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Case Report

Pulmonary involvement in Niemann–Pick disease: Case report and literature review

O. A. Minai*, E. J. Sullivan† and J. K. Stoller*

*Department of Pulmonary and Critical Care Medicine, The Cleveland Clinic Foundation, Cleveland, Ohio and †Division of Pulmonary and Allergy Drug Products, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, U.S.A.

Niemann–Pick disease (NPD) is a rare, inherited, autosomal recessive, lipid storage disease. The pathognomonic intracellular accumulation of sphingomyelin results in the production and accumulation of 'foam cells'. Interstitial lung disease is a rare manifestation of NPD. We present the case of a 48-year-old white female with NPD involving the lungs, liver and spleen. The chest radiograph showed bilateral, predominantly basal reticulonodular infiltrates and serial pulmonary function tests over a period of years showed preserved expiratory airflow and a severely decreased diffusion capacity for carbon monoxide (DLCO). In view of her visceral involvement, lack of neurological symptoms and survival into adulthood, we believe our patient represents a case of type B NPD. In this type of NPD, aside from prominent hepatosplenomegaly and sexual immaturity, significant pulmonary infiltration with 'Pick cells' has been reported. To date, no therapeutic modality has been shown to alter the natural history of this disease, which results in progressive debilitation and death. This case is unique in that it provides the longest physiological follow-up in the literature, and provides data on the natural history of pulmonary involvement in NPD.

Key words: Niemann–Pick disease; sea-blue histiocytosis; interstitial lung disease.

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Introduction

Niemann–Pick disease (NPD) is a rare syndrome characterized by the intracellular deposition of sphingomyelin. Presumed to be an infantile variant of Gaucher's disease in the initial report by Niemann (1), Pick later recognized it as a distinct entity (2,3). Over the years, it has become apparent that NPD is a clinically and biochemically heterogeneous disorder, with six variants of NPD (types A to F) currently described (4). The exact incidence of pulmonary involvement with NPD is difficult to determine since the literature mostly consists of isolated case reports. The disease is characterized by the presence of groups of lipid-laden (mainly spingomyelin and cholesterol) cells with 'foamy' cytoplasm, so-called 'Pick' cells, in various body tissues. The disease may become manifest in infancy and follow a rapid course of death by 3 years of age, or it may follow a more protracted course (5–7). The predilection for involvement of the reticuloendothelial system and, in some cases, the nervous system, results in bone marrow involvement, variable hepatosplenomegaly and, in some types, neurological symptoms. Type B NPD develops as a result of sphingomyelinase deficiency and is characterized by prominent hepatosplenomegaly, absence of neurologic involvement and a chronic, protracted course. Pulmonary parenchymal involvement may be a feature of several types of NPD, including type B.

The current report presents a patient with type B NPD with pulmonary involvement and reviews the available experience regarding pulmonary involvement with NPD.

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Correspondence should be addressed to: Omar A. Minai, M.D., Clinical Associate Staff, Department of Pulmonary and Critical Care Medicine, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Desk A-90, Cleveland OH 44195, U.S.A. Fax: 216 445 8160.

Case report

The patient is a 48-year-old white female who was referred to the Cleveland Clinic Foundation for an abnormal chest radiograph. She had a history of Niemann–Pick disease for which she underwent a splenectomy at 12 years of age (which revealed replacement of splenic pulp by PAS-positive large histiocytes and 'foam' cells) and an orthotopic liver transplant at 41 years of age. She was first noted to have an abnormal chest radiograph, characterized by bilateral predominantly basal reticulonodular infiltrates, at 41 years old. A flexible bronchoscopy with transbronchial

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biopsies was performed at an outside facility and was said to be consistent with 'fibrosis' but the slides were not available for review. At that time, she was able to function normally and required oxygen with exertion only.

At the time of her evaluation in our institution at 48 years of age, her pulmonary symptoms had been stable over the last few years. She was able to walk approximately 1 mile on a treadmill with oxygen and she did not have a cough. Apart from the NPD, her past medical history was significant for aortic valve replacement 3 years earlier for severe aortic stenosis, CMV pneumonia 6 years earlier and hypertension. She was a former smoker of 10–15 pack-years, having quit 11 years earlier.

