Anterior mediastinal seminoma with myasthenia gravis: A rare case report and literature review

YEN-CHANG WEN
Department of Surgery, Division of Thoracic Surgery, Chung Shan Medical University Hospital
JIUN-YI HSIA (d02zxc@gmail.com)
Department of Surgery, Division of Thoracic Surgery, Chung Shan Medical University Hospital
TUAN-YING KE
Department of Pathology, Chung Shan Medical University Hospital
JENG-DONG HSU
Department of Pathology, Chung Shan Medical University Hospital

Case Report

Keywords: seminoma, thymic follicular hyperplasia, myasthenia gravis

Posted Date: April 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1562197/v1

Abstract

Background:

Myasthenia gravis may be associated with thymic follicular hyperplasia or thymomas. We present a case of an anterior mediastinal tumor with myasthenia gravis, which turned out to be seminoma. We also review the literature on seminoma with myasthenia gravis in this article.

Case presentation:

A 34-year-old man presented to our hospital with a complaint of diplopia. Single fiber electromyography revealed ocular myasthenia gravis; chest computed tomography showed a 1.5 cm anterior mediastinum nodule suspected as thymoma. The patient underwent video-assisted thoracoscopic thymectomy. Histopathological findings revealed seminoma with thymic follicular hyperplasia.

Conclusion:

Anterior mediastinal seminoma with thymic follicular hyperplasia is rare and extremely rare with associated myasthenia gravis. Though rare, young male patient with anterior mediastinal tumor and myasthenia gravis, thymic seminoma is one possible cause. Testicular examination can be taken into consideration before operation.

Background

Myasthenia gravis may be associated with thymic follicular hyperplasia or thymomas [1]. Seminoma mimicking myasthenia gravis with anterior mediastinal tumor is rare. Germ cell tumors account for less than 4% of mediastinal tumors [2]. Non-seminomatous tumors are more common than seminomas [3]. Due to the indolent behaviour of seminomas, most of them are bulky when diagnosed. Patients with seminoma may present with symptoms, such as dyspnea, chest pain, cough, hemoptysis, hoarseness or even superior vena cava syndrome, caused by large anterior mediastinal tumor masses [2, 4]. These symptoms are non-specific; therefore, the diagnosis of seminomas is often incidental.

We present a case with double-seronegative myasthenia gravis and a 1.5 cm nodule in the upper anterior mediastinum (suspected as thymoma) revealed on chest computed tomography. After thymectomy, the histopathological findings revealed seminoma with thymic hyperplasia.

Case Presentation

A 34-year-old man experienced intermittent diplopia for 6 months. Serum test was negative for acetylcholine receptor antibody in Cheng Ching Hospital on 03/2021, where the patient was diagnosed with an unknown virus infection. He had diplopia again on 08/2021 and reported to Shin Kong Wu Ho-Su Memorial Hospital for further evaluation. Serum test was negative for muscle-specific receptor tyrosine kinase test; however, single fiber electromyography revealed ocular myasthenia gravis. Double-

seronegative myasthenia gravis was suspected, and chest computed tomography was performed, which showed a 1.5 cm nodule in the upper anterior mediastinum, suspected as thymoma (Fig. 1). The patient reported to Chung Shan Medical University Hospital for a second opinion.

Physical examination revealed a male in apparent good health and no distress. His temperature was 36.4 ℃, pulse rate was 66 per minute and regular, and blood pressure was 128/78 mmHg. The findings were within normal limits. There was no tracheal shift, and the thyroid gland was normal to palpation. Both lungs were clear to auscultation.

Laboratory data revealed a white blood cell count of 8,050 per microliter with 67% polymorphonuclear leukocytes; hemoglobin, 14.5 grams per deciliter; hematocrit, 43.1%. Serum electrolytes were normal. A pre-operative survey, including ultrasonography of the abdomen and whole-body bone scan, showed no liver or bone metastasis. Ultrasonography of the abdomen revealed mild fatty changes in the liver with bright echogenicity. A whole-body bone scan revealed no significant abnormal uptake.

