Case Report

A Case of Behçet's Syndrome with Rupture of a Pulmonary Aneurysm: Autopsy Findings and a Literature Review

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A 34 year old man suffering from oral and genital ulceration with uveitis (the complete type of Behçet's syndrome) developed fluctuating radiological opacities in the right lung and showed recurrent hemoptyses. Pulmonary angiography showed multiple aneurysms and obstruction of the pulmonary arteries. After he was treated with predonisolone, the symptoms and pulmonary manifestation improved temporarily. However, he died suddenly from a massive hemoptysis. An autopsy revealed the aneurysmal rupture of right basilar branch of pulmonary artery into the right B6 bronchus. Histopathological findings in the lung showed multiple organized thrombi, inflammatory infiltration and vascular wall destruction of pulmonary arteries of various sizes. Only 47 previously reported cases of Behçet's syndrome which showed pulmonary involvements were revealed by a search of the published literature.

Key Word: Behçet syndrome, Pulmonary aneurysm, Autopsy case

CASE REPORT

In 1975, a 27 year old man noticed painful ulcerations of the mouth and scrotum. In 1977, he developed chills and a fever. Chest X-ray showed opacities in the right lower lung field. Treatment with antibiotics was not effective but predonisolone was. However, unfortunately, he stopped taking the latter because he developed "moonface." In April 1978, he was admitted to Nagasaki University Hospital for further examination of hemospitum. Chest X-ray showed an infiltrative shadow in the right lower lung field and spherical opacities in bilateral middle lung field (Fig. 1a). Pulmonary angiography demonstrated the obstruction of both basilar branches of pulmonary artery (r-A.8.9, l-A.8.9) and two aneurysms in the right middle branch and left A6 branch of the pulmonary artery (Fig. 2a, b).

His condition was diagnosed as vascular Behçet's syndrome (complete type). Abdominal aortography, selective celiac angiography, femoral and

lower extremity angiography were performed, but no abnormal finding was observed. Predonisolone was again administered because the spherical opacity in the right lung increased in size (Fig. 1b). In November 1979, he was readmitted to the hospital in emergency because of massive hemoptysis (about 1,000 ml).

After stopping the hemoptysis, pulmonary angiography was again performed and showed an obstruction of the bilaterel basilar branches of the pulmonary artery (r-A.7.8.9.10, l-A.8.9) and disappearance of the aneurysms probably due to thrombosis (Fig. 1c).

In May 1980, he showed massive hemoptysis again. Estimated blood loss was again about 1,000 ml which necessitated bloodtransfusion. Chest X-ray showed that the spherical opacity in the right hilum had reduced in size (Fig. 1c).

In March 1982, he was readmitted to the hospital because of hemoptysis (400 ml) and Chest X-ray showed enlargement of right hilar shadow (Fig. 1d).

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Fig. 1. Spherical opacity of the right hilum in chest X-ray fluctuates its size by time, (A: 1978, b: 1979, c: 1980, d: 1982).

Physical examination on admission showed the following: Blood pressure was 100/70 mmHg with no difference between the upper and lower extremities. Pulse rate was 72/min and regular. Body temperature was 37.2°C . Respiration rate was 18/min. Several ulcers, 0.1–0.2 cm in diameter, were present on the tongue and scrotum. The palpebral conjunctiva was slightly anemic. The chest was clear. Bruit and venous dilatation were absent. There was no hepatosplenomegaly. Multiple erythema nodosum-like eruptions were present in both lower extremities and thrombophlebitis was seen in left leg. A needle reaction was positive. Neurological examination exhibited no abnormal signs. Ophthalmological examination showed the presence of serious iritis.

Laboratory data on admission were as follows. Neither anemia nor leucocytosis was seen in the peripheral blood. A mild elevation of GPT (31 mu/ml), LAP (109 mu/ml) and γ GTP (91 mu/ml) was noticed in the liver function test. CRP was positive. Mucoprotein (106 mg/dl) and erythro-

cyte sedimentation rate (30 mm at 1 hour) were increased slightly. No immunological abnormalities except a mild decrease of IgG (726 ng/ml) were noticed. Blood gas and ventilatory function were normal.

Chest X-ray on admission showed remarkable enlargement of the right hilum which increased in size up to 4 cm in diameter and compressed the right intermediate bronchus (Fig. 3a).

