Case Report

Enlarging cystic lymphangioma of the mediastinum in an adult: is this a neoplastic lesion related to the recently discovered PIK3CA mutation?

Shogo Tajima1, Yusuke Takanashi2, Kenji Koda3

1Department of Pathology, Shizuoka Saiseikai General Hospital, Shizuoka, Japan; Departments of 2Chest Surgery, 3Pathology, Fujieda Municipal General Hospital, Shizuoka, Japan

Received February 25, 2015; Accepted April 14, 2015; Epub May 1, 2015; Published May 15, 2015

Abstract: Cystic lymphangioma, a lymphatic system malformation, is usually observed in infants and children and is rarely found in adults. It most commonly occurs in the cervicofacial region, followed by the axilla. Mediastinal cystic lymphangioma is rare, accounting for 1.8% of all mediastinal cysts. Herein, we present an exceedingly rare adult case of mediastinal cystic lymphangioma that had increased in size over a 5-year period. Although fluid collection might be an alternative explanation for this increase in size, this lymphangioma might harbor a neoplastic nature related to the recently discovered PIK3CA mutation.

Keywords: Cystic lymphangioma, mediastinum, adult, PIK3CA

Introduction

Cystic lymphangioma is a lymphatic system malformation most often observed in infants and children [1]. In contrast, cystic lymphangioma is rarely observed in adults. This malformation is most often observed in the cervicofacial region (75%) and less frequently encountered in the axilla (20%) [2], whereas mediastinal cystic lymphangioma is rare [3]. Mediastinal cystic lymphangioma was reported to account for 1.8% of all mediastinal cysts over a 40-year period [4]. Accordingly, mediastinal cystic lymphangioma is exceedingly rare in adults [5].

Herein, we present a 66-year-old woman with a mediastinal cystic lymphangioma that had increased in size over a 5-year period. This enlargement might be attributed to the possible neoplastic nature related to the PIK3CA mutation recently discovered by Luks et al. [6], though fluid collection could be an alternative explanation for this increase in size.

Case report

A 66-year-old woman presented with chest radiograph abnormalities during her regular check-up. Five years earlier, an anterior mediastinal mass measuring 46 mm × 38 mm × 24 mm had been detected on computed tomography (CT) without any abnormal findings on chest radiography. The mass was sharply marginated and exhibited overall homogeneous water density. No solid areas were apparent (Figure 1A). A thymic cyst was suspected as a differential diagnosis for the cystic lesion arising from the anterior mediastinum. At the time of presentation, the mass had increased in size to 68 mm × 63 mm × 53 mm and did not feature a solid area (Figure 1B). Multiple hemangiomas were detected in the liver, and they did not change in size during the 5-year period (Figure 1C, 1D). Subsequently, video-assisted thoracic surgery with 3 ports was used to perform surgical resection of the mediastinal mass. There were no adhesions in the left thoracic cavity, and the tumor was resected smoothly. The patient’s postoperative course was uneventful.

The surgically resected specimen revealed a multilocular cystic lesion filled with serous fluid. The lesion had collapsed upon submission to the pathological division. The presumed sizes of the constituent cysts ranged from <1 mm to >2 cm.
Histopathologically, the lesion was almost devoid of fluid, probably due to spillage. The cyst walls contained focal lymphocytic aggregates (Figure 2A, 2B). The endothelial cells covered the walls of the cysts and they were flattened (Figure 2C). These findings were suggestive of lymphangioma. No hemangiomatous component was apparent.

Immunohistochemically, the endothelial cells were diffusely positive for CD31 (JC70A, 1:100; Dako, Glostrup, Denmark) (Figure 3A), focally positive for D2-40 (D2-40, 1:100; Dako) (Figure 3B), and rarely positive for CD34 (QBEnd 10, 1:100; Dako) (Figure 3C). Vessels expressing all these markers were observed. All areas exhibiting CD34 positivity were also positive for

Figure 1. Computed tomography findings. A. Five years earlier, the mass was sharply margined, measured 46 mm × 38 mm × 24 mm, and exhibited overall homogeneous water density. No solid areas were apparent. B. The mass increased in size to 68 mm × 63 mm × 53 mm, with no solid area. C. Two hemangiomas in the liver. D. Another hemangioma in the liver.
Enlarging mediastinal cystic lymphangioma in an adult

D2-40. Therefore, the constituent vessels, including the area of CD34 expression, were recognized as lymphatic vessels.