Her physical examination revealed a healthy female with a few faint crackles at both lung bases and a 3/6 systolic murmur at the base of the heart. No signs of cor pulmonale were noted.

Her chest radiograph [Figs 1(a) and (b)] showed diffuse interstitial markings bilaterally with an old granuloma in the right upper lobe. No lymphadenopathy or pleural effusion was noted. An echocardiogram showed a small left ventricular cavity with normal systolic function. A CT scan of the chest showed diffuse bilateral interstitial lung disease with basal predominance (Fig. 2). A few small calcified granulomata were seen in the lung bases. Her oxygen saturation was 94% at rest on room air. After walking 250 feet on $3\,l\,min^{-1}$ oxygen via nasal cannula, her saturation was 91%.

Her pulmonary function tests (Fig. 3) showed preserved flow rates and lung volumes with a severely decreased diffusion capacity for carbon monoxide (DLCO), $5{\cdot}58\,ml\,min^{-1}\,mm\,Hg^{-1}$ (29% of predicted).

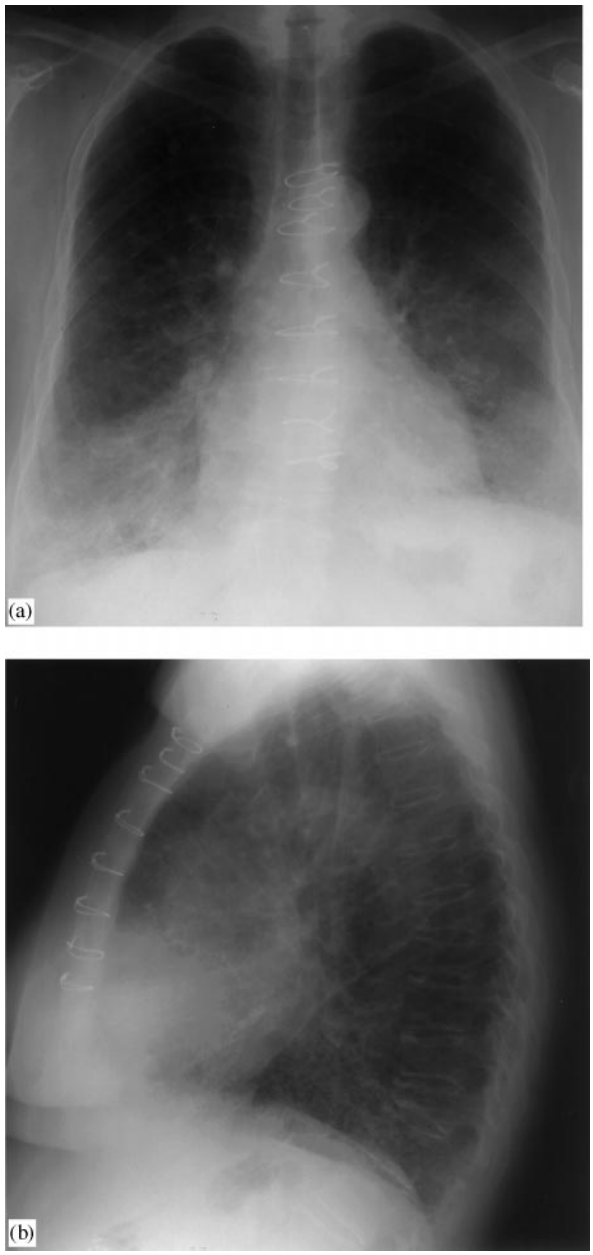

FIG. 1. (a) PA and (b) lateral views of the chest showing diffuse interstitial markings bilaterally with an old granuloma in the right upper lobe. No lymphadenopathy or pleural effusions were noted.

Discussion

Niemann–Pick disease is a rare, inherited, autosomal recessive disease characterized by abnormal sphingomyelin lipid storage. The pathognomonic intracellular accumulation of sphingomyelin in NPD may result from a variety of biochemical derangements, including lysosomal sphingomyelinase deficiency and altered intracellular cholesterol processing (4), which are associated with the accumulation of 'foam cells'. This biochemical heterogeneity may help to explain the significant variability noted in the clinical presentation. Although the diagnosis is usually established in childhood, the disease may rarely be first recognized in adolescence or adulthood (6).

