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Case Report

Human Pulmonary Dirofilariasis: Report of Six Cases

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Division of Pathology, and [1]Division of Surgery, Institute of Pulmonary Cancer Research, [2]Department of Parasitology, School of Medicine, Chiba University, Chiba 260-8670, and [3]Department of Respiratory Surgery, Chiba Rosai Hospital, Ichihara 290-0003

HIROSHIMA, K., IYODA, A., TOYOZAKI, T., FUJISAWA, T., AOSAI, F., KOBAYASHI, M., HATA, H., YANO, A., YUSA, T. and OHWADA, H. *Human Pulmonary Dirofilariasis: Report of Six Cases*. Tohoku J. Exp. Med., 1999, **189** (4), 307-314 —— We report six cases of pulmonary dirofilariasis diagnosed at our laboratory with clinical and pathological features. The nodules of dirofilariasis were round in three cases as previously reported, however dumbbell-shaped in two cases. The nodule did not attach to the pleura in four cases. Microscopically, the nodules were granulomas composed of central coagulation necrosis and peripheral fibrosis with round cell infiltration, histiocytes, and multinucleated giant cells. Necrotic pulmonary artery with single or multiple sections of degenerated nematode was observed in the center of the nodule. Dilated bronchioles with inflammation were observed in the nodule in four cases. Collapse of the alveoli, organizing pneumonia, hemosiderin-laden macrophages were observed around the nodule. We suppose that the nodule is not an infarction but a granuloma caused by antigen released from the nematode. Because the pulmonary dirofilariasis is difficult to be differentiated from primary or metastatic lung carcinoma, and the inflammation exists around the nodule, the nodule should be removed surgically. ———— pulmonary dirofilariasis; lung; granuloma; coin lesion

Dirofilaria immitis is a parasitic nematode which infects dogs, however other species of mammals have been reported to be infected with this nematode. Mosquitoes serve as vectors. Dashiell (1961) described the first case of pulmonary dirofilariasis in man and it has been thought to be rare. However, the incidence

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of this disease is increasing because the thoracoscopic surgery of the nodule to exclude the malignant disease is often performed recently. The nodule has been believed to be an infarct caused by the obstruction of a branch of pulmonary artery by Dirofilaria immitis (Gutierrez 1984; Fabbretti et al. 1990; Nicholson et al. 1992). In this report, we represent six cases of pulmonary dirofilariasis with clinical manifestations and pathological findings.

Case Report

Case 1

In a 60 year-old man, an asymptomatic 1.2 cm nodule was detected in the right midlung field in July 1991. The diagnosis of the nodule was not made with bronchoscopic examinations performed in August 1991 and in February 1994. An aneurysm was detected in his abdominal aorta and an aneurysmal segment was replaced with a synthetic graft in June 1994. At thoracoscopy, a mass in the anterior segment of the right upper lobe was removed in November 1994. Pathological analysis confirmed a granuloma with Dirofilaria immitis.

Case 2

In June 1996, a 71 year-old man was found to have an incidental 2 cm nodule in the right lower lobe. Bronchoscopy was negative. Right thoracotomy with wedge resection of the lesion in the posterior segment of the right lower lobe was perfomed in October 1996. The lesion was adherent to the parietal pleura. Pathological analysis demonstrated a granuloma containing Dirofilaria immitis.

Case 3

In June 1996, a 68-year-old asymptomatic man was found to have an incidental peripheral nodule in the right upper lobe. Chest computed tomography demonstrated a 28×26 mm round nodule with a cavity and surrounding small nodules (Fig. 1). Lung carcinoma was highly suspected. Transbronchial biopsy of the nodule was performed twice, but tumor cells were not detected. The patient underwent thoracotomy and right upper lobectomy in January 1997, because the possibility of lung cancer could not be ruled out. Pathological analysis demonstrated a granuloma with Dirofilaria immitis (Fig. 2). There were four separated nodules in the resected lobe. A cavity in the nodule detected radiographically was composed of a dilated bronchiole with the infiltration of small round cells.

