https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

CT FINDINGS OF THREE GIANT MEDIASTINAL TUMORS IN YOUNG AGE

Arifah[1], Dini Rachma Erawati[2]
[1]Resident of Radiology Specialist Program Study Program, Brawijaya University. Malang, East Java, Indonesia
[2]Radiology Department, Brawijaya University, Malang, East Java, Indonesia
*drarifahsign@student.ub.ac.id

Abstract

Background : Mediastinal teratoma and other mediastinal tumors are very challenging to be distinguished from other mediastinal tumors. Mediastinal tumors can be optimally evaluated with computed tomography (CT). In this paper we present three young male patients with similar symptom of chronic chest pain and chronic cough.
Materials and Methods: Conducting a literature review and medical records.
Results : All patients in this case are young age male, below two decades. All chest CT shows giant mass, but they have different enhancing pattern, different amount of solid, cystic, calcification component. To make correct diagnosis of the mediastinal mass is important because of treatment planning difference, surgery or chemoteraphy. The first case shows benign teratoma with characteristic of heterogenous mass with large amount of fat, with presence of solid and calcification component. The second case shows malignant germ cell tumor with feature of heterogenous mass with predominantly solid component and small amount of fat. It also shows metastatic process in lung and bone. The third case shows Hodgkin lymphoma with slight enhanced mass that narrowed pulmonary artery and caused pericardial effusion.
Conclusion: Various features of mediatinal tumors can be distinguished with CT modality.
Keyword: *Teratoma, malignant germ cell tumor, lymphoma.*

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

INTRODUCTION

Mediastinum is a segment of the thorax containing vital structures such as heart, great vessels, trachea, main bronchi, oesophagus, thymus, lymphatic and nerve structures.[1] The mediastinum is divided into three compartments: anterior (prevascular), middle (visceral), and posterior (paravertebral) compartments.[2]

Mediastinal masses are rather uncommon, but nevertheless include several entities, presenting with a large variety of clinical and pathological features. Age and sex represent important information, which need to be integrated with imaging and laboratory findings. Anterior mediastinum is the most common location of mediastinal tumors, which include various solid and cystic lesions. Several studies have reported the following figures: 35% thymic tumours, 25% lymphomas (Hodgkin lymphoma 13%, non-Hodgkin lymphoma 12%), endocrine tumours 15%, germ-cell tumours 20% (10% benign teratoma, 10% malignant germ-cell tumours) and 5% thymic benign lesions. Mediastinal lesions are optimally evaluated with cross-sectional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI).[1]

Germ cell tumors (GCTs) are rare neoplasms that originate from progenitor cells of the germ cell lineage. The GCT family is a heterogeneous group of neoplasms, which can affect gonads (ovaries and testes) and in rarer cases (approximately 5%) can occur in extragonadal sites (retroperitoneum, mediastinum, pineal gland). Pineal and mediastinal GCTs are considered primary tumors, while retroperitoneal tumors are suspected to be metastases of a misunderstood gonadal lesion in certain cases. Concerning extragonadal GCTs, it is widely accepted that they originate from an erroneous proliferation of mismigrated primordial germ cells, the same precursor of gonadal tumors. During the migration process to the genital ridge, primordial germ cells could fail to exit from the nerve branches and continue migration through the midline of the body.[4]

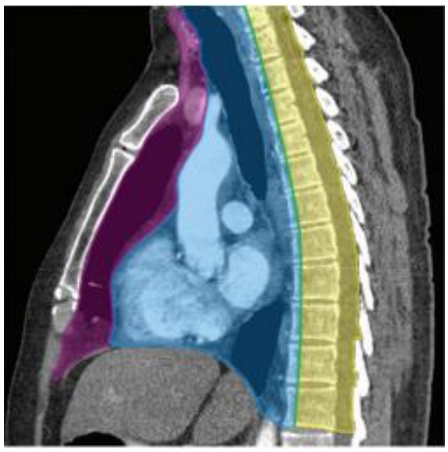

Figure 1. Note the prevascular compartment (purple) wraps around the heart and pericardium, the visceral compartment (blue). Yellow = paravertebral compartment.[3]