'Sea-blue histiocytes' have been described in patients with NPD and are known as 'Pick cells' (7–11). However, the relationship of NPD with the syndrome of 'sea-blue histiocytosis' has been an area of some controversy. In 1947, Moeschlin (12) described splenic macrophages that stained deep blue with May–Grunwald Giemsa stain. Since then, 'sea-blue histiocytes' have been described in approximately 30 different diseases (7,13) as well as in isolation, i.e. without a known primary disorder (14). Some (15) have argued that 'sea-blue histiocytes' represent a normal reticuloendothelial cell that contains partially digested cells.

To review all available reports, a Medline search of English language reports using the words 'Niemann–Pick disease' and 'lipid storage disease' was performed. Tables 1 and 2 present the clinical characteristics of patients with NPD and pulmonary involvement in 31 previous reports. The current patient extends this experience to 32 and is unique in many respects. It provides the longest physiological follow-up in the literature, provides data on the natural history of pulmonary involvement in NPD, and highlights the fact that lung volumes and flow rates may be preserved even in advanced NPD with interstitial infiltrates and severely decreased DLCO. Although it is tempting to speculate that the aortic stenosis may have been due to an infiltrative process such as NPD, the patients' histopathol-

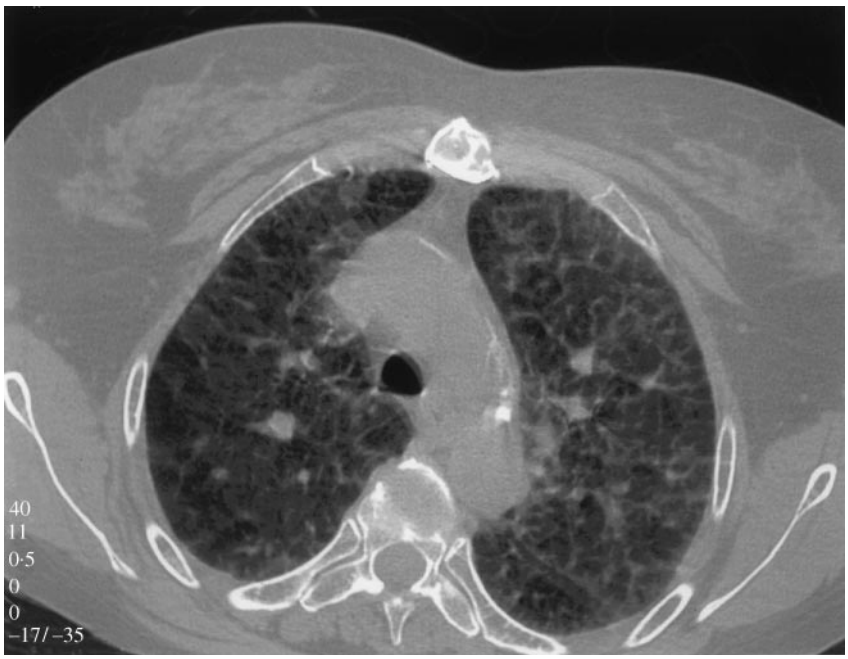

FIG. 2. A high resolution CT scan of the chest, at the level of the aortic arch, showing diffuse bilateral interstitial lung disease.