A Scintigram of the lungs revealed poor perfusion in the right middle lobe and left lower lobe (Fig. 3b).

Dynamic computed tomography of the chest was performed. Just after the bolus injection of the contrast media, the aneurysm of the right pulmonary artery was stained as dark as the aorta. The wall of the aneurysm was 5 mm thick and it was stenotic by the thrombus (Fig. 3c).

The first pulmonary angiography conducted in 1978 showed the obstruction of both sides of the basilar arteries and aneurysms in the right A5, left A4 and A6 (Fig. 2a, b). However, the

Fig. 2. Pulmonary angiography demonstrates the obstruction of both basilar branches of the pulmonary artery (right - A.8.9.10 left - A.8.9). Two aneurysms of the right middle branch and left A6 branch of the pulmonary artery fluctuate their size by time (a, b: 1978, c: 1979, d: 1982).

second pulmonary angiography in 1979 revealed the disappearance of the previous aneurysms and further obstruction of the right lower lobe arteries (Fig. 2c). A nodular shadow was seen at

the same lesion of the obstruction site probably caused by a thrombosed aneurysm.

The third pulmonary angiography in 1982 showed the aneurysm of the right lower trunk of the pulmonary artery which was identical to the right hilar enlargement. Right A7.A8.A9.A10 and left A8 were completely obstructed (Fig. 2d). Using a bronchofiberscope, engorged capillaries of the right intermediate bronchus and a smooth surfaced round blueish protrusion were noticed

Fig. 3. a: Tomography shows a right hilar nodular shadow which is about 4 cm in diameter, compressing the right intermediate bronchus.

b: A scintigram of the lungs shows reduced perfusion in the right middle and left lower lobes.

c: Computed tomography shows the aneurysm of the right pulmonary artery and the thick aneurysmal wall caused by thrombus.

d: Bronchofiber scopy shows engorged capillaries of the right intermediate bronchus and a smooth surfaced round blueish protrusion.

at the same place as the aneurysm (Fig. 3d).

Following this examination, surgery was considered necessary although unfortunately while awaiting the operation, the patient died suddenly from massive hemoptysis. A subsequent autopsy was performed.

Autopsy Findings

1. Macroscopic Examination

The upper respiratory tract, trachea and main bronchi contained diffuse hemorrhage in the pulmonary parenchyma and one aneurysm (caliber 2–3 cm) with a mural thrombus of pars basilaris in the right pulmonary artery penetrated to the right B6 segmental bronchus (Fig. 4a).

Pulmonary arteries at peripheral sites from this aneurysm showed occlusion with recanalization

due to organized thrombi. Similar changes of pulmonary arteries were seen in the left lower lobe but no aneurysmal lesions were detected clearly in this lobe. There was old infarction scar at the distal part of the right lower lobe. The pulmonary vein system appeared to be normal and the large systemic arteries and veins were free of thrombi.

2. Microscopic Examination

Microscopically, there were organized thrombi in the aneurysm of the parts basilaris in the right pulmonary artery. The wall of the aneurysm with mononuclear inflammatory infiltration showed irregular thickening and thinning. Furthermore, the inner elastic lamella and the elastic fibers of the media showed pronounced destruction and

Fig. 4. a: A Pulmonary aneurysm (pars basilaris of the right pulmonary artery) penetrates to the right B6 segmental bronchus. (An: Aneurysm, Br: Bronchus, Ca: Cartilage of the bronchus, Ep: Epithelium of the bronchus. Mural thrombus has been removed before hand) (1.HE)

b: Fibrinoid necrosis is recognised in aneurysms. (100.HE)

c: Organized thrombi with recanalization of the right pulmonary artery and prominent destruction of the inner lamella and elastic fibers of the media are seen. (20.HE)

d: Infiltration of mononuclear inflammatory cells in the wall of the septal arteriole and the perivascular region is seen. (200.HE)

fibrinoid necrosis (Fig. 4b) was detected in parts. There was proliferation of the vasa vasorum with mononuclear inflammatory infiltration in some places.

The medium-sized (muscular) and small pulmonary arteries of the bilateral lower and right medial lobes revealed organized thrombi and multiple recanalization (Fig. 4c). In various regions, there were intimal thickening, interruptions of the inner elastic lamella and the elastic fibers of the media without inflammatory infiltration.