Mediastinal germ cell tumor (MGCT) represents a small percentage of GCTs arising from the anterior mediastinum. They represent <5% of all GCTs and <4 % of all mediastinal neoplasm.[4]

MGCTs are classified into seminomatous and nonseminomatous GCTs. Seminomatous MGCT represents pure seminoma, whereas nonseminomatous MGCTs encompass pure yolk sac tumors, embryonal carcinoma, choriocarcinoma, mature or immature teratoma, and mixed GCTs with any combination of GCT types, including seminoma.[5]

More than 80% of GCTs are benign, with a large majority being mature teratomas. Mature teratomas occur with equal frequency in men and women, while malignant GCTs have a predominant distribution in males during the second to fourth decades.[6] Diagnosis is made on the basis of histological findings and excluding the presence of a testicular/ovarian involvement. Laboratory is pivotal for diagnosis of extragonadal germ cell tumors, often demonstrating high levels of human chorionic gonadotropin (β-HCG) and/or α-

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

fetoprotein (α-FP).[7]

Lymphomas are the second most diagnosed group of tumours arising in the anterior mediastinum following thymic disease, according to several studies. The classical phenotype is that of a young male/female (most commonly aged 10–40 years). When considering histology, Hodgkin lymphoma is the most common diagnosed subtype. The diagnosis of mediastinal lymphoma can be confidently suspected on the basis of clinical and imaging findings; however, tissue analysis is needed to confirm diagnosis and to fully identify the histological subtype.[1]

MATERIAL AND METHODS

Patient data were obtained from direct history-taking to the patient and from the patient's medical records of Saiful Anwar Hospital, Malang. The patient's imaging examination data were taken from the Radiology Information System of Saiful Anwar Hospital, Malang.

RESULTS AND DISCUSSION

Case 1

A 22-year-old man was transfered to our center with chest pain for 1 year and became heavy followed with chronic cough for past month. In the beginning, the symptoms did not disturbed the activity, until patient felt difficulty to move and sleep. The chest X-ray showed mass with well-defined margin, regular border mass and calcification, approximately 18,6 x 9,2 cm in size in right hemithorax, on lateral view is seen in anterior mediastinum and covered the retrosternal space.

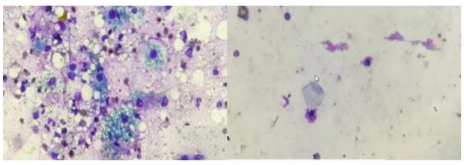

Fig. 2 – (Case 1) Intrathoracic guided-biopsy showed hypocellular containing macrofag cyst, adipose cells, lymphocyte and squamous cells suitable with teratoma.

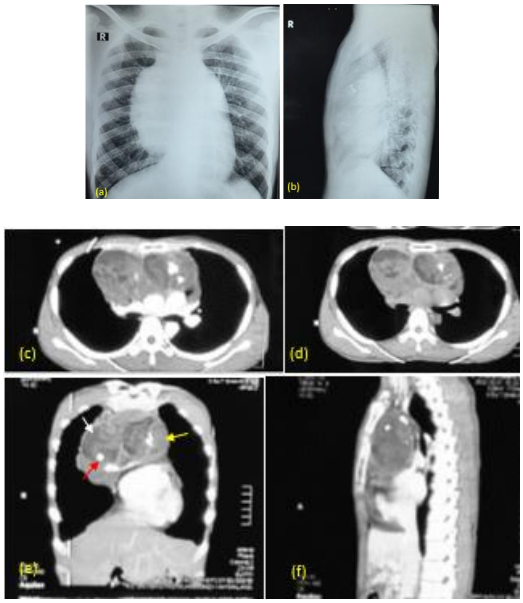

Fig 3-(Case 1) Mediastinal mature cystic teratoma in a 22-year-old man Frontal chest radiography and CT scan images: (a)(b) The frontal chest X-ray shows a calcified mediastinal mass; (c) the axial plain and (d) post contrast view, (e) the coronal post contrast view large amount of fat (white arrow), soft tissue (yellow arrow), and calcification component (red arrow), and (f) the sagittal

