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Three in one: A case presented with multiloculated thymic cyst, thymic Hodgkin lymphoma and pericardial cyst

Üçü bir arada: Multiloküle timik kist, timik Hodgkin lenfoma ve perikardiyal kist birlikteliği olan bir olgu sunumu

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ABSTRACT

Multiloculated thymic cyst is a cystic reaction of medullary epithelium to inflammatory process. In most cases, the exact cause of the inflammation is not known. Hodgkin lymphoma and multiloculated thymic cyst coexistence is a rare condition and may cause significant diagnostic difficulties. Herein, we present a rare case who underwent surgery for multiloculated thymic cyst and was subsequently diagnosed with Hodgkin lymphoma and had a concurrent pericardial cyst.

Keywords: Anterior mediastinal mass, multiloculated thymic cyst, pericardial cyst, thymic Hodgkin lymphoma.

ÖZ

Multiloküle timik kist, iltihaplanma sürecine medüller epitelin kistik bir reaksiyonudur. Çoğu olguda iltihabın kesin nedeni bilinmemektedir. Hodgkin lenfoma ve multiloküle timik kist birlikteliği nadir bir durumdur ve önemli tanısal zorluklara neden olabilir. Bu yazıda, multiloküle timik kist nedeniyle ameliyat edilen ve daha sonra Hodgkin lenfoma tanısı konan ve eş zamanlı perikardiyal kist bulunan nadir bir olgu sunuldu.

Anahtar sözcükler: Ön mediasten kitlesi, multiloküle timik kist, perikardiyal kist, timik Hodgkin lenfoma.

Thymic cysts are relatively rare lesions and constitute approximately 3% of mediastinal masses. The differential diagnosis of acquired multiloculated thymic cysts (MTC) from congenital thymic cysts is vital. They may be associated with malignancy (thymoma, thymic carcinoma, Hodgkin lymphoma [HL]) and may cause compression on adjacent structures and may recur, if not completely resected.[1] Hodgkin lymphoma and MTCs coexistence is a rare condition and may cause significant diagnostic difficulties.[2] Herein, we present a case who underwent surgery for MTC and was subsequently diagnosed with HL and had a concurrent pericardial cyst.

CASE REPORT

A 25-year-old female patient was admitted to hospital with facial paralysis thrice in a year. She received methylprednisolone (1 mg/kg/day) therapy on admissions. Her physical examination and radiological evaluation, including ultrasound (US) of the cervical region and magnetic resonance imaging (MRI) of the ear and brain, revealed no pathology. In her medical history, she had a mass-diagnosed fibroadenoma in her left breast. She had no smoking history, tuberculosis, or any other disease. Left hilar enlargement was present on chest radiography and, then, thoracic computed tomography (CT) was

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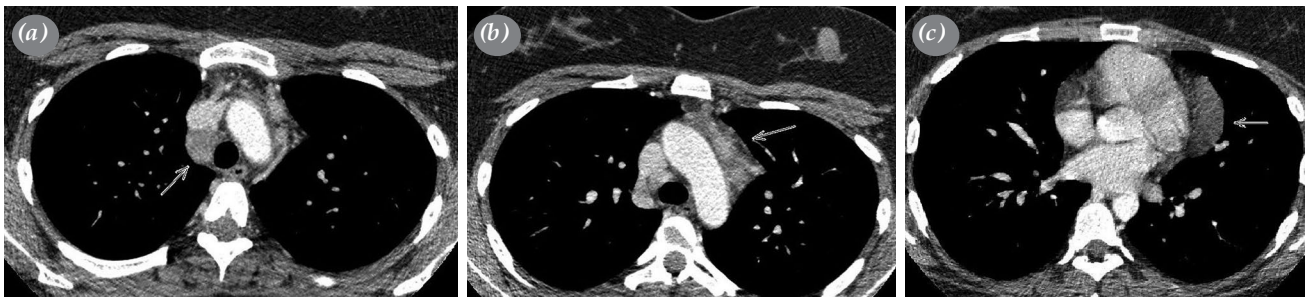

Figure 1. Axial enhanced computed tomography scan showing enlarged mediastinal lymph nodes. **(a)** The most prominent lymph node is located at right upper paratracheal region (arrow). **(b)** An ill-defined soft tissue mass in the paraaortic area (arrow). Note that there is a well-defined soft tissue mass in the left breast, which is proven as fibroadenoma pathologically. **(c)** Well- marginated cystic lesion without solid component on left paracardiac region, which may belong to the thymic cyst or pericardial cyst (arrow).