A few septal arterioles with transmural inflammatory infiltration were detected (Fig. 4d) but no pathological changes were found in the septal capillaries.

In addition to the above, periadventitial fibrosis was observed in pulmonary arteries of all sizes which showed the above-mentioned alterations. Furthermore, smooth muscle metaplasia developing around the arterioles was apparent in periadventitial fibrous tissue of the thrombosed arteries next to the aneurysm.

1. Behçet's disease (vasculo-, complete):

1) vascular lesions

- a) multiple aneurysms of the bilateral pulmonary arteries
- b) post-vasculitis healed scar, bilateral pulmonary arteries (mild vasculitis was demonstrated in a few septal arterioles)

2. rupture of pulmonary aneurysm (right pars basilaris into segmental bronchus (right B6)

3. massive intra-alveolar hemorrhage due to #2, both lungs (left 330 g, right 410 g)

DISCUSSION

Behçet's syndrome is a systemic inflammatory disease characterized by chronic and recurrent symptoms such as aphthous stomatitis, genital ulceration and ocular lesions.

Pulmonary manifestations in Behçet's syndrome are very rare. Only forty seven patients of Behçet's syndrome with pulmonary abnormalities have been described previously in the literatures¹⁻³⁹, according to our survey (table 1). Forty one cases were male and four were female (2 unknown), i.e. an extreme predominance of males (84%). The age distribution was from 14

to 58 with an average of 29 years. Seventeen cases were complete type of Behçet's syndrome with aphthous stomatitis, skin lesion, ocular lesions and genital ulcers. Fifteen cases were the incomplete type (17 were unknown). Hemoptysis and hemosputum were observed in 39 of 44 cases (89%) and the mortality rate in these cases was considerably higher (47%) than that in cases of Behçet's syndrome without pulmonary manifestation.

Hemoptysis may result from acute inflammatory destruction of pulmonary artery aneurysms, pulmonary infarcts, erosion of pulmonary artery aneurysms into adjacent bronchi, extensive inflammatory disruption of alveolar capillaries or rupture of a bronchial vein caused by increased pressure of the azygos vein due to superior vena cava thrombi³⁾.

Chest X-ray showed abnormal findings with diffuse infiltrates and round opacities in all 47 cases. The infiltrates, distributing over many areas with varying size, are probably the radiographic expression of hemorrhage and they appear during the acute phase of the disease. They usually resolve within a few days and are then replaced by round opacities. Peripheral, often multiple opacities probably correspond to hemorrhage and necrotic pulmonary infarctions. Proximal opacities of the hilum correspond to pulmonary artery aneurysms. Pulmonary angiography assesses the severity of the pulmonary artery lesions like occlusion by thrombosis or aneurysm.

Among the 47 cases, 20 case were investigated histologically (Table 2). Aneurysms of the pulmonary arteries were observed in 15 of these (75%) which indicated a high incidence of aneurysm in Behçet's disease compared with other diseases such as syphilis, mycotic aneurysm, trauma or chronic pulmonary hypertension. The size of aneurysm usually varies over a period of time as observed in our case. A reduction in size may be explained by recanalization of thrombi in the aneurysm. Whilst an enlargement is induced by derangement of the elastic fiber of the pulmonary artery and destruction of the arterial wall. This sometimes erodes the bronchial wall and finally leads to rupture.