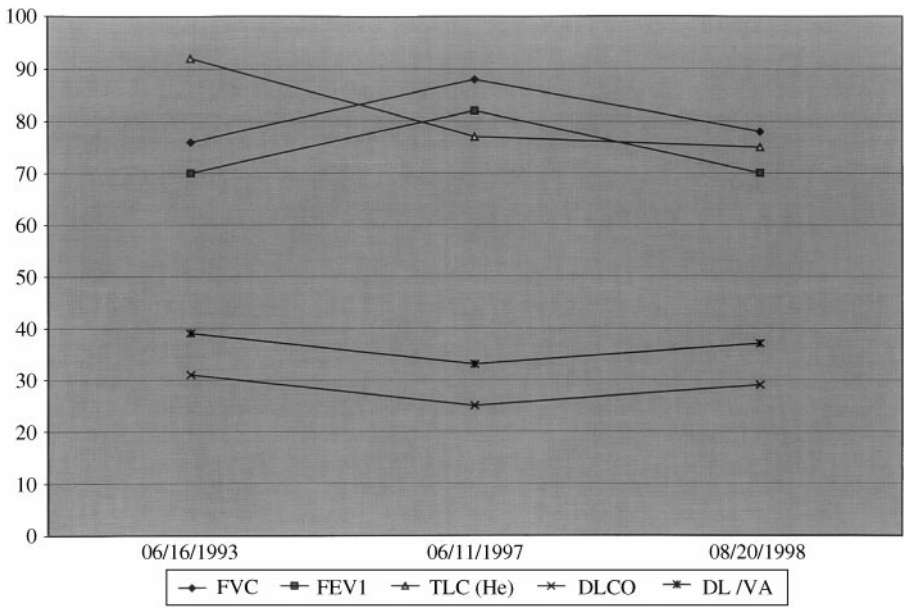

FIG. 3. Graph showing results of serial pulmonary function testing in our patient (in % predicted). These showed preserved spirometric flow rates and lung volumes over time, with severely decreased DLCO and DLVA. ◆: FVC; ■: FEV_1; △: TLC (He); ×: DLCO; *: DLVA.

ogy was not available for review and our review of the literature did not reveal any previous reports of valvular involvement specifically with NPD.

RADIOGRAPHIC FEATURES

As presented in Table 2, radiographic features of NPD include diffuse linear interstitial and nodular infiltrates with basal predominance, and honeycombing (7,30,36,40). The infiltrates may initially involve only the base and later progress to involve the entire lung field (30). High resolution computed tomography of the lung (Table 2) may show ground-glass opacities in the upper lung zones, possibly due to partial filling of the alveoli with 'Pick cells' and thickening of the interlobular septa in the lower lung zones (6,36,37). Pleural disease and lymphadenopathy have not been observed (6,36,37) and cavitary infiltrates are rare,

TABLE 1. Demographic features and presenting characteristics of reported patients with pulmonary involvement in Niemann–Pick disease*

Reference	Age at diagnosis, gender	Age at report	Type	Presentation	Physical examination	Diagnostic test
Knox [16]			NK	HSM	HSM, cherry spot on fundus	Autopsy
Bloom [17]	16 months	16 months	NK	GR, DD, diarrhea	LAN, rash, rales	Autopsy
	7 months	7 months	NK	Cough, fever, coma, seizures	Comatose, HSM	Autopsy
Abt [18]	14 months	14 months	NK	HSM, rhinopharyngitis	HSM, fever	Liver, splenic bx
Karelitz [19]	NR	NR	NK	HSM, listlessness, nystagmus	HSM, rotatory nystagmus	BM smear
Videbaek [20]	26 months	26 months	NK	DD, HSM, skin pigmentation (26 months). Epistaxis (4 years)	SM, LAD	BM, liver, splenic bx
Terry [21]	53 years	53 years	NK	Easy fatigability, SOB, cough, hemoptysis	Cyanosis, HSM	Lung bx, autopsy
Crocker [6]	1 month — 6 years, M	NR	NK	18 patients With variable symptoms. Bouts of bronchopneumonia	SM, Fe, LAN	Bm bx, LN bx
Forsythe [22]	10 years	19 years	NK	DD	SM	Splenic bx
	4 years	9 years 2 months	NK	Abdominal distension	SM	BM bx
	5 years	10 years	NK	SM	SM	BM bx
Fritts [23]	51 years	51 years	NK	Confusion, weakness, SOB	Cyanosis	Autopsy
Lynn [24]	19 years	19 years	?B	Night sweats, mild SOB, fatiguability	HSM, LAN	BM bx, LN bx
Lowden [25]	18 months	3 years 10 months	B	PMR, DD	HSM, retinal 'cherry red' spot	BM
Skikne [26]	12 years, M	NR	NK	Abnormal CXR	Unremarkable	Lung bx
Kawai [27]	2 years, M	2 years	B	SOB, fever, stridor, vomiting	HSM	BM bx
Long [7]	3 years, F	33 years	NK	HSM, SS, DSM	HSM, clubbing (33 years)	BM bx, liver bx
	15 years, F	15 years	NK	HSM, abnormal, CXR, easy bruising	DSM, SN, ecchymosis	liver bx
	15 years, F	15 years	NK	Anorexia, recurrent epistaxis, GIB	HSM, bruises	BM bx
Fried [11]	17 months	NR	B	HSM, anemia	HSM	BM bx
Dewhurst [9]	25 years	25 years	B	Malaise, abdominal distension	HSM,CLD, DSM	BM
Reich [28]	2 years, M	5 years	B	HSM	HSM	BM bx
Hammeren [29]	2 years 8 months	4 years	B	Bronchopneumonia, HSM	HSM	BM bx