performed. Thoracic CT was obtained via a 64-row slice CT scanner (Toshiba Aquilion 64, Otawara, Japan). One mL/kg of intravenous contrast agent (350/100 Omnipaque, GE Healthcare, Oslo, Norway) was administered at a rate of 2.5 mL/sec via the antecubital vein. Thoracic CT revealed enlarged lymph nodes in the mediastinum. The largest node's axial diameter, located at station 4R, was 21×16 mm (Figure 1a). Additionally, CT scan demonstrated an ill-defined soft tissue attenuated mass in the left side of the anterior mediastinum, which might belong to thymic hyperplasia or thymic lymphoid hyperplasia (Figure 1b). On the left paracardiac area at the caudal edge of the soft tissue mass, a well-marginated cystic lesion with a diameter of 52×20 mm was observed (Figure 1c). On positron emission tomography (PET)/CT, the mass in the anterior mediastinum had a maximum standardized uptake value (SUVmax) of 6.6, and the right paratracheal lymph node had a SUV_{max} value of 5.6. Endobronchial US-guided fine-needle aspiration (EBUS-FNA) of the right paratracheal lymph node was performed and it was reported as negative in terms of malignancy or granulomatous reaction; therefore, we decided to follow the patient. In the follow-up thoracic CT three months later, progression was observed in the soft-tissue attenuation mass, which was located in the left anterior mediastinum. The paracardiac cyst was excised, and the mass lesion was biopsied by a left-sided video-assisted thoracoscopic surgery (Figure 2). Intraoperative frozen-section diagnosis was deferred to paraffin sections during this procedure, as the differential diagnosis could not be performed between the possible diagnoses of thymoma and lymphoma. The pathological diagnosis on permanent sections was a MTC with an accompanying pericardial cyst (Figure 3). Thereafter, extended thymectomy via median sternotomy was planned. After sternotomy, an invasive lesion with a diameter of 6 cm in the anterior mediastinum was observed. The mass was resected *en bloc* with a wedge resection of the invaded lung, and the right paratracheal lymph node was dissected. The final histopathological diagnosis was classical nodular sclerosing type HL (NSHL) both for the mass and paratracheal lymph node and accompanying MTC (Figure 4). The patient was discharged on postoperative Day 4 without any complications. The diagnosis was limited-

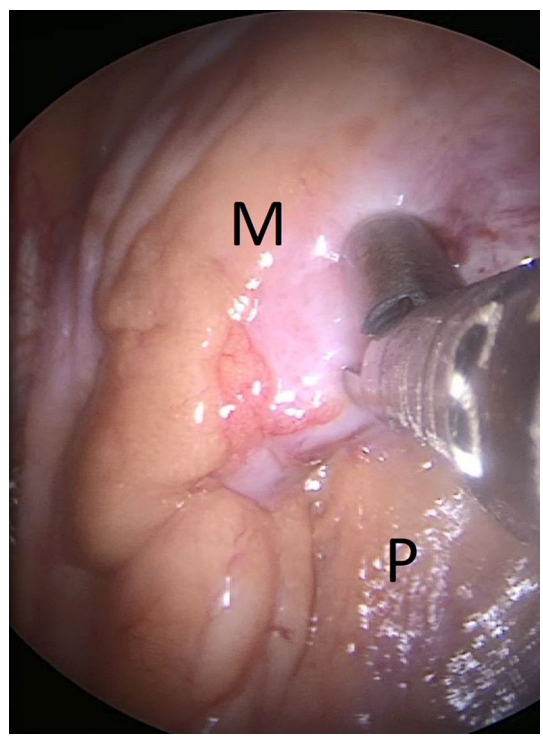

Figure 2. Thoracoscopic view of the mass.
M: Mass; P: Pericardium.

