ALK-Negative Lung Inflammatory Myofibroblastic Tumor in a Young Adult: a Case Report and Literature Review of Molecular Alterations

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Case report

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Abstract

Background: Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor and is prevalent among children and adolescents. Surgery is the most important therapeutic approach for IMT and complete resection is recommended. Although 50% of IMTs present anaplastic lymphoma kinase (ALK) rearrangements, an efficacy has been shown by the use of Crizotinib . However the genetic landscape of this tumor is not fully understood and the therapeutic options are limited in particular for the remaining percentage of negative ALK tumors.

Case presentation: In our case, we detail the clinical history of 18-year-old female patient diagnosed with pulmonary IMT negative for ALK, subjected to surgery and subsequently to follow-up. The initial pathology report oriented for a salivary gland lung cancer. Afterwards due to a second look by another pathologist an ALK negative IMT of the lung was diagnosed. We also perform a literature review based on IMT and other kinase fusions found in addition to ALK such as ROS proto-oncogene 1 (ROS1), rearranged during transfection (RET), neurotrophic receptor tyrosine kinases (NTRKs) and platelet derived growth factor receptor (PDGFR beta).

Conclusions: IMT is a very rare disease involving children and adolescents. Little is known about the clinical and molecular characteristics, pathological diagnosis, prognosis and optimal management strategy of IMT. Since there is no "standard of care" therapy for IMT, identifying feasible genomic alterations could redefine the management of patients with negative ALK disease.

Introduction

Inflammatory Myofibroblastic Tumor (IMT) is a rare mesenchymal tumor with an incidence of 0.04%. IMT is more frequent in female than in male for soft tissue origin and 1:1 ratio for lung one and usually involves children, adolescents and young adults even if it can occur at any age (1)

The lungs are the most common site of IMT onset, although it can be detected in others anatomic sites such as the retroperitoneum, abdomen, and pelvic cavity. Despite the low metastatic potential surgery remains the gold standard therapeutic approach for localized resectable disease. However despite of this IMT can be locally invasive and in 10% of cases is could be associated with distant metastasis. (2, 3) The IMT prognosis is good with a 5-year survival rate of 74–91%. (4)

Approssimately 50% of IMT cases harbor a clonal translocation that activates the anaplastic lymphoma kinase (ALK)-receptor tyrosine kinase gene located at 2p23 locus. (5) As a result ALK protein is overexpressed and can be detected with immunohistochemical tests. ALK acquire an oncogenic potential as a result of a gene fusion, such as in anaplastic large cell lymphoma, lung cancer and also in IMT, or due to a missense mutation as seen in neuroblastoma and anaplastic thyroid cancer. (6)

ALK positivity to immunohistochemical test, as an expression of *ALK*-based gene fusions, is more prevalent in pediatric IMT patients compared to the adult counterpart. However, it remains unclear if this

discrepancy depends by an intrinsic difference in biology of IMT between the two age groups (children vs adult), or instead is merely a reflection of a wider spectrum of genetic alterations. (7, 3)

IMTs display a wide morphologic spectrum, ranging from an inflammatory ‘pseudotumor’ with predominant hyalinization and chronic inflammation and only a paucity of lesional spindle cells, to a highly cellular myofibroblastic proliferation and occasionally defined as sarcomatous neoplasm due to the lacking of significant inflammatory or/and fibromyxoid stromal component. The diagnosis of ALK-negative IMTs is often hard due to its markedly variable phenotype and lack of objective immunoprofile regarding a potential waste-basket of different entities, including reactive/inflammatory processes, such as the fibro-inflammatory IgG4 related disease, idiopathic retroperitoneal fibrosis, and at the other end of the spectrum, other spindle cell/pleomorfic sarcoma. (8, 9)

Metastatic patients harboring alk alteration can be effectively treated using ALK inhibitors. (10, 11)

However, outside alk inhibitors treatment options are limited for patients with unresectable/andvanced disease and for negative ALK tumors. (12)

In order to increase the knowledge about this very rare disease we report a case of ALK negative lung IMT surgically resected in a AYA patient

Furthermore a we carried out a literature review on emerging genetic alteration in ALK-negative IMT such as ROS1, NTRK, RET or PDGFR beta in order to suggest targetable biomarkers that can be improve the management of patients with negative ALK disease.

