Bronchogenic Cyst with High Carbohydrate Antigen 19-9 in the Cyst Fluid and the Serum

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A mass of 8 cm in diameter was revealed in the right upper lung field of a 46-year-old female patient. The chest X-ray film taken one year previously revealed only a linear shadow in the same position, which was thought to be a vacant cyst. The levels of carbohydrate antigen (CA) 19-9 in cyst fluid and serum were elevated, at 410,000 and 130 U/ml, respectively. After surgical resection, serum CA19-9 returned to normal. Pathologically, the cyst wall was lined with bronchial epithelium with no evidence of malignancy. Immunohistochemical study revealed CA19-9 positivity in the bronchial epithelium of the cyst wall.

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Introduction

Bronchogenic cysts are congenital anomalies that arise early in gestation from the budding of the developing respiratory systems (1). Bronchogenic cysts are seldom seen in adults, and most are thought to be asymptomatic and free of complications unless they become infected (2-4).

Carbohydrate antigen (CA) 19-9, a colorectal antigen detected by monoclonal antibody (5), is frequently elevated in patients with gastrointestinal carcinomas, pancreatic carcinomas or lung adenocarcinomas, and thus it is used as a tumor marker (6, 7). However, the relation between of CA19-9 and bronchogenic cyst has been previously reported in only a few cases (8-13).

Here, we report a patient with a bronchogenic cyst which caused an exceptionally elevated level of CA19-9 in the serum and cystic fluid, and which grew rapidly during a one-year period, appearing as an 8 cm mass shadow on chest X-ray film. These findings are important in recognizing the natural history of bronchogenic cysts.

Case Report

A 46-year-old woman was admitted to Konan hospital on June 14, 1994 due to an abnormal shadow on her chest X-ray film. Annual physical examinations for six years previously had

shown no abnormalities on the chest X-ray films. She was a non-smoker and had no episode of exposure to excess dust or fumes. Her past history and family history were unremarkable.

On admission, physical examination profiled a medium-sized woman with body temperature of 36.7°C. Her breath sound was weak in the upper right chest, but no surface lymph nodes were palpable. Laboratory examinations on admission gave the following results: Leukocyte counts 6,200/mm³, an erythrocyte sedimentation rate (ESR) of 11 mm/hr, and level of C-reactive peptide (CRP) within normal range. Biochemical and other serological examinations were all in the normal ranges. The serum level of CA19-9 was high at 130 U/ml (normal <37), but the serum level of carcinoembryonic antigen (CEA), human chorionic gonadotropin (HCG), neuron specific enolase (NSE) and squamous cell carcinoma-related antigen (SCC) were in the normal ranges (Table 1). The chest X-ray film on admission showed a mass as large as 8 cm in diameter in the right upper lung field (Fig. 1). Chest computed tomograph revealed a huge cystic mass immediately adjacent to the superior vena cava and the trachea. The density of the fluid inside the cyst was lower than in the adjacent muscle (Fig. 2).

We obtained approximately 300 ml fluid from the cyst by percutaneous aspiration. The fluid was prulent and the level of CA19-9 was elevated at 410,000 U/ml. The fluid protein was 5.5 g/dl; glucose, 0 mg/dl; lactate dehydrogenase (LDH), 10,010 IU/l; leukocyte counts, 51,800/mm³ (Table 1). Examinations

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Table 1. Laboratory Findings

Peripheral blood		Cyst fluid	
White cells	6,200/mm ³	White cells	51,800/mm ³
Protein	6.2 g/dl	Protein	5.5 g/dl
Glucose	96 mg/dl	Glucose	0 mg/dl
LDH	229 IU/l	LDH	10,010 IU/l
CA19-9	130 U/ml	CA19-9	410,000 U/ml
CEA	0.9 ng/ml	CEA	5.2 ng/ml
HCG	<1.0 MIU/ml	HCG	<1.0 MIU/ml
NSE	3.6 ng/ml	NSE	33 ng/ml
SCC	<1.0 ng/ml	SCC	120 ng/ml

LDH: lactate dehydrogenase, CA19-9: carbohydrate antigen 19-9, CEA: carcinoembryonic antigen, HCG: human chorionic gonadotropin, NSE: neuron specific enolase, SCC: squamous cell carcinoma-related antigen.

Figure 1. Chest X-ray film on admission. A huge mass was seen in the right upper lung field.

for malignant cells and bacteria, including mycobacterium tuberculosis, were negative.

After aspiration, the outer line of the cyst on the chest X-ray moved toward the mediastinum in the form of an arch (Fig. 3A, B). Upon close examination of the previous chest X-ray film taken one year earlier, a linear shadow was found in the inner zone which was suspected to be the outer line of the cyst, because there were no markings of pulmonary vessels inside the liner shadow (Fig. 3C). These facts indicated that the cyst was present at least one year previously, and further that communication between the airways and cyst was blocked, due to the large increase of the fluid volume inside. We suspected that this disease was bronchogenic cyst, however, malignant disease

Figure 2. Chest computed tomograph on admission. A large mass was immediately adjacent to the superior vena cava and trachea.

could not completely be ruled out due to the elevated level of CA19-9.