Chest CT demonstrated solid-cystic mass in the anterior mediastinal approximately 11,4 x 5x 11,5 cm in size with regular border and calcification component. The mass pushed heart and aorta to the posteroinferior side. There is no invasion to heart and vascular. In contrast additional the mass showed inhomogenous enhancement. This mass suspected with teratoma dd thymoma. Intrathoracic guided-biopsy taken from right parasternal showed hypocellular containing macrofag cyst, adipose cells, lymphocyte and squamous cells suitable with teratoma.

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

Laboratory finding showed normal value of AFP (1,85) Ng/mL, CEA (0,766) Ng/mL, NSE (15,63) Ng/mL, and Beta-HCG <0,10 mlu/mL, and LDH was also normal (191 U/L).

Case 2

A 17-year-old man was transfered to our center with fatigue and chronic cough for 3 months that worsened in one month. The patient also has symptoms : intermittent fever for the past month and back pain in 3 weeks. The chest X-ray showed opacity in the right parahilar and paracardiac region formed silhoute sign with heart, and opacity in right hemithorax covered costophrenic angle and right hemidiaphragm, suspected with mediastinal mass dd lung tumor and right pleural effusion.

The chest CT showed heterogenous mass containing fat, soft tissue, and calcification approximately 13x12,9x19,7 cm in size in the right anteromedial mediastinum. There is heterogenous contrast enhancement in soft tissue component. The mass pushed bronchus partially, and caused right middle lung collapse, also pneumonic reaction and fluid density in right hemithorax are seen. In visualized liver showed hypodensity of multiple nodule. This mass suitable with teratoma with pneumonic reaction and multiple hypodense nodule in liver, and right pleural effusion.

Intrathoracic guided-biopsy that taken from thorax region showed necrosis and hemorhage, from liver showed round-oval-pleomorphic cells, irregular nucleus membrane, prominent nucleolus, partial of cytoplasma is narrow or wide. It also showed matrix of fibrous tissue and lymphocyte with erythrocyte field. It is suspected with metastasis process of malignant germ cell tumor dd small cell carcinoma.

Because of back pain and difficulty of walking, patient was underwent bone survey with the result collapse of vertebral body of Lumbal 2 in the anteromiddle side with decreased vertebral thickness <50 % and multiple osteolytic in frontal bone because of metastasis process. Magnetic resonance also depicts bone marrow changes in multiple level of thoracolumbal.

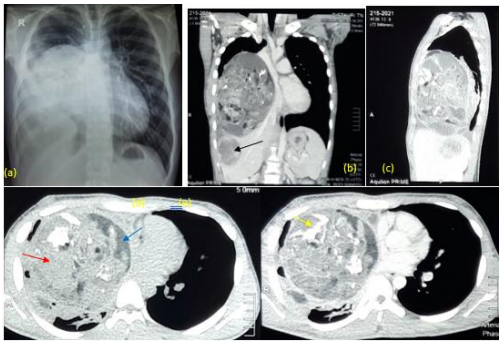

Fig. 4 – (Case 2) Malignant teratoma in a 17-year-old man. Frontal chest radiography (a) showed opacity in the right parahiler and paracardiac formed silhoute sign with heart, coronal (b), axial (d) and sagittal view (c,e)with contrast showed heterogenous mass dominantly soft tissue (red arrow), small fat (blue arrow), calcification (yellow arrow), also liver mass (black arrow)

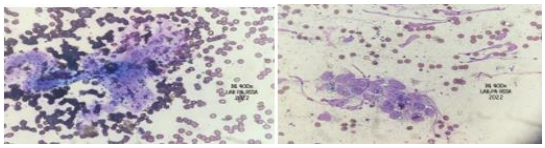

Fig 5 (Case 2). Left : Intrathoracic guided-biopsy from thorax region showed necrosis and hemorhage, Right : from liver showed round-oval-pleomorphic cells, irregular nucleus membrane, prominent nucleolus