Case Presentation

In December 2015 a 18-year-old girl was admitted to the hospital due to a car accident. A CT scan was performed to esclude lung injury and a broncopulmonary nodule with a diameter of 14 mm at the apical segment of the right lower lobe (RLL) was incidentally detected. She had been in hers usual state of good health prior to this referral and specifically denied fever or chills. Her past medical history was negative as the family history for inherited diseases. Due to the radiological characteristics and the young age a prudential follow up was decided with a chest CT scan. In December 2018 a slight increase (16 x 12 vs 14 x 10 mm) in the longest diameters of the broncopulmonary nodule was noted. A ^{18}F- fluoro-2-deoxy-D-glucose- (^{18}FDG) and ^{68}Gallium (^{68}Ga) DOTATATE Positron Emission Tomography/Computed Tomography (PET/CT) were perfomed showing an increased standardized uptake value (SUV) max of the nodule of 3.5 and 3.4 respectively. (Fig. 1)

An endobronchial hamartoma was suspected and patient underwent a videothoracoscopic segmentectomy of the apical segment of right lower lobe (RLL) with ilo-mediastinal lymphadenectomy. Histopathological examination showed a complex lesion regarded as a salivary gland lung neoplasm. The epithelial component shows well defined solid and acinar architecture without a capsule, with low degree of malignancy, IHC positive for cam5.2, naspin, TTF1 and weak positivity for sinaptofysin and

negative for chromogranin A, CD56, DOG1 and SOX10. Intense cytoplasmic positivity for PAS was also reported. 8 lymph nodes founded was negative for metastasis. No pleural infiltration was detected. The clinical-morphological and immunophenotypic features were diagnosed as salivary gland lung cancer.

After surgery patient was admitted at our Institution for a second opinion where a second revision of the histopathology diagnosis from an another expert pathologist is mandatory according Rare Tumors Guidelines. The pathology revision showed a central area of compact fascicular spindle cells, sometimes with eosinophilic citoplasm which are mixed with numerous inflammatory elements including plasma cells and lymphocytes inserted in a dense fibrous stroma.

On the periphery of the nodule there are numerous epithelial elements, cubic cells without atypia or mitosis which at immunohistochemical characterization were positive for Ck7 and napsin and TTF1 **(A)** and negative for CD117, chromogranin and synaptophysin previously considered as neoplastic but propably reactive to the real lesion. The IgG plasma cells are numerous mostly in the periferical fields,but the IgG4 ratio is normal. The spindle cell component was positive for smooth actin **(B)** and negative for ALK **(C)** using Vysis LSI ALK (2p23) Dual Color, Break Apart Rearrangement probe. The Ki67 was 5%. These findings oriented for a diagnosis of an inflammatory myofibroblastic tumor (IMT). (Fig. 2)

Thereafter, discussed in the multidisciplinary board of Soft Tissue Sarcoma of our Institute, no adjuvant treatment was decided and the patient was placed on a 3-monthly follow-up program.

To now, patient has been in clinical follow-up for 18 months, with no signs of recurrent disease.

Discussion

IMT is a rare neoplasm which belongs to a subtype of soft tissue sarcoma, with an overall prevalence of approximately 0.04%-0.7% (13, 14)

It may occur at any age but it is more common in children and adolescents, constituting less than 1% of adult lung tumors. (15, 16)

Therapeutic options for patients with unresectable and/or advanced IMT are limited in particular for ALK negative cases. (17)

Other treatments besides surgery include radiation and chemotherapy.(18)

Dishop et al. reported a case treated with vincristine and etoposide as the first line and cisplatin, adriamycin, and methotrexate as the second line after incomplete resection. (19)

In addition, complete remission was reported using vincristine, ifosfamide, doxorubicin, and celecoxib (20)

Steroid and non-steroidal anti-inflammatory drugs have also been reported as effective for IMT. However the patient’s phenotype that can have a benefit for the treatment is stil debate. Steroids have been

reported as effective for both IMT containing and IMT patients without IgG4SD features (21, 22)