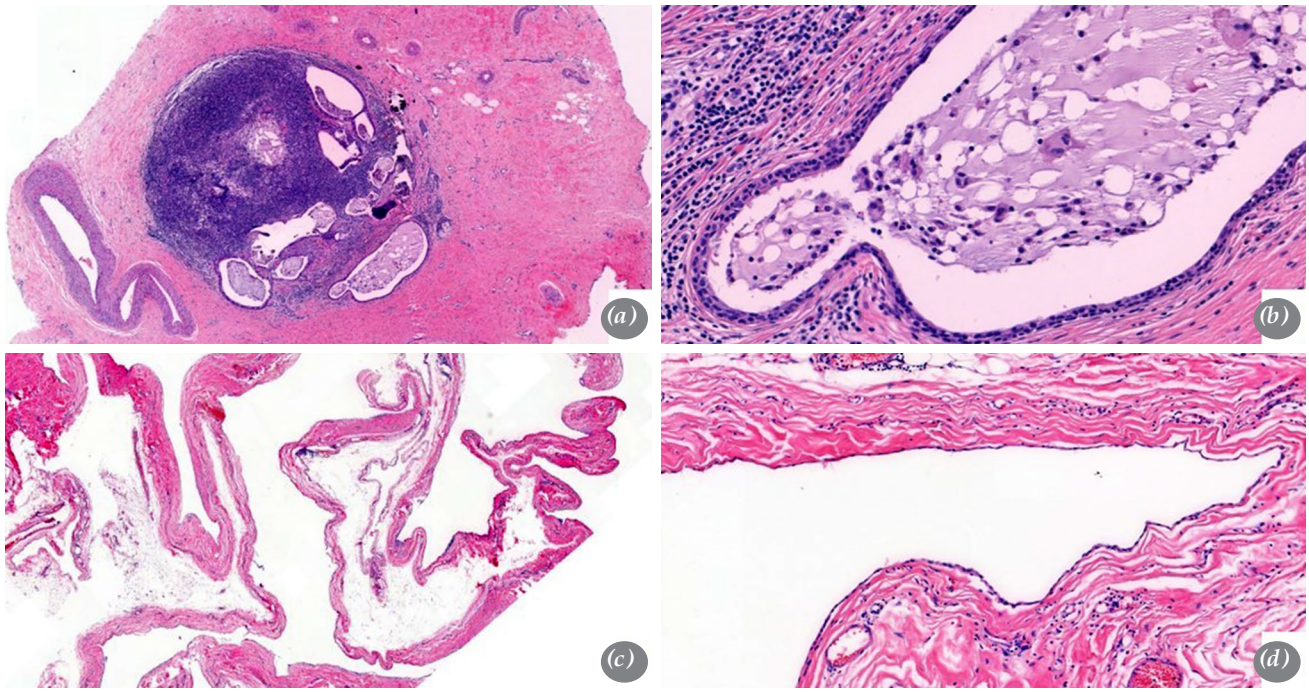

Figure 3. Multiloculated thymic cyst lined with ciliated epithelium **(a)** (H&E, ×5), **(b)** (H&E, ×40). Pericardial cyst lined by bland mesothelium **(c)** (H&E, ×2), **(d)** (H&E, ×20).

stage classical HL, nodular sclerosing type, clinical Stage II A according to the European School of Medical Oncology (ESMO) guidelines. The patient received three cycles of ABVD (adriamycin 50 mg/m^2, bleomycin 20 mg/m^2, vinblastine 12 mg/m^2, dacarbazine 750 mg/m^2) followed by external radiotherapy in 15 fractions with a total dose of 3,000 cGy. The PET/CT positivity of the lesion resolved completely during the interim PET and end of treatment PET. The patient has been under follow-up for nine months without any recurrence and symptoms.

DISCUSSION

Thymic cysts are rare mediastinal masses and classified as congenital unilocular and acquired multilocular cysts. Congenital unilocular cysts originate from the foregut, and can be lined with different types of epithelium (i.e., squamous, respiratory, columnar, or mesothelial).[3] Multiloculated thymic cysts are cystic reactions of medullary epithelium to inflammatory process. In most cases, the exact cause of the inflammation is not known; however, MTC have been reported in patients with Sjögren syndrome, aplastic anemia, myasthenia gravis, systemic lupus erythematosus, human immunodeficiency virus (HIV) infection, radiotherapy, surgical trauma, and also malignancies such as thymoma, thymic carcinoma, and HL.[1] Cystic spaces of MTC are lined by squamous, cuboidal or flat epithelium. The lining of the cyst often shows continuity with residual Hassall corpuscles. Chronic inflammation, hemorrhage, fibrosis, cholesterol clefts, lymphoid follicular hyperplasia can be seen in the wall of the cysts. Tumors that may show cystic features such as HL, seminoma, teratoma, and thymic epithelial tumors are in the differential diagnosis of MTC. They may have an identical gross pathological appearance with MTC.[4] Suster and Rosai[5] published 18 MTC cases in 1991. Thymoma cases with cystic degeneration, unilocular thymic cysts, thymic Hodgkin disease and thymic seminomas were not included in this study. Three (16%) of 18 patients were female, and the average age was 42. The majority of the patients were asymptomatic. Recurrence was observed in three patients. While two of them had no accompanying tumor, one had thymic carcinoma. Re-excision followed by radiotherapy was applied to those who had no cancer. Both patients were followed without recurrence. Aplastic anemia in one patient, Sjögren syndrome in one patient, thymoma in two patients, thymic carcinoma in two patients, and chronic myeloid leukemia in one patient were reported. Tight