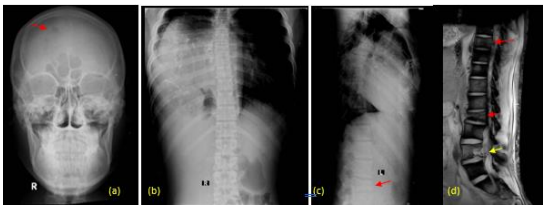

Fig Fig. 5 – (Case 2) Metastatic process from malignant teratoma in a 17-year-old man. Skull AP (a) showed multiple osteolytic in

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

frontal bone, Thoracolumbal AP (b) and lateral view (c) showed collapse of vertebral body of Lumbal 2 in the anteromiddle side with decreased vertebral thickness <50 % (c) bone marrow changes, (d) MR imaging shows bone marrow changes in multiple levels of thorolumbal

Laboratory finding showed markedly increased value of AFP (54009) ng/mL and Beta-HCG 737,20 mIu/mL).

Case 3

A 19-year-old man was transfered to our center with chronic cough for 5 months and unexplained 20 kg-weight loss in 5 months. Chest Xray showed lobulated mass in left parahilar formed silhoute sign with upper left heart border. The chest CT showed isodense solid mass with lobulated margin in the anteromedial of mediastinum that enhanced after additional contrast approximately ±11,8x9,2x14,3cm in size. It adhered to retrosternal space and covered and narrowed left pulmonal artery, pulmonal truncus, aorta arch, descendens aorta, and also adhered to left atrium, and left ventricle. It also covered subclavian and left common carotid artery. The chest CT also depicted pericardial effusion.

Intrathoracic guided-biopsy that taken from thorax region showed growing tumor, forming diffuse-solid structure, separated with fibrous tissue. Tumor consist of round cells, partially giant cells, round-oval nucleus, irregular nuclear membrane, hyperchromatic, thin cytoplasma. There are inflammatory cells : erythrocyte dan lymphocyte. Suspicious for Hodgkin Lymphoma.

Immunohistochemistry examination for CD3 and CD30 shows positive for T lymphocyte around atypic cells, PAX5 shows weak positive.

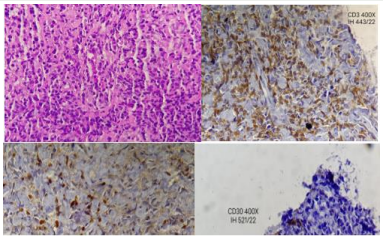

Fig 6 (Case 3). a) . Tumor consist of round cells, partially giant cells, round-oval nucleus, irregular nuclear membrane, b) CD3, positive for T lymphocyte around atypic cells forming rosete pattern, c) PAX5, weak positive in nucleus of atypic cells, d) CD30, positive in nucleus of atypic cells

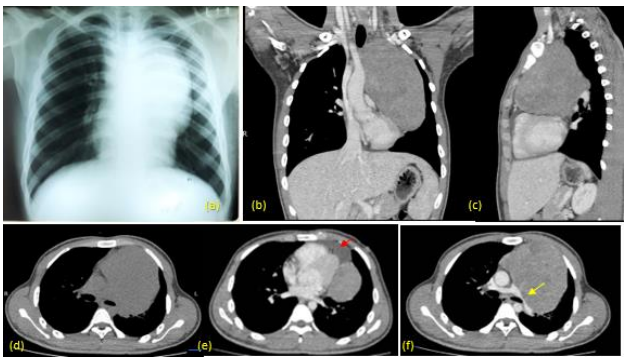

Fig.75– (Case 3) Mediastinal mass in a 19-year-old man. Frontal chest radiography showed lobulated mass in left perihilar and CT scan images: (b-f) showed a isodense solid mass with lobulated marginin the anteromedial of mediastinum that enhanced after additional contrast. It narrowed left pulmonal artery (yellow arrow). We can see also pericardial effusion red arrow).