On the other hand, Cerfolio et al. reported two cases where the remaining tumor showed no growth after incomplete resection during 4 to 9 years follow-up and the cases did not receive any additional treatment, although the biological features of those cases were not showed. (23)

ALK and / or ALK expression gene rearrangement has been described as a good prognostic marker in IMT, while ALK negative IMT appears to be more aggressive with a higher frequency of metastasis than ALK positive IMT (7, 3)

Among ALK rearrangements have been identified more than 10 different ALK fusion partner genes in IMT, including the most common TPM3/4, RANBP2, TFG, CARS, ATIC LMNA, PRKAR1a, CLTC, FN1, SEC 31A, and EML4 .Chromosomal translocation led to the formation of an ALK fusion protein which exhibits kinase activity independent of the ligand due to the self-phosphorylation of the chimeric protein. This results in prolonged survival of the cancer cell, hyperproliferation and enhanced cell migration. (24–29)

In contrast, actionable genomic alterations have not yet been described in about 50% of IMT samples that are negative for ALK by IHC. ALK-negative IMTs may be more aggressive than ALK-positive IMT with a higher frequency of metastasis. (3)

Our case showed a slowly growing ALK negative IMT in a AYA patient. Initially IMT was misdiagnosed and patients underwent radiological follow up for 4 years without any morphological modifications. After surgery the pathology report oriented for a salivary gland tumor of the lung and only after a second look the IMT was defined. This reflects the challenge in the diagnosis in case of ALK negative IMT.

Furthermore in case of ALK negative tumors little is known about their potential oncogenic drivers, so there are no targeted therapies available.

Recent studies have shown ALK-negative IMT might harbor other kinase fusions such as ROS1, NTRK, RET or PDGFR beta, which initiated genome-level research into potential tumorigenic drivers in ALK-negative subsets of IMTs.

In 2014 was published a study in which other possible IMT actionable targets were reported for the first time, involving ROS1 and PDGFR beta fusions. A genetic analysis was performed by NGS on 33 IMT samples, 11 of which were ALK negative specimens. In cases in which there was sufficient tumor material available, the kinase fusions were verified with RNA sequencing. Kinase fusion different from ALK fusion were identified in 6 of 11 ALK negative cases. Four contained distinct ROS1 fusions (sample L3/L4, YWHAE-ROS1, sample L6, TGF-ROS1) and 2 contained a PDGFR beta fusion (samples L7/L10, NAB2-PDGFR beta). They are both actionable targets of FDA-approved drugs. Notably, they also detected ALK fusions in 2 of 11 IMT samples that tested negative for ALK expression by IHC.(30)

ROS1 rearrangements are reported in approximately 9–13% of IMT, all ALK-negative cases (25, 31). Clinical cases of children/adolescents with pulmonary IMT with a TGF-ROS 1 rearrangement are present

in literature. They all benefited from treatment with crizotinib (250 mg) with a significant reduction in tumor size. (31–34)

Jia He et al found for the first time a double amplification of CDK4 and MDM2 with protein overexpression by NGS and IHC in a 68-year- old woman with a gastric IMT with local invasion of spleen and diaphragm(35).

Furthermore, Antonescu et al. found correlations between the genotypes and certain clinic-pathologic characteristics of the IMT .(36) All cases have been tested for ALK gene rearrangements. ALK negative tumors have been further studied by FISH and RNA sequencing in some cases for abnormalities in ROS1, PDGFRB, NTRK1 and RET. About 6 ROS1 rearranged IMTs all except one is presented in children, mainly in the lung and intra-abdominal, with a specific growth of spindle cells with long cell processes. RET rearrangement was found in a 27-year-old pulmonary IMT characterized by a solid pseudosarcomatous growth and a fatal clinical outcome.