The patient underwent video-assisted thoracoscopic thymectomy. Diplopia resolved after surgery, and the patient was discharged in stable condition on postoperative day 4.

In 12/2021, follow-up physical examination showed no epididymal or testicular lesions. Follow-up positron emission tomography showed no active lesion. Follow-up tumor markers, such as lactate dehydrogenase, alpha-fetoprotein and beta-human chorionic gonadotropin, were within normal range.

Pathology

Macroscopically, the thymus (with tumor) measured 20.0 × 7.0 × 2.0 cm and weighed 124.6 grams. A soft to solid, mild irregular and well-defined tumor (about 1.5 × 1 × 1 cm) in the high body of thymus was noted (Fig. 2A). The tumor measuring 1.3 × 1.0 × 0.8 cm showed a homogeneous yellow-white to flesh cut surface with a rubbery consistency (Fig. 2B).

Histologically, the lesion shows the characteristic appearance of nests of large, uniform polygonal cells with clear or eosinophilic cytoplasm and distinct cell membranes. Marked thymic follicular hyperplasia with numerous germinal centers is seen (Fig. 3A). High-power field shows squared-off nuclei and prominent central nucleoli (Fig. 3B).

Immunohistochemical staining shows positive CD117 with strong and diffused circumferential cytoplasmic membrane reactivity (Fig. 3C). Positive SALL4 with strong, uniform nuclear staining (Fig. 3D). Negative for CK, P63, CD20, CD3, CD68, CD79a and Tdt stain.

Overall, the appearance is consistent with primary mediastinal seminoma with thymic follicular hyperplasia. The surgical margins are free.

Discussion

Mostly, symptoms of anterior mediastinal seminoma, such as dyspnea, chest pain and cough, are tumor-size dependent [2, 4]. We reviewed previous literature on anterior mediastinal seminoma with thymic follicular hyperplasia and found only 12 case reports of mediastinal seminoma with lymphoid hyperplasia. In 1985, a paper by Williams et al. [5] described a case with symptoms of ocular myasthenia gravis. In 1986, Burns et al. [6] described 3 case reports. In 2015, Weissferdt et al. [7] described 6 case reports with a median tumor size of 4 cm (ranging from 3 ~ 5 cm), mostly presenting symptoms of chest pain. In 2016, Lee et al. [8] described a case with asymptomatic synchronous thymoma. In 2021, Holmes et al. [9] described a case report with symptoms of breathlessness on lying down. Among the case reports mentioned above, only one patient presented ocular myasthenia gravis symptoms, similar to our patient.

The most common association of thymic pathology with myasthenia gravis is thymus follicular hyperplasia or thymoma. The association between seminoma and follicular lymphoid hyperplasia is still uncertain. Willis et al. [10] found that the microenvironment of seminoma produced specific antigens, which could be associated with follicular lymphoid hyperplasia. Weissferdt and Moran hypothesised that the mechanism of thymus follicular hyperplasia was associated with a characteristic distribution of antigen-presenting dendritic cells in mediastinal seminomas [7]. Further research is needed.

Mediastinal seminomas are morphologically similar to testicular seminomas. However, secondary changes are noticed in mediastinal seminomas sometimes, including the presence of thymic remnants, prominent cystic changes, reactive follicular lymphoid hyperplasia and epithelioid granulomas [6, 11, 12]. These secondary changes lead to more differential diagnoses. For example, differential diagnosis of anterior mediastinal cyst should include thymic cyst, cyst formation of thymoma or Hodgkin lymphoma and seminoma with cystic change [11]. Similarly, in the case of anterior mediastinal tumors with symptoms of myasthenia gravis, thymoma, thymus hyperplasia and seminoma with reactive follicular lymphoid hyperplasia should be considered for differential diagnosis.