Case 4

In August 1997, a 68 year-old asymptomatic man was found to have a 1.5 cm right upper lobe nodule on routine chest radiography. A chest roentgenogram in 1992 had been normal. Bronchoscopic biopsy specimens were nondiagnostic. He underwent thoracoscopic wedge resection of the nodule in October 1997. An

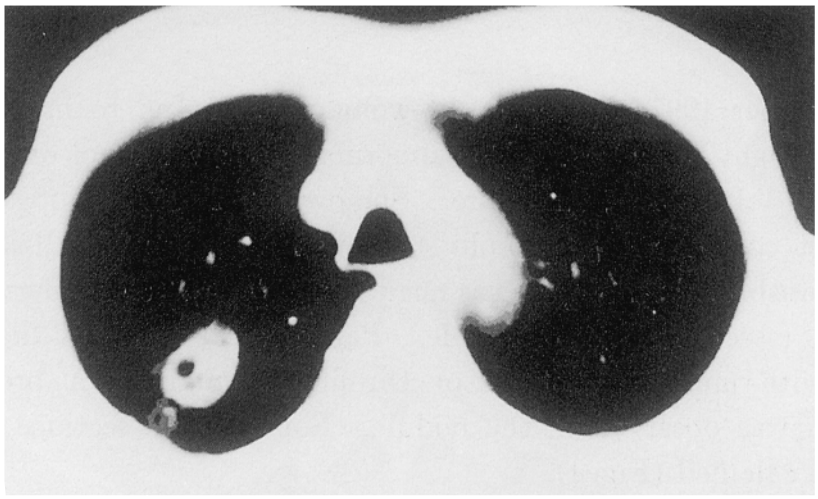

Fig. 1. Chest computed tomograph of Case 2 showing a round nodule with a cavity in the right upper lobe. A small nodule with a cavity attaches to this nodule.

Fig. 2. Microscopic photograph of the organism observed in the nodule of Case 2. Cuticle, somatic muscles, and two tubules are observed in the organism. (H & E, ×33).

organism was detected in the nodule macroscopically at the time of the surgery. It was removed and confirmed to be Dirofilaria immitis by light microscopy. Pathological analysis demonstrated a granuloma, however, sections of Dirofilaria immitis was not observed.

Case 5

In September 1997, a 65-year-old man was found to have an incidental peripheral coin lesion in the right lower lobe. He had underwent resection of stomach and colon because of gastric carcinoma and colon carcinoma, respectively, in August 1995. Chest computed tomography demonstrated a 1.0 cm round nodule. The patient underwent thoracoscopic wedge resection of the nodule. Pathological analysis demonstrated a calcified granuloma with Dirofilaria immitis.

Case 6

In September 1997, a 52-year-old woman was found to have a peripheral nodule in the right lower lobe. The abnormal shadow did not exist in her chest roentgenogram taken one year before. She owns her cats and dogs inside of her house. Chest computed tomography demonstrated a dumbbell-shaped nodule (Fig. 3). Transbronchial biopsy was negative. The patient underwent thoracoscopic wedge resection of the nodule. Pathological analysis demonstrated a granuloma with multiple sections of Dirofilaria immitis. A bronchiole with inflammation was observed in the nodule. Some of the sections of Dirofilaria immitis were calcified (Fig. 4).

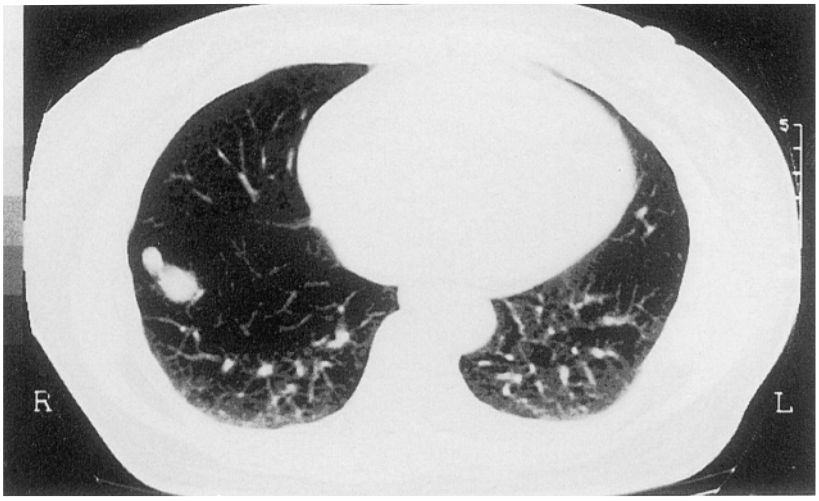

Fig. 3. Chest computed tomograph of Case 6 showing a dumbbell-shaped nodule in the right lower lobe.