DISCUSSION

Almost 40% of people who have mediastinal tumors experience no symptoms. Most of the growths are often discovered on a chest x-ray that is performed for another reason. When symptoms are present they are often a result of the compression of surrounding structures, such as the spinal cord, heart or the pericardium (the heart's lining), and may include: shortness of breath, chest pain,

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

cough, fever, chills, night sweats, coughing up blood, hoarseness, unexplained weight loss, lymphadenopathy, (swollen or tender lymph nodes), wheezing, stridor (a high-pitched, noisy respiration, which can be a sign of respiratory obstruction, especially in the trachea or larynx).[8]

Dyspnea is the most common symptom followed by cough, fever, chest pain, hemoptysis and dysphagia. Localising symptoms are secondary to tumour invasion (respiratory compromise; paralysis of the limbs, diaphragm and vocal cords; Horner syndrome; superior vena cava syndrome), while systemic symptoms are typically due to the release of excess hormones, antibodies or cytokines.[8]

In the cases we have reported, all patients had clinical symptoms : chronic cough, chest pain, activity disturbance and weight loss, and CT revealed that the tumors were large in size.

A frontal chest radiograph will show that, mediastinal mature teratomas often create an obtuse angle with the lungs, silhouette the cardiac borders, and demonstrate the hilum overlay sign. The hilar vessels are still visible through a mediastinal mass. This indicates the mass does not arise from the hilum. On a lateral chest radiograph, the mass can be compartmentalized into the anterior, middle, or posterior mediastinum. Masses that tend to obliterate the retrosternal clear space are in the anterior mediastinum.[9]

Chest X-ray and CT examination can show round or round mass in the anterior mediastinum, partial lobulated, calcification in the tumor and even tooth or bone. Mature teratomas are mostly cystic or cystic masses, while immature teratomas are mostly solid masses. Most mediastinal teratomas are located in the anterior mediastinum, which are easily misdiagnosed as thymoma before operation, and should be carefully identified.[10]

In the cases we have reported, all the xray showed round mass located in the anterior mediastinum, create an obtuse angle with the lungs, silhouette the cardiac borders, obliterate the retrosternal clear space.

The radiologic examination of choice is a chest CT scan in mediastinal teratomas which can better evaluate the location, extension, and vascularity of such lesions compared to conventional radiography. The typical CT features in mediastinal teratomas include well-demarcation with lobulated structure regions of fat, cystic fluid contents, and areas of calcification. The presence of the fat-fluid level is pathognomonic for teratomas. The characteristic findings of teratoma are the presence of well-differentiated tissues such as the teeth and hair.[11] In case 1 and case 2 showed solid cystic mass with heterogenous enhacement and mass containing calcification component.

Pancreatic enzymes are reported to have a role in the rupture of tumors. If teratoma is ruptured, the findings can be fat globules at the site of rupture, air space opacities such as consolidation or atelectasis in the adjacent lung parenchyma, and pleura effusion.[11] There is parenchymal concolidation, lung collapse in the middle lobe, and pleural effusion in case 2, whether pericardial effusion is presence in case 3.

Comprehensive analysis must be combined with clinical manifestations and imaging characteristics to improve the accuracy of diagnosis. During the diagnosis and follow-up of mediastinal teratoma, it is necessary to monitor serum tumor markers, and lack alpha-feto-protein (AFP) and beta-human chorionic gonadotropin (β-HCG) should be monitored. Benign teratomas commonly revealed normal AFP and β-HCG. Elevated serum AFP or β-HCG level indicates a malignant component to the teratoma, such as embryonal carcinoma, endodermal sinus tumor, or choriocarcinoma.[10]