For small, resectable anterior mediastinal seminomas, surgical removal of the tumor with thoracoscopic or thoracotomy is the first-line treatment. The decision to use postoperative radiotherapy depends on histopathological features of surgical resection margins [13, 14]. Patients with advanced disease should receive chemotherapy and radiotherapy because seminomas are highly sensitive to chemotherapy and radiotherapy [14]. Moreover, monitoring tumor markers of human chorionic gonadotropin and alpha-fetoprotein for detecting recurrence of advanced seminoma has been recommended by Gilligan et al. However, they did not recommend using markers for detecting recurrence of stage I seminoma [15].

Conclusion

Anterior mediastinal seminoma with thymic follicular hyperplasia is rare and extremely rare with associated myasthenia gravis. The clinical presentation was attributed to the secondary changes in the thymic seminoma. For anterior mediastinal tumors with myasthenia gravis symptoms, thymic seminoma with thymic follicular hyperplasia should be included in differential diagnoses, especially in young male patients.

Abbreviations

CD117: Cluster of differentiation 117

SALL4: Spalt like transcription Factor 4

CK: Cytokeratins

P63: Tumor protein 63

CD20: Cluster of differentiation 20

CD3: Cluster of differentiation 3

CD68: Cluster of differentiation 68

CD79a: Cluster of differentiation 79a

TdT: Terminal deoxynucleotidyl transferase

Declarations

Ethics approval and consent to participate:

This case is in accordance with the ethical standards of the Ethics Committee of Chung Shan Medical University Hospital, Taiwan (R.O.C.) (date: March 4, 2022, approval number: CS2-22027) and the Declaration of Helsinki and its later amendments.

Consent for publication:

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials:

Not applicable.

Competing interests:

All authors declare that they have no competing interests.

Funding:

Not applicable.

Authors' contributions:

YCW, first author, reviewed the medical record and drafted the manuscript.

JYH, corresponding author, performed the operation, carried out clinical treatments and drafted the manuscript.

TYK and JDH reviewed the medical record and carried out histopathological studies.

All authors read and approved the final manuscript.

Acknowledgements:

Not applicable.

References

1. Le Panse R, Bismuth J, Cizeron-Clairac G, Weiss JM, Cufi P, Dartevelle P, De Rosbo NK, Berrih-Aknin S. Thymic remodeling associated with hyperplasia in myasthenia gravis. Autoimmunity. 2010 Aug;43(5–6):401–12.
2. Takeda S, Miyoshi S, Ohta M, Minami M, Masaoka A, Matsuda H. Primary germ cell tumors in the mediastinum: a 50-year experience at a single Japanese institution. Cancer. 2003 Jan 15;97(2):367–76.
3. Bokemeyer C, Nichols CR, Droz JP, Schmoll HJ, Horwich A, Gerl A, Fossa SD, Beyer J, Pont J, Kanz L, Einhorn L, Hartmann JT. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. J Clin Oncol. 2002 Apr 1;20(7):1864-73.
4. Moran CA, Suster S, Przygodzki RM, Koss MN. Primary germ cell tumors of the mediastinum: II. Mediastinal seminomas–a clinicopathologic and immunohistochemical study of 120 cases. Cancer. 1997 Aug 15;80(4):691–8.
5. Williams IM, Gee DC, Cooper E, Dickinson P, Sandeman TF, Sum AC. Thymic seminoma and myasthenia gravis. J Clin Neuroophthalmol. 1985 Dec;5(4):254–7.
6. Burns BF, McCaughey WT. Unusual thymic seminomas. Arch Pathol Lab Med. 1986 Jun;110(6):539–41.
7. Weissferdt A, Moran CA. Mediastinal seminoma with florid follicular lymphoid hyperplasia: a clinicopathological and immunohistochemical study of six cases. Virchows Arch. 2015 Feb;466(2):209–15.
8. Lee HI, Jang IS, Jeon KN, Ko GH, Lee JS, Kim DC, Song DH, Lee JH. Thymoma and Synchronous Primary Mediastinal Seminomas with Florid Follicular Lymphoid Hyperplasia in the Anterior Mediastinum: A Case Report and Review of the Literature. J Pathol Transl Med. 2017 Mar;51(2):165–170.
9. Holmes C, Loo PS, Barnard S. Primary mediastinal seminoma with florid follicular lymphoid hyperplasia: a case report and review of the literature. Diagn Pathol. 2021 Aug 21;16(1):76.