Fig. 4. Microscopic photograph of the nodule of Case 6. Five sections of organism are observed in a pulmonary artery (upper right). Calcium is deposited on two of the organisms. A bronchiole with infiltration of small round cells is observed in the nodule (arrow). (H & E, ×8).

Clinical features

Clinical features of six cases are summarized in Table 1. Males outnumbered females, i.e., 5 males to 1 female. The age of the patients ranged from 52 to 71 years old, and the highest concentration of cases occurred in the 60- to 69-year age group. All patients had no symptoms at all, and the nodules had been discovered on routine radiographs of the chest. In Case 5 the nodule was discovered on the check up after surgical resection of gastric cancer and colon cancer. The duration between the time of observation of the nodule and the time of resection of it was from one month to three years and four months. Four cases were owners of dogs and/or cats. Five of the patients live at outskirts of Chiba Prefecture and one live at urban area.

All the patient had the nodule in the right lung. Five patients had a single nodule and Case 3 had four nodules in the same lobe. In three patients the nodule existed in the right upper lobe, and in three in the right lower lobe. The pulmonary nodules ranged from 9 to 24 mm in diameter. The nodule was round in four cases as previously reported, however dumbbell-shaped in two cases. The nodule faced to the pleura in two cases and the shape of the nodule was pyramidal in one case. The nodule had not attached to the pleura in four cases. The nodules were enucleated by thoracoscope in five cases, and lobectomy of the lobe with the nodule was performed in one case.

Pathological features

Pathological features of six cases are summarized in Table 1. All nodules were composed of central coagulation necrosis and peripheral fibrous capsule. Pulmonary architecture was still discernible with elastic stain. The organisms were identified in the artery at the center of the necrotic zone. More than one sections of the nematode were observed in the artery in four cases. The cross-sectional diameter of the organism ranged from 0.3 to 0.5 mm. Cuticle, somatic muscles, and one to several tubules were observed in the organism in some cases, however, the structure of the organism was obscure and its diameter was small due to disintegration in other cases. Calcium was deposited on the organism in two cases. The range of diameter of the artery which include the organism was from 1 to 9 mm. The organism was observed macroscopically at the time of operation in three cases. Fibrous capsule with hyalinization was observed at the periphery of the nodule, and cellular infiltration, mainly lymphocytes and plasma cells, histiocytes, foreign body multinucleated giant cells, proliferation of fibroblasts and collagen fibers were observed outermost layer of the nodule. Neither hemorrhage nor accumulation of hemosiderin-laden macrophages was observed in the nodule. Cavities composed of dilated bronchioles with the infiltration of small round cells were observed in the nodule in four cases. Denudation of epithelium and focal squamous metaplasia in the dilated bronchiole was observed. Choles-

TABLE 1. *Summary of clinical, pathological and immunological features in cases with pulmonary dirofilariasis*

Case	Age	Sex	Nodule			Inside the nodule			Outside the nodule				Ouchterlony	ELISA Index
			Location	Size (mm)	Shape	Artery[a]	Dirofilaria[b]	Cavity	Collapse	Macrophages	Hemosiderin	Eosinophils		
1	63	M	rS3	12	Dumbbell-shaped	1.3	2	+	+	+	+	+	+	78
2	71	M	rS10	20	Pyramidal	1.0	2	+	+	+	+	−	NT	84
3	68	M	rS2	16	Round	9.0	1	+	+	+	+	+	+	(+)
4	68	M	rS3	15	Round	N	N	−	−	+	+	+	NT	NT
5	65	M	rS10	9	Round	1.0	2	−	−	+	−	−	NT	87
6	52	F	rS8	24	Dumbbell-shaped	2.0	Multiple	+	+	+	−	+	NT	94