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

Approximately 90% of patients present with markedly elevated serum levels of a-FP or b-HCG, is often highly suggestive of NSGCTs especially it occurred in men below the age 0f 40 years. Approximately 10% of patients with seminoma demonstrate slightly elevated serum levels of b–human chorionic gonadotropin (b-HCG); however, a-fetoprotein (a-FP) level is usually normal. Although serum lactate dehydrogenase (LDH) levels are usually elevated, this may be seen with other malignancies such as lymphoma.[3]

Elevated serum AFP or β-HCG level are present in case 2, while in case 1 showed normal value. Case 1 showed benign characteristic, while case 2 showed malignant characteristic compatible with radiological finding and laboratory finding. There is no metastatic process in case 1, while case 2 showed metastatic process in lung parenchym and pleura, liver, and bone (osteolytic in skull and lumbar vertebrae).

On histological examination, mature teratomas are constituted by several tissues such as epidermis, intestinal, bronchial, pancreatic tissue, nervous tissue, bone and cartilage, thyroid, smooth muscle and different components derived from the three germinal layers.[1] It is suitable with histology finding in case 1 : hypocellular containing macrofag cyst, adipose cells, lymphocyte and squamous cells suitable with teratoma.

From histological appearance, malignant germ cell tumor shows large and monotonous tumour cells, separated by fibrous septae showing infiltration by chronic inflammatory cells, mainly lymphocytes. Tumor cells have abundant eosinophilic cytoplasm, well defined cell borders, large ‘squared-off’ nuclei with prominent nucleoli and numerous mitoses.[12] It is compatible with case 2.

The treatment of choice is surgery by completely excising the tumor in non-malignant teratomas. There is an excellent prognosis with a survival rate of almost 100% in mature teratomas. In immature teratomas, the lesions might depict aggressive behavior in adults and with poor prognosis. Surgery is also helpful in establishing the diagnosis as well as maintaining longterm cure diminishing recurrence. The preferred method is the median sternotomy because it provides ease of access. Lateral thoracotomy can be useful in cases where an extension to hemithorax is noted. Although mediastinal teratomas are not life-threatening by themselves; however, complications of extensive surgery that are carried out can be fatal, for instance, pneumonectomy which can lead to death. The combination of surgery with chemotherapy can increase the survival rate in malignant teratoma.[11] Patient with benign teratoma was planned for sternotomy debulking, but patient refused.

Patient with malignant germ cell tumor was treated with chemoteraphy. GCTs are sensitive to chemotherapy and radiotherapy. Radiation delivery with advanced techniques may provide eloquent alternative to surgical salvage for refractory and relapsed tumors. Complete en-block resection should be achieved for better survival and local control. Patient selection always plays a major role while deciding for surgery; assessment of resectability is based on radiological findings and performance status of patients. Extensive stage disease may require assistance of cardiopulmonary bypass or a great vessel replacement; hence, experience of surgical oncology or cardiovascular surgery team also plays a crucial role while going for surgery.[13] Etoposide was the perfect agent to combine with carboplatin in high-dose chemotherapy (HDCT) because its main toxicity is myelosuppression.[14]

Primary malignant nonseminomatous germ-cell generally carrying a poor prognosis, respond poorly to chemotherapy, with 40–50% overall survival. Metastatic disease at diagnostic assessment further worsened the prognosis, with only 25% survival.[1] Follow up 3 months after

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 7-16
e-ISSN 2830-506X
p-ISSN 2830-6007

chemoteraphy shows poor response, RECIST (*Response Evaluation Criteria in Solid Tumours)* shows overall progressive disease compatible with worsening of clinical condition. Then chemoteraphy regiment was changed to Docetaxel. But unfortunately, after once administration of Docetaxel, patient passed away.

Lymphomas are the second most diagnosed group of tumours arising in the anterior mediastinum following thymic disease, according to several studies. The classical phenotype is that of a young male/female (most commonly aged 10–40 years), clinically asymptomatic or presenting with mild-to-moderate respiratory symptoms and/or B symptoms (fever, drenching night sweats, loss of body weight).[1] Or it may be asymptomatic and discovered incidentally at thoracic radiography, or it may be revealed by cough and sometimes dyspnea (secondary to bronchial compression and irritation), fever, itching and night sweats.[1] In case 3, the main symptom are chronic cough for 5 months and unexplained 20 kg-weight loss in 5 months.