10. Willis SN, Mallozzi SS, Rodig SJ, Cronk KM, McArdel SL, Caron T, Pinkus GS, Lovato L, Shampain KL, Anderson DE, Anderson RC, Bruce JN, O'Connor KC. The microenvironment of germ cell tumors harbors a prominent antigen-driven humoral response. J Immunol. 2009 Mar 1;182(5):3310-7.
11. Moran CA, Suster S. Mediastinal seminomas with prominent cystic changes. A clinicopathologic study of 10 cases. Am J Surg Pathol. 1995 Sep;19(9):1047–53.
12. Schantz A, Sewall W, Castleman B. Mediastinal germinoma. A study of 21 cases with an excellent prognosis. Cancer. 1972 Nov;30(5):1189–94.
13. Napieralska A, Majewski W, Osewski W, Miszczyk L. Primary mediastinal seminoma. J Thorac Dis. 2018 Jul;10(7):4335–4341.
14. Petrova D, Kraleva S, Muratovska L, Crcareva B. Primary Seminoma Localized in Mediastinum: Case Report. Open Access Maced J Med Sci. 2019 Jan 25;7(3):384–387.
15. Gilligan TD, Seidenfeld J, Basch EM, Einhorn LH, Fancher T, Smith DC, Stephenson AJ, Vaughn DJ, Cosby R, Hayes DF; American Society of Clinical Oncology. American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. J Clin Oncol. 2010 Jul 10;28(20):3388 – 404.