Thrombosis was observed in 15 of the 20 cases

Table 1. Cases of Behcet's syndrome with pulmonary involvement

Author	Sex	Age	Life Status	Hemoptysis Hemosputum	Type	Reference
1 Chajek	M	20	L	+	C Diffuse infiltration	1)
2 Davies	M	29	D	+	C Diffuse infiltration	2)
3 Kansu	M	29	D	+	C RLL density	3)
4 "	M	23	L	+	C	
5 Hills	M		L	+	C Transient infiltrate	4)
6 Decroix	M	52	L	—	C Diffuse infiltrate and nodule	5)
7 Bank	M		D	+	Round density	6)
8 Payan	M	30	D	+	C Diffuse infiltrate	7)
9 Dascalopoulis	M	35	L	+	C RVL opacification	8)
10 Jensen	M	22	L	+	C RLL infiltrate	9)
11 Boe	F	58	D	—	C Diffuse infiltrate and nodule	10)
12 Godeau	F	21	L	—	I Diffuse infiltrate and small cavitation	11)
13 Cadman	F	22	L	+	C Diffuse infiltrate	12)
14 Petty	F	48	L	+	I Patchy infiltrate	13)
15 Okamoto	M	25	L	+	I RLL densities	14)
16 Ichikawa	M	41	L	—	I Diffuse infiltrate	
17 Iwaki	M	32	L	+	I RL opacity	15)
18 Simizu	M	38	L	+	I RML opacity	16)
19 "	M	39	L	+	I RML opacity	
20 "	M	22	D	—	I Diffuse infiltrate and cavitation	
21 Sawata	M	23	L	+	C Patchy infiltrate	17)
22 Sulhein						18)
23 Bobkov	M	33	D	+	Fleeting circular opacities	19)
24 Gamble						20)
25 Beattie	M	21		+		21)
26 Pirani	M	14		+		22)
27 Hughes	M	35		+		23)
28 "	M	14		+		
29 Charlton	M	25		+		24)
30 Kopp	M	30		+		25)
31 Slavin	M	34	L	+	C RLL infiltrate, pleural effusion	26)
32 Reza	M	24	L	+	C RLL infiltrate	27)
33 Bonse	M		D	+	Hilar and perivascular opacity	28)
34 Basex	M	48	D	+	Hilar and perivascular opacity	29)
35 Marchi	M	42	L	+	Hilar vascular prominence, nodular opacities	30)
36 Ohta	M	34	D	+	I 2 RLL confluent shadows	31)
37 Tsukamoto	M	27	L	+	C Nodular shadows	32)
38 Nishimoto	M	21	D	+	I Nodular shadows	33)
39 Yasuda	M	38	L	+	I Nodular shadows	34)
40 Koyama	M	26	L	+	C Infiltration and nodular shadow	35)
41 Durieux	M	35	L		I Infiltration and nodular shadow	36)
42 "	M	32	D	+	I Round excavated density	
43 "	M	35	D	+	I Nodular shadow	
44 "	M	31	D	+	I Nodular shadow	
45 Charlier	M	32		+	Nodular shadow	37)
46 Mayaud						38)
47 Bonnel	M	24	L	+	Nodular shadow	39)

L: live D: dead C: complete I: incomplete

Table 2. Pathology of pulmonary lesions in reported Behcet's syndrome

No. of cases in Table 1	Aneurysm	Vascular inflammation	Thrombosis	Infarction	Periarterial fibrosis	Others
2	+	+	+			vascular necrosis
6		perivascular	+		diffuse	cavitation
7	+	infiltration	+	+	fibrosis thickened artery	
8		vasculitis	+	+	fibrosis	hemorrhage nodule
11					nodular fibrosis	vascular necrosis
22					+	
23	+	+	+			
24		+				
25	multiple		+			bronchial erosion
26	multiple rupture	+	+	+	+	
27	+(2)	+	+	+	+	bronchial erosion
28	+(3)	+	+		+	metaplastic artery
29	multiple	+	+	+	+	metaplastic artery
30	multiple	+	+	+	+	bronchial erosion
31	+(2)	+	+	+	+	metaplastic artery
36	+	+	+	—		bronchial erosion
38	+	+				
39	+					

(75%) and infarction in 7 (35%). Thrombosis is mostly related to the underlying vasculitis or hypercoagulation. In Behcet's syndrome, hyperplatelet aggregation was reported and was suggested to be related to multiple thrombosis⁴⁰. Occlusion of branches of the pulmonary arteries is often observed as in our case and is mainly due to thromboembolism, which usually causes pulmonary infarction.

Vasculitis was observed in 15 cases (75%) and periarterial fibrosis in 12 (60%). Vasculitis occurs in pulmonary vessels of all sizes with acute and chronic inflammatory cells. Vascular inflammation is sometimes associated with necrosis such as fibrinoid necrosis and inflammation increases vascular permeability causing deposition of im-

mune complexes. Various segments of arteries and capillaries are subjected to repeat bouts of inflammatory injury and thus subsequent repair. This is putatively responsible for the development of perivascular fibrosis. However, etiology of vasculitis is still not clear.

Because of the high mortality rate (39.4% in 47 cases) in Behcet's syndrome with pulmonary involvement, treatment is extremely difficult. Steroids and anticoagulants are usually administered. However if the pulmonary aneurysm increases in size, surgical intervention is necessary before rupture occurs.

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