On imaging, Hodgkin lymphomas appear as solid and lobulated lesions without calcifications. Hodgkin lymphomas may be very large, infiltrating into adjacent tissues (lung, nerves, vessels); lesions are firm and n lobulated, with some foci of necrosis.[1] In case 3, the chest CT showed isodense solid large mass with lobulated margin in the anteromedial of mediastinum that enhanced after additional contrast. It adhered to retrosternal space and covered and narrowed left pulmonal artery, pulmonal truncus, aorta arch, descendens aorta, and also adhered to left atrium, and left ventricle. It also covered subclavian and left common carotid artery. The chest CT also depicted pericardial effusion.

Laboratory tests may identify elevation of LDH, bone marrow involvement or neoplastic cells in pleural effusion.[1] The chest CT also depicted pericardial effusion in case 3.

The diagnosis of mediastinal lymphoma can be confidently suspected on the basis of clinical and imaging findings; however, tissue analysis is needed to confirm diagnosis and to fully identify the histological subtype, in order to set up the treatment. When considering histology, Hodgkin lymphoma is the most common diagnosed subtype.[1]

Lymphomas in the mediastinum account for 15% of mediastinal masses; they arise either in the thymus or from the mediastinal lymph nodes and only about 10% are primary. Hodgkin lymphoma of classic type (cHL) of thymic origin represents the most frequent mediastinal lymphoma. Among the lymphoma occurring in the mediastinum, T cell lymphomas of precursor type predominate in pediatric age, whereas, in the young adult and in adult age, the most frequent lymphomas are of B cell origin or are classic Hodgkin Lymphoma (cHL) of the thymus. The diagnosis relies on the demonstration of typical C30+ cells, which are often very rare, in a mixed fibroinflammatory background. Immunophenotypical from cHL is positive for CD30 whereas B Lymphoma is >80% weak for CD30. PAX5 in cHL is weaker than that of B Lymphoma.[15]

The diagnosis of mediastinal lymphoma can be confidently suspected on the basis of clinical and imaging findings; however, tissue analysis is needed to confirm diagnosis and to fully identify the histological subtype. A unique Hodgkin lymphoma (HL) characteristic is the tight adherence of rosetting CD41 T cells to Hodgkin tumor cells.[16]

Third patient was treated with regiment doxorubicin, bleomycin, etoposide, and dacarbazine. NCCN (The National Comprehensive Cancer Network) recommendations for stage I–II unfavorable, bulky mediastinal disease or adenopathy >10 cm the preferred regimen, ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) category 1, is initially administered for 2 cycles followed by interim

restaging with PET.[17]After one cycle of regiment, RECIST showed partial response, and clinically improved.

CONCLUSION

All patients in this case are young age male, below two decades. All chest CT depicts giant mass in anterior mediastinum adhered heart and large vessels. But they have different amount of solid, cystic, calcification component, or enhancing pattern. Mediastinal teratoma has soft tissue and calcification components with large amout of fat, while malignant germ cell tumor has large amount of soft tissue or solid component. The characteristic of mediastinal Hodgkin lymphoma was slightly enhanced without calcification component.

Laboratory test and histology are very important in mediastinal tumor cases, AFP, β-HCG, and LDH. AFP and β-HCG are marker to diagnose malignant or benign germ cell tumor. AFP and β-HCG are markedly increased in malignant germ cell tumor, LDH is increased in lymphoma.

It is important to decide right diagnosis of the mediastinal mass because of treatment planning difference, surgery or chemoteraphy. Mediastinal teratoma is cured with surgery, in many cases chemoteraphy is favorable by decreasing the size of tumor. Malignant germ cell tumor has better outcome if no lung metastasis . Mediastinal lymphoma is sensitive with chemoteraphy.