As reported above IMT has an increased incidence in children, adolescents and young adults (AYA). Our case was an asymptomatic young adult female of 18 yo. Initially due to the radiological characteristic of the nodule, the lacking of risk factors for neoplastic disease and the young age it was decided to follow radiologically the lung nodule and it was decided to perform the surgery only after a increasing in the size of the nodule. We would like to focus our attentntion onto the attitude into diagnostic and therapeutic strategies in cases of AYA should be different from that used in adult cases. Unfortunately there is a lacking of AYA specialized centers that should be implemented

Conclusions

In summary, we report a case of a pulmonary alk negative IMT surgically resected.

No further gene rearrangements have been investigated to date other than that for ALK. However, from literature data available, it seems to be hat the majority of IMTs shows kinase fusions. Conventional detection methods, such as IHC and FISH, may fail to detect a range of actionable gene rearrangements, such as ROS1, RET, NTRK, and PDGFRβ, in IMTs and sometimes a broader molecular testing, such as NGS, is necessary to explore the comprehensive genetic characteristics. This could present an important resource in clinical practice in order to increase potentially drug targets for patients with IMT, especially for those identified as ALK negative.

Abbreviations

ALK: anaplastic lymphoma kinase

AYA: adolescents and young adults

IHC: Immunohistochemistry

IMT: Inflammatory myofibroblastic tumor

NTRK: neurotrophic receptor tyrosine kinases

PDGFr: platelet derived growth factor receptor

RET: rearranged during transfection

RLL: right lower lobe

ROS1: ROS proto-oncogene 1

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by Comitato Etico della Romagna – CEROM.Patient provided her written informed consent to participate in this study..

Authors ensured compliance with EQUATOR Guidelines (CARE Case Report Checklist).

Consent for publication

The authors obtained patient consent for publication of clinical data and images

Authors' Contributions

SAD and AB equally contributed to draft the manuscript. SV ADV and LM carried out the literature review. FP and DD provided the images and the pathology review. TI supervised the study and revised the manuscript for intellectual content. VF NR and LG were responsibleof the clinical management of the patient. All authors read and approved the final version of the manuscript for submission.

Availability of data and materials

Not applicable.

Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Gleason BC, Hornick JL. Inflammatory myofibroblastic tumours: where are we now? J Clin Pathol. 2008;61:428–437.
2. Fletcher, C.; Bridge, JA.; Hogendoorn, PC., et al. WHO Classification of Tumours of Soft Tissue and Bone. IARC; Lyon: 2013.
3. Coffin C. M., Hornick J. L., Fletcher C. D. M. Inflammatory myofibroblastic tumor: comparison of clinicopathologic, histologic, and immunohistochemical features including ALK expression in atypical and aggressive cases. *The American Journal of Surgical Pathology*. 2007;31(4):509–520. doi: 10.1097/01.pas.0000213393.57322.c7
4. Cerfolio RJ, Allen MS, Nascimento AG, et al. Inflammatory pseudotumor of the lung. Ann Thorac Surg. 1999;67:933–936. doi: 10.1016/S0003-4975(99)00155-1.
5. Morris SW, Naeve C, Mathew P, James PL, Kirstein MN, Cui X, et al. ALK, the chromosome 2 gene locus altered by the t(2;5) in non-Hodgkin's lym- phoma, encodes a novel neural receptor tyrosine kinase that is highly related to leukocyte tyrosine kinase (LTK). 1997;14:2175–88
6. Chiarle, R., Voena, C., Ambrogio, C. et al. The anaplastic lymphoma kinase in the pathogenesis of cancer. Nat Rev Cancer 8, 11–23 (2008).
7. Chan JK, Cheuk W, Shimizu M. Anaplastic lymphoma kinase expression in inflammatory pseudotumors. Am J Surg Pathol. 2001;25:761–768.
8. Saab ST, Hornick JL, Fletcher CD, et al. IgG4 plasma cells in inflammatory myofibroblastic tumor: inflammatory marker or pathogenic link? Mod Pathol. 2011;24:606–612.
9. Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. 2006;367:241–251.
10. T. M. Theilen, J. Soerensen, K. Bochennek, M. Becker, D. Schwabe, U. Rolle, T. Klingebiel, T. Lehrnbecher, Crizotinib in ALK(+) inflammatory myofibroblastic tumors-current experience and future perspectives, Pediatr. Blood Cancer 65 (2018), https://doi.org/10.1002/pbc.26920.
11. A. Ono, H. Murakami, M. Serizawa, K. Wakuda, H. Kenmotsu, T. Naito, T. Taira, Y. Koh, Y. Ohde, T. Nakajima, M. Endo, Drastic initial response and subsequent response to two ALK inhibitors in a patient with a highly aggressive ALK-rearranged inflammatory myofibroblastic tumor arising in the pleural cavity, Lung Cancer 99 (2016) 151–154, https://doi.org/10.1016/j.lungcan.2016.07.002.
12. N. Panagiotopoulos, D. Patrini, L. Gvinianidze, W.L. Woo, E. Borg, D. Lawrence,Inflammatory myofibroblastic tumour of the lung: a reactive lesion or a true neo-plasm? J. Thorac. Dis. 7 (2015) 908–911
13. Panagiotopoulos, D. Patrini, L. Gvinianidze, W.L. Woo, E. Borg, D. Lawrence,Inflammatory myofibroblastic tumour of the lung: a reactive lesion or a true neo-plasm? J. Thorac. Dis. 7 (2015)