Lever [30]	7 years, F	26 years	?B	HSM, GR, abn CXR	HSM	BM bx
Pavone [31]	2 years, F	17 years	B	Recurrent pulmonary infections, Abnormal CXR	HSM, skin rash, DSM, GR	BM bx, liver bx
Lipson [32]	14 months	NR	B	HSM, episodes of pneumonia	HSM	BM, liver bx
Takada [33]	15 months, F	5·5 years	?B	HSM	HSM, macular 'change'	BM bx
Zina [13]	38 years, M	38 years	NK	Skin involvement	Skin rash and exophytic lesions[‡]	BM bx, skin bx
Putterman [10]	12 years	36 years	B	DSM, CLD,HSM	CLD,HSM	BM
Viana [34] (on four patients)	3·5–22 years, 2F/2M	3·5–22 years	B	NR	HSM, poor breast development	BM bx, liver bx
Gogus [8]	8 years,F	8 years	?B	Failure to thrive	SM	BM bx, lung bx
	3 years, M	3 years	?B	Abnormal CXR	HSM	BM bx
Niggemann [35]	2 years, F	13 years	B	Abnormal CXR	SM	BM bx
	3.5 years, M	3.5 years	B	Excessive sweating, abnormal CXR	HSM, PMR	BM
Ferretti [36]	10 years,F	23 years	?B	Tpenia, abnormal CXR	SM	lung bx
Kovesi [37]	18 months, M	NR	C	Respiratory, distress, dry cough, jaundice, hypotonia, DD	HSM	BM asp
Muntaner [38]	62 years, F	62 years	B	Epigustric pain, N/V	HSM	BM bx, liver bx
Schofer [39]	3 months	3 months	C	Severe interstitial pneumonia	HSM	OLBx, liver, BM, skin bx
Minai[§]	12 years, F		B	HSM	HSM	

*Case reports identiifed by Medline search with key words 'Niemann–Pick disease' and 'lipid storage disease'.
[†]Single case reports unless otherwise indicated.
[‡]Disfiguring exophytic lesions on face, hands and feet.
[§]Present report.
Abbreviations: BM: bone marrow; bx: biopsy; CLD: chronic liver disease; CXR: chest radiograph; DD: developmental delay; DSM: delayed sexual maturity; F: female; GR: growth retardation; HM: hepatomegaly; HSM: hepatosplenomegaly; LAN: lymphadenopathy; LN: lymph node; M: male; N: nausea; NK: not known; NR: not reported; PMR: psychomotor retardation; SM: splenomegaly; SN: spider nevi; SOB: shortness of breath; SS: short stature; Tpenia: thrombocytopenia; V: vomiting.
Types of NPD. A: acute neuronopathic; B: chronic non-neuropathic; C: chronic neuronopathic; D: Nova Scotia variant; E: adult non-neuronopathic; ?denotes type is presumed.

Table 2. Characteristics of pulmonary involvement in patients with Neimann–Pick disease*