Figures

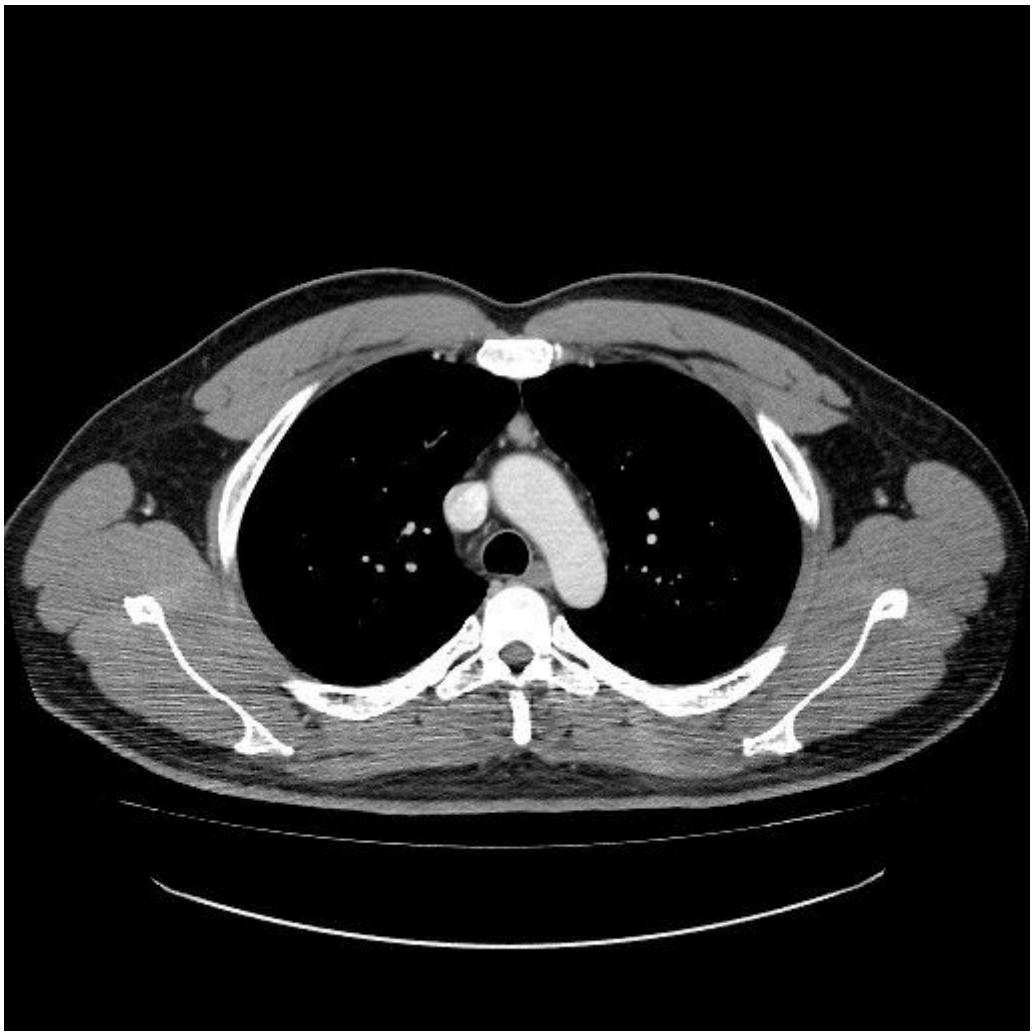

Figure 1

Homogeneous 1.5 cm nodule in the upper anterior mediastinum with mild contrast enhancement, suspected as thymoma.