908–911

14. Goldin SB, Osborne D, Paidas C, Iannello J Gilbert-Barness E, Karl R, Wilsey MJ Jr. Inflammatory myofibroblastic tumor of the midesophagus. Fetal Pediatr Pathol. 2007;26(5-6)243-254
15. Ufuk F., Duygu H., Karabulut N. Inflammatory Myofibroblastic Tumor of the Lung: Unusual Imaging Findings of Three Cases. Pol J Radiol. 2015; 80: 479–482. doi: 12659/PJR.894902
16. Mirshemirani,Tabari AK., Sadeghian n., Shariat-Torbaghan S., Pourafkari M., Mohajerzadeh L. Abdominal Inflammatory Myofibroblastic Tumor: Report on Four Cases and Review of Literature. Iran J Pediatr. 2011 Dec; 21(4): 543–548.
17. Panagiotopoulos, D. Patrini, L. Gvinianidze, W.L. Woo, E. Borg, D. Lawrence,Inflammatory myofibroblastic tumour of the lung: a reactive lesion or a true neo-plasm? J. Thorac. Dis. 7 (2015) 908–911
18. Watanabe H., Yamasaki N. et al. Successful treatment based on molecular biological assessment of invasive anaplastic lymphoma kinase-positive inflammatory myofibroblastic tumor of the lung. Surg Case Rep. 2019 Dec; 5: 118. doi: 1186/s40792-019-0674-x
19. Dishop MK, Warner BW, Dehner LP, Kriss VM, Greenwood MF, et al. Successful treatment of inflammatory myofibroblastic tumor with malignant transformation by surgical resection and chemotherapy. J Pediatr Hematol Oncol. 2003;25:153–158. doi: 10.1097/00043426-200302000-00014.
20. Johnson K, Notrica DM, Carpentieri D, Jaroszewski D, Henry MM. Successful treatment of recurrent pediatric inflammatory myofibroblastic tumor in a single patient with a novel chemotherapeutic regimen containing celecoxib. J Pediatr Hematol Oncol. 2013;35:414–416. doi: 10.1097/MPH.0b013e3182915cef.
21. Kamisawa T, Nakajima H, Egawa N, et al. igG4-related sclerosing disease incorporating sclerosing pancreatitis, cholangitis, sialadenitis and retroperitoneal fibrosis with lymphadenopathy.
22. Saab Shahrazadb T, Hornick Jason L, Fletcher Christopher D, Olson Sandra J, Coffin Cheryl M. IgG4 plasma cells in inflammatory myofibroblastic tumor: inflammatory marker or pathogenic link? Modern Pathology. 2011;24(4):606–612. doi: 10.1038/modpathol.2010.226.
23. Cerfolio RJ, Allen MS, Nascimento AG, et al. Inflammatory pseudotumor of the lung. Ann Thorac Surg. 1999;67:933–936. doi: 10.1016/S0003-4975(99)00155-1.
24. Zhao Z, Verma V, Zhang M. Anaplastic lymphoma kinase: role in cancer and therapy perspective. Cancer Biol Ther. 2015;16(12):1691.1701.
25. Lovly CM, Gupta A, Lipson D, Otto G, Brennan T, Chung CT, Borinstein SC, Ross JS, Stephens PJ, Miller VA, et al. Inflammatory myofibroblastic tumor harbor multiple potentially actionable kinase fusions. Cancer Discov. 2014;4(9):889-895.
26. Debelenko LV, Arthur DC Pack SD, Helman LJ, Schrump DS, Tsokos M . Identification of CARS-ALK fusion in primary and metastatic lesions of an inflammatory myofibroblastic tumor. Lab Invest. 2003;(9):1255-1265.