Age at Pulmonary diagnosis	Pulmonary symptoms	Pulmonary examination findings	Chest radiograph	CT scan	PFT
	NR	NR	NR	ND	ND
16 months	Pneumonia	Basal rales	Marked diffuse mottling bilaterally	ND	ND
7 months	Cough	Coarse rales	NR	ND	ND
14 months	Rhinopharyngitis	'Stertorous' breathing	Accentuated bilateral bronchial markings and infiltration 'along the finer ramifications'	ND	ND
NR	None	NR	Diffuse nodular infiltration	ND	ND
26 months	OM, cough, bronchopneumonia	None	Diffuse bilateral speckled, lacy pattern	ND	ND
53 years	Cough, hemoptysis	Cyanosis, bilateral inspiratory rales	Extensive symmetrical reticulated pattern (EAB)	ND	ND
6 months–19 years	Cough	None	11 of 18 patients with abnormal CXR. Most commonly 'miliary infiltration' ($N=6$)	ND	ND
10 years	None	NR ling	Diffuse miliary mottling (7 years), coarse mottling and reticular (18 years)	ND	ND
4 years	None	None	Symmetrical soft mottling bilaterally	ND	ND
5 years	None	None	Diffuse fine mottling bilaterally	ND	ND
51 years	SOB	Cyanosis	Bilateral mottling, hilar shadows	ND	Mild restrictive defect
19 years	Mild DOE	None	Diffuse coarse retic pattern (EAB). No LAN	ND	ND
18 months	URTI	NR	Bilateral diffuse perihilar infiltration (18 months), fine retic network of increased densities (3 years), heavy diffuse infiltration (3 years 10 months)	ND	ND

12 years	None	None	Diffuse mottling	ND	ND
2 years	Dyspnea, stridor	None	NR	ND	ND
3 years	DOE (age 33 years)	Clubbing	Diffuse mottling, widespread internal shadows	ND	Normal lung volumes flow rates, decreased DLCO (TF)
15 years	None	None	Widespread interstitial shadows, septal lines at bases (age 15 years) Reportedly abnormal at age 5 years.	ND	HI, decreased DLCO (<50% predicted)
15 years	Recurrent epistaxis	None	Diffuse fine reticular (EAB)	ND	ND
17 months	None	None	Fine symmetrical reticular densities bilaterally thick ILF	ND	ND
25 years	None	None	Generalized infiltration (25 years). First noted at age 7 years	ND	Mild restrictive defect
NK	None	None	Bilateral interstitial infiltration (2 years). Increased at 4 years	ND	ND
2 years 8 months	Pneumonia	Pneumonia	Bilateral diffuse RN infiltration (first noted at 11 months). Stable over time	ND	ND
7 years	Dyspnea	Cor pulmonale	Coarse reticular shadows bilaterally (EAB). Worsening infiltration at 18 years	ND	Restrictive defect (see text)
2 years	Recurrent pulmonary infections	None	Coarse, bilaterally RN infiltration	ND	ND
3·5 years	Pneumonia	Pneumonia	Bilateral diffuse interstitial infiltration (stable over time)	ND	Normal
15 months	None	None	Diffuse, bilateral, RN infiltration	ND	ND
38 years	None	None	Diffuse nodular infiltration + cavitation	ND	ND
34 years	None	NR	Markedly increased interstitial markings (EAB)	ND	Severe restrictive lung disease
3·5–22 years (four patients)	NR	None	Diffuse interstitial infiltration	ND	ND
8 years	None	None	Bilateral diffuse RN infiltration	ND	ND
3 years	None	None	Bilateral fine reticular infiltration	ND	ND
13 years	None	None	Bilateral symmetrical RN infiltration	ND	Normal (see text)
3·5 years	None	None	Bilateral fine reticular infiltration Unchanged 6 months later	ND	ND

Table 2. (*continued*)

Age at Pulmonary diagnosis	Pulmonary symptoms	Pulmonary examination findings	Chest radiograph	CT scan	PFT
23 years	None	None	Fine reticular basal infiltration	UL+ML: nodular, CL GGO, thick ILS LL: Thick ILS, less GGO, no nodules. No LAN, normal BVB	Normal spirometry+ volumes. Moderately decreased DLCO (56%) Normal ABG
3 years	Dyspnea, dry cough	Adventitial sounds	Diffuse reticular pattern, increased density R lung + L perihilar (36 months)	Diffuse interstitial + AS involvement (42 months)	ND
62 years	None	None	NR	Mild interstital pattern	ND
3 months	Severe interstitial pneumonia	Pulmonary insufficiency	Diffuse RN infiltration (3 months) increased lung density (4 months)	ND	ND
41 years	None	None	Bilateral basal RN infiltration	Diffuse bilateral Basal RN infiltration	See Fig. 1