A diagnosis of cystic lymphangioma of the mediastinum was rendered. No other type of vascular malformation coexisted with this lesion.

The patient had no familial history of vascular malformation, and physical examination did not detect any significant vascular lesions on the skin. Eighteen months after surgery, the patient remains free of recurrent disease.

Discussion

Lymphangiomas arise from abnormal lymphatic system development during the early phase of angiogenesis [1]. In normal lymphatic vessels, endothelial cells express CD31 and usually do not express CD34 [7]; however, these cells do express the specific lymphatic marker D2-40 [8]. In contrast, in lymphangiommas, lymphatic vessels are more likely to express CD34 [9]. In our case, few endothelial cells in the cystic lesion expressed CD34 concomitantly with D2-40 and CD31 expression. Whereas this expression pattern is not expected in normal lymphatic vessels, it may be observed in endothelial cells from lymphangiommas. The diagnosis of lymphangioma was supported by the predominant expression of D2-40 over CD34 and co-expression of D2-40 at the site of CD34 expression, along with the fact that lymphocytic aggregate in the cyst walls, which were observed in our case, is a feature of lymphangioma [10].

The conventional term lymphangioma might be better replaced by lymphatic malformation (LM); this term was proposed in the widely used International Society for the Study of Vascular Anomalies (ISSVA) classification, which was expanded in 2014 [11]. According to this classification, the mediastinal lesion in our case was a mixed cystic LM, as the sizes of some constituent cysts exceeded 2 cm whereas others were smaller. The multiple hemangiomas of the liver in our case were considered venous malformations (VMs) under this classification. Some syndromes manifest as LM, and both LM and VM can be observed in syndromes such as Klippel-Trenaunay syndrome and CLOVES syn-
Enlarging mediastinal cystic lymphangioma in an adult

Figure 3. Immunohistochemical findings. (A) Endothelial cells were diffusely positive for CD31 (400 × magnification). (B) Patchily distributed D2-40-positive endothelial cells were observed (400 ×). (C) CD34-positive cells are visible on a cyst wall (arrow) in this field, which corresponds to the area indicated by arrows in (A and B). Arrowheads indicate a mural CD34-positive vessel; this is the same vessel indicated by arrowheads in (A and B) (400 ×).

drome [11]. However, this patient did not present any other manifestations consistent with these syndromes. Regardless, an underlying mechanism prone to inducing vascular malformation development might have led to the occurrence of both LM and VM in this case.

Although LM is not considered neoplastic in the ISSVA classification [11], a PIK3CA mutation in LM was very recently found by Luks et al. [6]. The mechanism by which a PIK3CA mutation that arises during embryogenesis results in malformation is not well elucidated, but is likely attributable to the role played by PI3K in signaling pathways such as the vascular endothelial growth factor pathway [12]. The finding by Luks et al. that PIK3CA-mutant cells were present at low frequencies (≤10%) in affected LM tissue samples suggests that mutant cells can recruit wild-type cells to the malformation process [6]. On the other hand, Luks et al. stated that it is difficult to enrich biopsies solely for affected tissue; accordingly, biopsy samples used to examine PIK3CA mutations are likely to include normal tissue as well as affected tissue, possibly resulting in a low PIK3CA-mutant cell detection rate. In our case, it is possible that the lesion enlargement was due to the neoplastic nature of LM; fluid collection in the lesion is an alternative explanation.

In conclusion, this is a rare case of mediastinal cystic lymphangioma in an adult. Although it corresponded with the non-neoplastic LM according to the ISSVA classification, the more recent finding of a PIK3CA mutation in LM suggests the possibility of a neoplastic lesion. The enlarged size of the lesion in our case might be related to its neoplastic nature or due to fluid collection.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Shogo Tajima, Department of Pathology, Shizuoka Saiseikai General Hospital, 1-1-1 Oshika, Suruga-Ku, Shizuoka 422-8021, Japan. Tel: +81-54-285-6171; Fax: +81-54-285-5179; E-mail: stajima-tky@umin.ac.jp

References

Enlarging mediastinal cystic lymphangioma in an adult