REFERENCES

1. Ghigna, M. R., & Thomas de Montpreville, V. Mediastinal tumours and pseudo-tumours: a comprehensive review with emphasis on multidisciplinary approach. European respiratory review : an official journal of the European Respiratory Society. 2021. 30(162), 200309.
2. Jeffrey Klein et al. Brant and Helms' Fundamentals of Diagnostic Radiology 5th Edition. 2018.709
3. Carter, B. W., Benveniste, M. F., Madan, R., Godoy, M. C., de Groot, P. M., Truong, M. T., Rosado-de-Christenson, M. L., & Marom, E. M. ITMIG Classification of Mediastinal Compartments and Multidisciplinary Approach to Mediastinal Masses. Radiographics : a review publication of the Radiological Society of North America, Inc. 2017 37(2) 413–436.
4. Urbini, M., Schepisi, G., Bleve, S., Virga, A., Gianni, C., Gurioli, G., Ulivi, P., & De Giorgi, U. Primary Mediastinal and Testicular Germ Cell Tumors in Adolescents and Adults: A Comparison of Genomic Alterations and Clinical Implications. Cancers. 2021. 13(20), 5223.
5. El-Zaatari ZM, Ro JY. Mediastinal Germ Cell Tumors: A Review and Update on Pathologic, Clinical, and Molecular Features. Adv Anat Pathol. 2021 Sep 1;28(5):335-350.
6. Nakazono, T., Yamaguchi, K., Egashira, R., Mizuguchi, M., & Irie, H. Anterior mediastinal lesions: CT and MRI features and differential diagnosis. Japanese journal of radiology. 2021. 39(2), 101–117.
7. Dell'Aversana S, et al. Germ cell tumors in male patients without gonadal involvement: computed tomography/magnetic resonance imaging findings and diagnostic workflow. Quantitative imaging in medicine and surgery. 2019. 9(12), 2000–2007.

8. Malik, Maajid. Role of CT in evaluation of Mediastinal masses. International Journal of Advanced Medical and Health Research. 2019; 5. 41-45
9. Duc, V. T., Thuy, T., Bang, H. T., & Vy, T. T. Imaging findings of three cases of large mediastinal mature cystic teratoma. Radiology case reports. 2020; 15(7), 1058–1065.
10. Tian Zhenhuan, et al. Surgical treatment of benign mediastinal teratoma: summary of experience of 108 cases. Journal of Cardiothoracic Surgery. 2020;15. 10.1186/s13019-020-1075-8.
11. Foladi, N., Farzam, F., Rahil, N. *et al.* CT features of mature teratoma in the mediastinum of two young adults—a report of two cases. Egypt J Radiol Nucl Med 2020;51, 234.
12. Kaur, Baljeet. Pathology of malignant ovarian germ cell tumours. Diagnostic Histopathology. 2020. Elsevier
13. Kumar, N., Madan, R., Dracham, C. B., Chandran, V., Elangovan, A., Khosla, D., Yadav, B. S., & Kapoor, R. Primary mediastinal germ cell tumors: Survival outcomes and prognostic factors - 10 years experience from a tertiary care institute. Rare tumors. 2020; *12*, 2036361320972220.
14. Giunta, E. F., Ottaviano, M., Mosca, A., Banna, G. L., & Rescigno, P. Standard versus high-dose chemotherapy in mediastinal germ cell tumors: a narrative review. Mediastinum (Hong Kong, China). 2022; *6*, 6.
15. Marino, M., & Ascani, S. An overview on the differential diagnostics of tumors of the anterior-superior mediastinum: the pathologist's perspective. *Mediastinum (Hong Kong, China)*. 2019;*3*, 6.
16. Veldman, J., Visser, L., Huberts-Kregel, M., Muller, N., Hepkema, B., van den Berg, A., & Diepstra, A. Rosetting T cells in Hodgkin lymphoma are activated by immunological synapse components HLA class II and CD58. Blood. 2020; *136*(21), 2437–2441.
17. Hoppe RT,er al. Hodgkin Lymphoma, Version 2. NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2020;18(6):755–7.