On July 21, a thoractomy was carried out for the purpose of definite diagnosis and treatment. A cystic tumor of about 8 cm in diameter was enveloped by pleura pulmonalis, and pleura mediastinalis was found intact, enabling us to perform a complete resection.

Histologically, the cyst wall was composed of loose connective tissue lined with ciliated bronchial epithelium. Bronchial glands were also observed. No malignant lesions were found. In the area of adhesion with the lung, the cystic wall became thick with granulation tissue and included a few dilated bronchioles, but inflammatory cell infiltration in the area was slight (Figs. 4, 5). Immunohistochemical study with anti-CA19-9 monoclonal antibodies showed that ciliate epithelial cells, cells of the glands and the material in the lumina were strongly positive (Fig. 6). The post-operative serum level of CA19-9 returned to the normal range (18.8 U/ml).

Discussion

Bronchogenic cysts are benign tumors caused by abnormal budding of the bronchial tree (1). They are divided into two types according to location: mediastinal type and intrapulmonary type. The difference is due to the different times when the anomaly occurs in physical development (14–16). The present case was included in the intrapulmonary type because pleura mediastinalis was intact.

Monoclonal antibodies against CA19-9 can detect a monosialoganglioside antigen that is mainly present in gastrointestinal or pancreatic adenocarcinoma cells, and the serum level of CA19-9 is a more sensitive tumor marker than that of CEA of pancreatic cancers (5, 7). A small amount of CA19-9 is also present in normal cells, such as those of pancreatic duct, biliary duct, salivary gland ducts, and prostate and bronchial glands (17). Serum CA19-9 is sometimes known

Figure 3. Enlarged right upper lung on admission (A). After 300 ml aspiration the outer line moved to the mediastinum drawing the arch (B). A linear shadow is shown in the inner zone in the film taken one year previously (C).

to be elevated to more than 100 U/ml in benign digestive tract diseases such as chronic pancreatitis or cholelithiasis (18). Okubo et al first reported a case of bronchogenic cyst with high level of CA19-9 in both serum and cystic fluid in 1989 (8). Since then there have been five reports that indicate the relationship between bronchogenic cysts and increase of the CA19-9 level in the serum or the cyst fluid (9–13). The elevation in the levels of tumor markers in the cystic fluids is thought to be due to their production and accumulation in the cyst. Leakage of the cystic

Figure 4. Microscopic appearance of the cyst wall. There is a large amount of fibrous tissue and a few dilated bronchioles, but few inflammatory cells were seen between the cyst wall and the lung (HE stain, $\times 40$).

Figure 5. The cyst wall was lined with ciliated bronchial epithelium (HE stain, $\times 200$).

Figure 6. Immunohistochemical staining with anti CA19-9 monoclonal antibody. The ciliated bronchial epithelium was positive for CA19-9 ($\times 200$).

fluids into the serum is responsible for increased levels in the serum. In this case, CA19-9 was demonstrated positive inside bronchial glands, epithelial cells of bronchial glands, and ciliated bronchial epithelial cells in the cyst. Therefore, we assume a common reason for the increase of CA19-9 between cyst fluid and serum. After resection, the serum level of CA19-9 returned to normal range, indicating that the bronchogenic cyst had caused the increased serum level of CA19-9 in this case.

Patients with bronchogenic cysts usually have no symptoms: these cysts are revealed during health examinations by chest X-ray films (2–4). To the best of our knowledge, only two previous cases have been followed up by chest X-ray films retrospectively (12, 19). In one case, Takagi et al were unable to find abnormalities in an earlier chest X-ray (19), because the bronchogenic cyst was located in the middle lobe and abnormalities behind the lower vessels and bronchus are not typically

visible in standard chest X-ray film. However, in another case, there had been a vacant cyst before the mass shadow appeared in the chest X-ray film (12), and in the present case, we were able to identify a vacant cyst in the chest X-ray film taken one year previously, a cyst which increased in size to 8 cm within a year. These two cases suggest that the same bronchogenic cyst can demonstrate various abnormalities in chest X-ray films over a short period of time.

In the present case, it is important to discuss why the cyst became so large over a relatively short term. Though examinations for bacteria were negative, local infection might have played an important role in obstructing the formally patent bronchial communications because the fluid glucose was 0 mg/dl and leukocyte count was $51,800/\text{mm}^3$. Furthermore, pathological findings revealed post inflammatory changes between the cyst wall and the lung. These findings could mean that the inflammatory changes blocked the communication between the cyst and airways, and that the cyst became enlarged due to accumulation of fluid inside the cyst.

Finally, it is important to emphasize two points in this unique bronchogenic cyst case: CA19-9 levels in both the serum and the cyst fluid were high; and a large mass shadow will be visible on chest X-ray film, when bronchogenic cysts have interrupted a patent bronchial communication, presumably because of accumulated fluid inside the cyst. Therefore, internists should bear in mind that, while bronchogenic cyst is a single-symptom condition, it can display a variety of X-ray shadows in even one patient in a relatively short term. This case is important for consideration of the natural history of bronchogenic cysts.

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