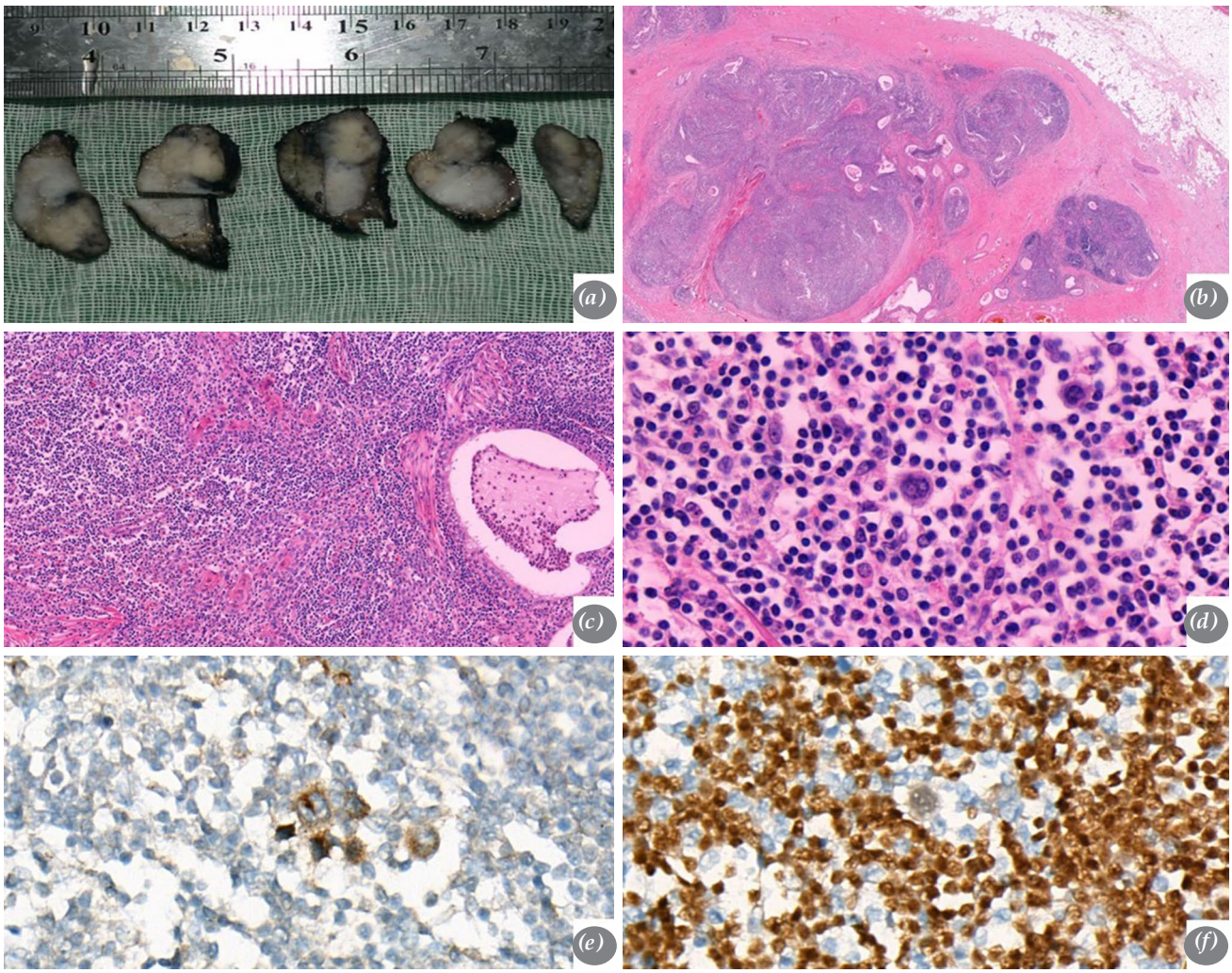

Figure 4. A solid lesion was detected in microscopic examination **(a)**. The solid lesion was composed of a small, microscopic multiloculated thymic cyst and Reed-Stenberg cells **(b)** (H&E, ×2), **(c)** (H&E, ×20), **(d)** (H&E, ×100). Reed-Stenberg cells were positive with CD30 **(e)** (×40) and PAX5 **(f)** (×100).