M, male; F, female. N, dirofilaria was not observed microscopically, however, it had been observed macroscopically at the time of surgery and removed; NT, not tested; ELISA Index, ([absorption value for sample] − [absorption value for negative control])/([absorption value for positive control] − [absorption value for negative control]) × 100. [a]Diameter of occluded artery (mm). [b]Number of sections of dirofilaria observed. Because Dot ELISA was performed for Case 3, ELISA Index was not obtained.

terin clefts were observed in the periphery of the nodule in one case. In the pulmonary parenchyma surrounding the nodule, bronchitis, organizing pneumonia, microabscess, recanalization of the pulmonary arteries, collapse of the alveoli, hemosiderin-laden macrophages were observed, and epithelial hyperplasia composed of cuboidal cells around the nodule was observed in one case. Eosinophilic infiltration at the periphery of the nodule was observed in four cases.

Immunological analysis

Antibodies against Dirofilaria immitis were confirmed in two of six cases with Ouchterlony method (Hornbeck 1996), and IgE against Dirofilaria immitis was confirmed in all cases except Case 4 with enzyme-linked immunosorbent assay (ELISA) (Table 1).

Discussion

Roentgenographically, pulmonary dirofilariasis is reported to present a subpleural coin-like lesion (Ro et al. 1989; Milanez de Campos et al. 1997). Two of our cases presented a dumbbell-shaped nodule in the lung and a cavity was observed in the nodule in one case. Microscopically, cystic dilated bronchioles existed in the nodule in four cases. These findings have not been reported in case reports of pulmonary dirofilariasis so far. We propose that inflammation in the nodule expanded in a complex manner and caused bronchiolitis and peribronchiolitis around the nodule.

The nodule caused by Dirofilaria immitis was thought to be formed by infarction due to the embolism of the pulmonary artery by the organism (Gutierrez 1984; Milanez de Campos et al. 1997). It is true that the muscular artery was partially occluded by tightly coiled organism, because multiple cross sections of the organism are observed in a single artery. However, pulmonary infarction is not necessarily induced by occluded pulmonary artery, because bronchial artery can supply blood to peripheral lung tissue. There is another idea concerning the etiology of the nodule that some antigen from the dead nematode are released from the worms (Chesney et al. 1983; Flieder and Moran 1999). We found several findings support the latter idea. First, when pulmonary infarction occurs, it is usually hemorrhagic, and accumulation of hemosiderin-laden macrophages may be found even after healing by organization. However, in our cases, hemosiderin-laden macrophages were observed outside of the nodule rather than in the nodule. Second, the shape of the lesions are grossly round or even dumbbell-shaped and not pyramidal, as in infarct. Third, if the nodule is infarct, eventual enlargement of air spaces near the nodule may occur due to shrinkage of the infarct. However, air space around the nodule partially collapsed in four cases. Finally, inflammation of airway existed both inside and outside of the nodule, and cystic dilated bronchioles are observed inside of the nodule in four cases.

Suspicion of malignancy in pulmonary dirofilariasis is frequently heightened

by the patient's advanced age and smoking history (Ro et al. 1989). The number of the primary lung cancer patients has been increased these days. Pulmonary metastatic nodule after the resection of primary carcinoma is also resected in some cases. A case of pulmonary dirofilariasis after the resection of transitional cell carcinoma of the urinary bladder was reported (Kahn et al. 1983). Case 5 in our study has underwent resection of stomach and colon because of gastric carcinoma and colon carcinoma, respectively. In these cases, preoperative diagnosis of the nodule was not made but metastasis of the primary carcinoma was highly suspected. Cases of pulmonary dilofilariasis with coexisting non-small cell carcinoma were also reported (Flieder and Moran 1999). Bronchitis, organizing pneumonia, and microabscess were observed around the nodule in our study. We propose that the resection of the nodule is needed to rule out the possibility of lung carcinoma, to prevent the further damage of peripheral lung tissue, and to obtain the precise pathological diagnosis of the lesion even if the serological examination shows that the patient is exposed to the Dirofilaria immitis before the resection of the nodule.

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