discussion of endovascular embolisation as a possible management option.
Changes in the text: However, we highlight the importance of careful collaboration with interventional radiologists to reduce potential bleeding risk in managing high risk intrathoracic vascular anomalies. In addition to surgical resection, management options of AVMs also include coil or ONYX embolization. This method may be used as a primary treatment option or as a preoperative procedure to minimise risk of haemorrhage (9). (Line 249-252)

Reviewer B

I appreciate the opportunity to review the paper by Dr. Hurley and colleagues, which describes two cases of mediastinal arteriovenous malformations that were successfully treated by a surgical approach by the thoracic surgery department. The abstract is well-written, and the paper has a coherent structure, with an appropriate number of tables and figures to effectively convey the key findings.

Although the report is interesting and provides information on this extremely rare condition, there are some limitations to consider. Firstly, the study was conducted in only one center and by the same surgical team. Additionally, the report included a small number of patients. The findings presented in the work do not provide sufficient guidance for clinicians managing this pathology, as most of the patients' symptoms are caused by the mass effect of the lesion. Furthermore, there are several points of interest that were not adequately addressed. For instance, although a robotic approach was mentioned in Case 2, no description of the approach used in Case 1 was provided. Additionally, the paper did not mention whether the patient's symptoms in Case 2 were resolved after surgery. These sections limit the quality of the work and may pose a hindrance to its publication. However, I believe that these cases are of great interest due to their rarity, and as such, the work has the potential to be published in a journal, provided that the aforementioned sections are addressed.

Reply: Approach included for Case 1 and symptoms included for Case 2.

Changes in the text:

C1: After a multidisciplinary meeting discussion, the patient was referred to thoracic surgery and underwent a median sternotomy and resection of the anterior mediastinal mass with repair of Superior Vena Cava (SVC) tear and right hemidiaphragmatic plication (Line 131-134)

C2: On her follow up appointment 8 weeks post operation, she reported improved neuropathic pain and respiratory symptoms (Figure 9). (Line 197-198)

Reviewer C

The authors present 2 interesting cases of arteriovenous malformation in the anterior mediastinum managed with surgical resection. This is a rare entity indeed and after a thorough workup for the most common anterior mediastinal masses can be considered. There is at least one other case report of this entity (Arteriovenous Malformation in the Anterior Mediastinum by Tennyson et al. The Annals of Thoracic Surgery, Volume 90, Issue 1, E9-E10, July 2010).

Revisions:

1. This is a report of two cases; not a case series. A case series typically includes 3 to 10 cases. Please revise the title and the description in the text (Lines 24 and 102).

Reply 1: Title amended

Changes in the text: Successful resection of arteriovenous malformation from the

anterior mediastinum: A case report of two presentations (Line 2-3)

2. Include reference to the previously described case of AVM in the anterior mediastinum (see above) in the paper.

Reply 2: Reference included

Changes in the text: In more recent literature there has been one report of an anterior mediastinal AVM being resected (9). (Line 222-224)

3. Line 41/42: Anterior mediastinum is incorrectly defined. It is posterior to the sternum and anterior to the pericardium and below the thoracic plane.

Reply 3: Updated description of ant mediastinum

Changes in the text: The anterior mediastinum is defined as the region below the thoracic plane, posterior to the sternum and anterior to the pericardium. It contains the thymus, fat and lymph nodes. Mediastinal masses are uncommon entities with 54% of them arising from the anterior mediastinum. (Line 80-85)

4. As incomplete resection can lead to recurrence, were the margins negative in both cases?

Reply 4: Comment on margins included

Changes in the text:

C1: A portion of the pericardium overlying the right atrium was resected en bloc with the tumour. (Line 139-140)

C2: She underwent a robot-assisted thoracoscopic anterior mass resection where the thymic tissue and peri-thymic fat was removed en bloc from the internal mammary vessels to the phrenic nerve and from the superior horn of the thymus to the diaphragm. Extra pericardial margin was obtained. (Line 185-189)

5. What is the role for embolization in these cases?

Reply 5: same as reply #5 to Reviewer A

6. Were further investigations undertaken to rule out other AVMs such as cerebral or gastrointestinal? Since both cases had CT chests it is assumed no PAVMs were identified and both cases did not have a history of hereditary hemorrhagic telangiectasia.

Reply 6: Comment including peripheral AVM investigation included

Changes in the text: In both cases a CT Chest was performed that ruled out pulmonary AVMs. Neither patient had a past medical history of hereditary haemorrhagic telangiectasia (Line 212-214)

7. Line 105: Please indicate the SUVmax of the lesion for Case 2 as included in Case 1.

Reply 7: Added SUVmax to C2

Changes in the text: thymic remnant or thymic reactivation rather than a malignant process with a standardized uptake value of 3 (Figure 8). (Line 182-183)

8. Units: Be consistent when describing the size of the lesions. Case 1 uses millimeters and Case 2 uses centimeters.

Reply 8: Updated units

Changes in the text: All units are in centimeter

Case 1 revisions:

1. What surgical approach was used. On the postoperative CXR there are sternal wires. Was this VATS or RATS converted to trans-sternal?

Reply 1: same as reply to Reviewer B

2. Was there direct communication to the SVC? Did the SVC need resection +/- reconstruction?

3. Why was the diaphragm plicated?

4. Why was the lung resected?

5. What was the estimated blood loss?

Reply 2-5: Increased detail of description of intraoperative findings

Changes in the text: After a multidisciplinary meeting discussion, the patient was referred to thoracic surgery and underwent a median sternotomy and resection of the anterior mediastinal mass with repair of Superior Vena Cava (SVC) tear and right hemidiaphragmatic plication. The solid mass was found in the anterosuperior mediastinum overlying the SVC. The mass was attached to the confluence of the right and left brachiocephalic vein where it becomes the SVC. The right phrenic nerve was also involved in the tumour with no prospect of preserving it and was therefore divided. A small portion of the right upper lung was wedge resected out to free it from the mass. A portion of the pericardium overlying the right atrium was resected en bloc with the tumour. Upon mobilisation, it became clear that the mass was directly connected to the vasculature. A Satinsky clamp was placed across the base of the tumour as it was cut free from the SVC, necessarily taking a portion of the vasculature. A 2cm defect in the SVC was closed with 4/0 running prolene with good effect. After resection of the mass, the right hemidiaphragm was plicated. The patient was transfused 4 units of blood intraoperatively with an estimated blood loss of 1400mls. (Line 131-146)

Edits required:

Line 60: "… further investigated further with a CT…" change to "…further investigated with a CT"

Line 62/63: "… being in a close proximity…" change to "…being in close proximity…"