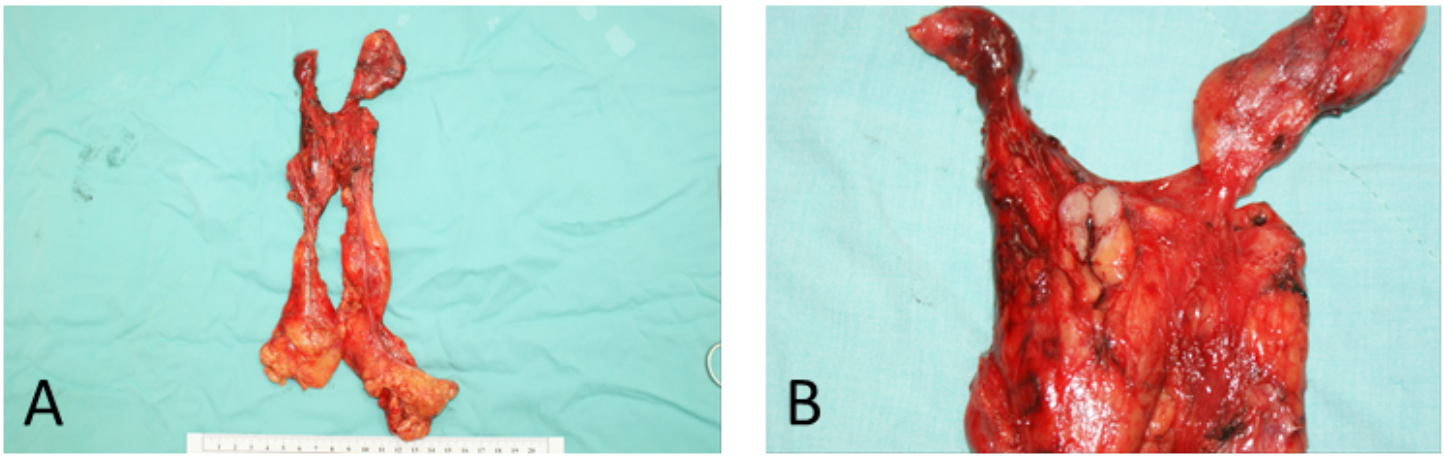

Figure 2

A. Well-defined tumor about 1.5 × 1 × 1 cm in the high body of thymus.

B. Encapsulated tumor with homogeneous yellow-white to flesh cut surface.

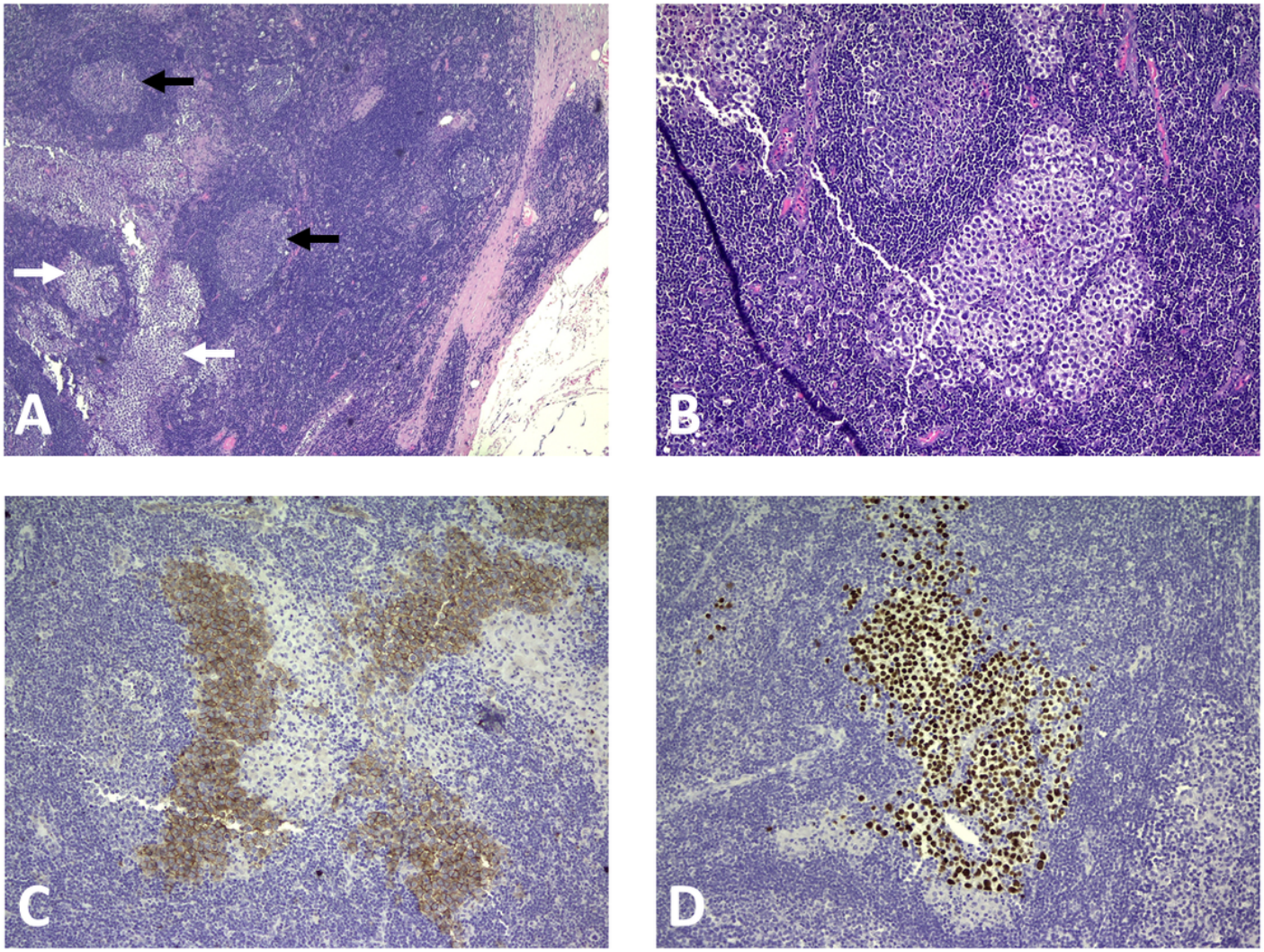

Figure 3

A. Hematoxylin and eosin staining at ×20 magnification. Seminoma cells with clear cytoplasm (white arrows) and germinal centers (black arrows).

B. Hematoxylin and eosin staining at ×100 magnification. Seminoma cells with squared-off nuclei and prominent central nucleoli.

C. Immunohistochemistry CD117 at × 100 magnification, confirming the diagnosis of seminoma.

D. Immunohistochemistry SALL4 at × 100 magnification, confirming the diagnosis of seminoma.