27. Butrynski JE, D'Adamo DR, Hornick JL et al. Crizotinib in ALK-rearranged inflammatory myofibroblastic tumor. N Engl J Med. 2010; 363: 1727-1733
28. Gleason BC Hornick JL. Inflammatory myofibroblastic tumours: where are we now?. J Clin Pathol. 2008; 61: 428-437
29. Cools J Wlodarska I Somers R et al. Identification of novel fusion partners of ALK, the anaplastic lymphoma kinase, in anaplastic large-cell lymphoma and inflammatory myofibroblastic tumor. Genes Chromosomes Cancer. 2002; 34: 354-362
30. Lovly CM, Gupta A, Lipson D, Otto G, Brennan T, Chung CT, Borinstein SC, Ross JS, Stephens PJ, Miller VA, et al. Inflammatory myofibroblastic tumor harbor multiple potentially actionable kinase fusions. Cancer Discov. 2014;4(9):889-895
31. Sugganth Daniel, Laurie M.Gay, Jo-Anne Vergilio, Jeffrey S.Ross. A clinical and genomic profile of inflammatory myofibroblastic tumors. Journal of Clinical Oncology (May 20, 2017) 1538-1538.
32. Lovly CM, Gupta A, Lipson D, Otto G, Brennan T, Chung CT, Borinstein SC, Ross JS, Stephens PJ, Miller VA, et al. Inflammatory myofibroblastic tumor harbor multiple potentially actionable kinase fusions. Cancer Discov. 2014;4(9):889-895.
33. Shijie Maia , Gang Xionga , Dingwei Diaoa , Wenjing Wangb , Yujie Zhoub , Ruijun Cai. Case report: Crizotinib is effective in a patient with ROS1-rearranged pulmonary inflammatory myofibroblastic tumor. Lung cancer. 128 (2019) 101-104
34. Hornick JL,Sholl LM, Dal Cin P, Childress MA, Lovly CM. Expression of ROS1predicts ROS1 gene rearrangements in inflammatory myofibroblastic tumors. Mod Pathol. 2015;28(5):732-739).
35. Jia He, Xinyi Z, Cheng HYan Y, Lu Z, Chongmei L, Fang Y, Shanqing L. Double amplifications of CDK4 and MDM2 in a gastric inflammatory myofibroblastic tumor mimicking cancer with local invasion of the spleen and diaphragm. Cancer Biology and Therapy. 2018; Vol. 19, NO. 11, 967-972
36. Antonescu Cristina R, Suurmeijer Albert JH, Zhang L. et al. Molecular chacacterization of inflammatory myofibroblastic tumors with frequent ALK and ROS1 fusions and rare novel RET gene rearrangement. M J Surg Pathol.2015 July; 39(7):957-967.)

Table

Table 1

Summary of the main case series on ALK negative IMT

STUDY	Lovly et al. (2014)	Shijie et al. (2019)	Hornick et al. (2015)	Jia et al. (2018)	Antonescu et al. (2015)
TYPE OF STUDY SUBJECTS	Case report N=1	Case report N=1	Molecular study N=30 (9 ALK -)	Case report N=1	Molecular study N=67 (27 ALK-)
MUTATIONS	TGF-ROS1	TGF-ROS1	ROS1 (TGF-ROS1 fusion, YWHAE-ROS1 fusion,fusion partner unknown)	double amplification of CDK4 and MDM2	ROS1, RET
TREATMENT	Crizotinib (250 mg)	Crizotinib (250 mg)	-	-	-
RESULTS	continued decrease in tumor burden	continuous remission with significant reduction in tumor size	-	-	-