Slides were scanned with the digital scanner (Pannoramic 250 Flash III, 3DHISTECH Ltd., Hungary) in ×40 objective and photographed with CaseViewer 1.4 (3DHISTECH Ltd., Hungary) in ×40 magnification.

Table 1. Publications presenting Hodgkin lymphoma with associated multiloculated thymic cyst

No	Publication	Year	Age/Sex	Cyst type	Lymphoma type
1	Scully et al.[12]	1982	21/F	MTC	NSHL
2	Kim et al.[13]	1985	39/M	MTC	NSHL
3	Lindfors et al.[9]	1985	20/F	MTC	NSHL
			19/M	MTC	NSHL
			39/M	MTC	NSHL
4	Ul Haque et al.[14]	1994	27/M	MTC	TCL
5	*Present case*		25/F	MTC	NSHL

MTC: Multiloculated thymic cyst; NSHL: Nodular sclerosing Hodgkin lymphoma; TCL: T-cell lymphoma.

adhesion to surrounding organs may be observed during surgery, and this may be interpreted in favor of invasion as in our case. Radiological appearance is not specific for MTC and, also, some MTCs have a unilocular appearance on CT.[1] Microscopic tumor foci can be found on the walls of only some of the cystic structures. Therefore, complete surgical excision is recommended for MTCs.[6] In our case, although we took multiple biopsies from the mass, we could not manage to get HL diagnosis apart from MTC.

Thymic HL was formerly considered a variant of thymoma. Thymic HL is more common in men in their 20s to 30s, while systemic HL is more common in both 20s to 30s and after 50s in women. Patients are usually asymptomatic, until extrathymic involvement is seen. Thymic involvement of Hodgkin disease often causes cystic changes, and the incidence of these cystic changes increases after radiotherapy.[7] The presence of Reed-Sternberg cells in the cyst wall and immunohistochemical studies are required for the diagnosis of HL.[4] The mechanism of thymic cyst formation in Hodgkin disease has not been fully understood, yet. Nevertheless, there are opinions that it may be secondary to therapeutic effect or tumor infiltration.[8-10] In particular, in the presence of accompanying lymph nodes, the diagnosis of lymphoma should be kept in mind. Lymph node sampling is useful for a definitive diagnosis. Mediastinoscopy may be better than EBUS-FNA for a through lymphoma diagnosis and, also, it should be in our case. Most lymphomas involving the thymus are NSHL.[11] Systemic symptoms are rarely seen at the time of diagnosis. Our case was similarly a NSHL and had no systemic symptoms.

Hodgkin lymphoma and MTC association is a rare condition. In the literature, there are five publications reporting seven patients.[12-14] Three of seven (42.8%) patients, including this case, were female and the average age was 27.1 years. Only one patient had T cell lymphoma; all the others had NSHL (Table 1). The fact that MTC is seen particularly with the NSHL subtype suggests that the inflammation caused by the tumor rather than the tumor itself plays a more critical role in the development of MTC.

Although cranial nerve involvement can be seen in lymphomas, this is rare in HL. In our case, although the cause of facial nerve involvement could not be determined radiologically, the recovery and non-recurrence of facial paralysis after lymphoma treatment suggests that there may be a relationship between lymphoma and facial paralysis as paraneoplastic neuropathies are seen in association with 4 to 5% of cancers.[15]

Pericardial cysts are also rare masses. It constitutes 4 to 7% of all mediastinal masses. They are usually asymptomatic and are detected incidentally. In the literature, there is no case with pericardial cyst and MTC coexistence.[16]

In conclusion, complete resection should be performed in all cases with suspected multiloculated thymic cysts. It is difficult to make a definitive diagnosis with incisional biopsies or to detect accompanying tumors. If there are enlarged lymph nodes, coexisting Hodgkin lymphoma should be suspected and they should be sampled using appropriate methods.

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