Figures

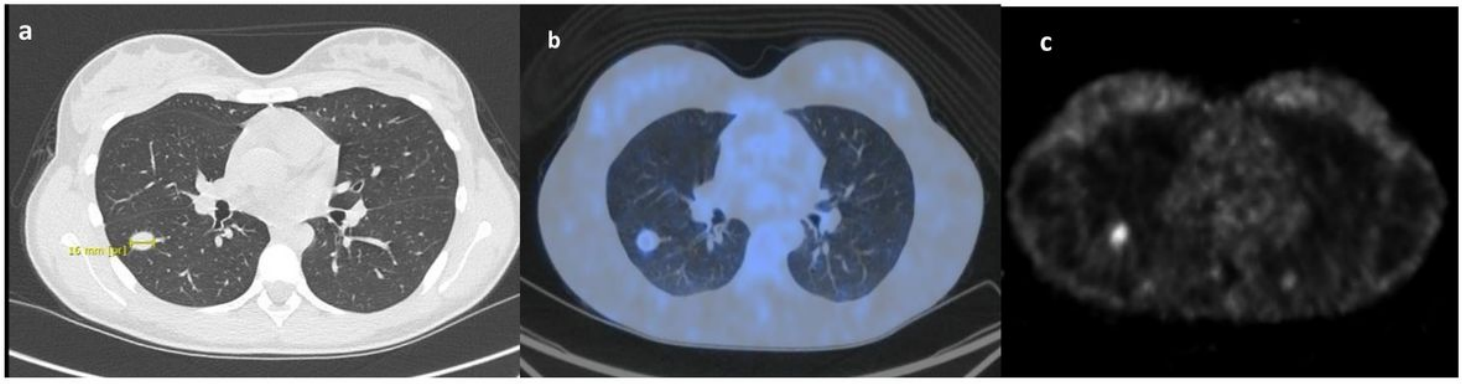

Figure 1

The broncopulmonary nodule detected with diameter of 16 mm was located at the apical segment of of the right lower lobe (RLL) (a) and show a SUVmax of 3.5 at the FDG PET/CT (b) and 3.4 at the 68GaPET/CT (c)

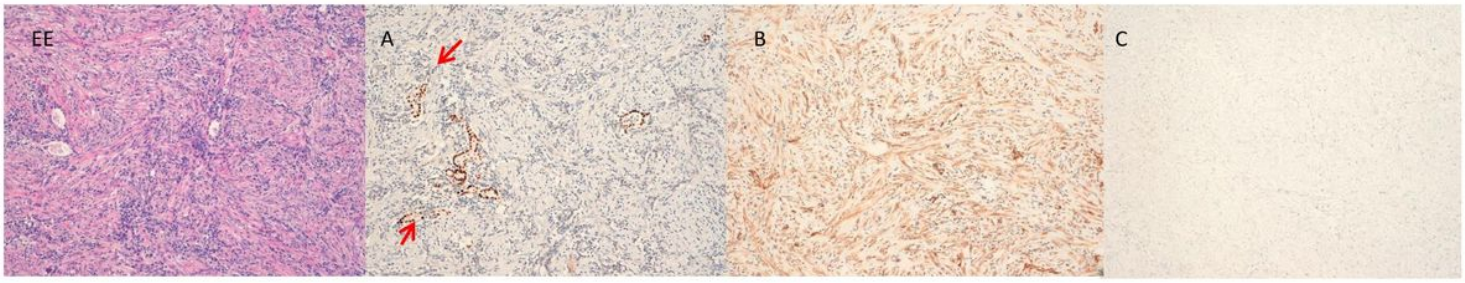

Figure 2

Figures with 10x magnification show cubic cells (EE) without atypia positive for TTF1 (A)(red arrow), Ck7 and napsin and negative for CD117, chromogranin and synaptophysin The IgG plasma cells are numerous mostly in the periferical fields, but the IgG4 ratio is normal. The spindle cell component was positive for smooth actin (B) and negative for ALK (C).

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