*Case reports identified by Medline Search with key words 'Niemann–Pick disease' and 'Lipid storage disease'.
Abbreviations: AS: airspace; BVB: bronchovascular bundles; CL: centrilobular; CT: computerized tomographic scan; CXR: chest radiograph; EAB: especially at the bases; GGO: ground glass opacity; HI: hyperinflation; ILF: interlobar fissures; ILS: interlobular septa; LAN: lymphadenopathy; LL: lower lobe; ML: middle lobe; ND: not done; NK: not known; NR: not reported; OM: otitis media; PFT: pulmonary function tests; RN: reticulonodular; TF: transfer factor; thick: thickened; UL: upper lobe; URTI: upper respiratory tract infection.

TABLE 3. Pulmonary histopathological findings reported in 16 patients described with Niemann–Pick disease

Reference	Type of biopsy	Pathology
16	Autopsy	LM: Thickened interstitium with infiltration by 'vacuolated' cells. Large pale cells in the walls of pulmonary arteries and veins with patchy luminal obliteration.
17	Autopsy	Gross: Large, dark red, congested, edematous. No induration. No LAN. LM: Large, multi-nucleate, foam cells filling alveolar spaces, peribronchial connective tissue, alveolar capillaries and pulmonary artery branches, PMN alveolar infiltrate. An area of 'lymphoid' cells.
17	Autopsy	Gross: Reddish. No masses. Mottled, gray, pink on section. LM: Alveoli completely filled with large, spheroidal or polygonal foam cells (especially in subpleural and paraseptal alveoli). Foam cells also seen in bronchi and pulmonary artery branches. The cells stained intensely black with Weigert's iron hematoxylin stain.
19	Autopsy	Widespread involvement of the lungs with Niemann–Pick foam cells.
21	Lung bx, autopsy	Lung bx: Collections of intra-alveolar foam cells. Autopsy: Gross: gray-green pleural surface with minute, yellow points. A frothy, greasy material which did not float on water was expressible from the cut surface. Normal tracheobronchial tree. Hilar lymph nodes moderately enlarged. LM: Lipid Laden histiocytes (30–60 μ, cytoplasm filled with acidophilic foam, large nuclei 2–3 cells) filling alveoli and to a lesser extent alveolar septa which were 'sclerotic'. Slight hyperplasia of the subintimal layer of the small pulmonary arteries and arterioles.
6	Autopsy (11 of 18 had lungs examined)	8 to 11 patients had Niemann–Pick cells (foamy cells) in alveoli, alveolar septae, tracheal and bronchial walls and pleura. Variable severity. Bronchopneumonia in all autopsy specimens.
23	Autopsy	Fat-laden cells with a high phospholipid content almost completely replacing the alveoli.
25	Autopsy	Gross: 'Yellowish infiltration' and marked increase in weight. LM: Foam cells.
26	Not known	EM: Alveoli filled with 'foamy' cells containing membranous cytoplasmic bodies made up of stacks of lamellae, alternately osmiophilic and osmiophobic, giving a vacuolated appearance. Alveolar epithelial cells containing 'myelin bodies'. Edema of the basement membrane.
27	Autopsy	Foamy cells in intra-alveolar spaces.
5	Autopsy	Foamy cells present in alveoli.
35	Not known	Foamy cells in alveolar spaces and interstitium.
8	OLBx	LM: Nodular clusters of Oil Red O and Sudan Black B positive foamy histiocytes in alveoli especially in perivascular, peribronchial and subpleural areas. 'Sea-blue' histiocytes appearance in some cells. EM: Intracytoplasmic lamellated membranous bodies or fine granular material
36	OLBx	Foamy macrophages (20–90 μm diameter, vacuolated cytoplasm) in alveoli + thickened alveolar walls, filling lymphatic spaces around peripheral bronchi and peripheral. PA branches and subpleural and interlobular connective tissue. Rare giant cell forms. No granulomas, no fibrosis.
37	OLBx	LM: Large foamy macrophages in alveolar spaces and in thickened alveolar walls. Alveoli showed changes 'typical of alveolar proteinosis'. EM: Intra-alveolar macrophages containing membrane bound cytoplasmic vacuoles with concentric lamellated bodies 'typical of storage cells seen in NPD'.
39	OLBx	Massive alveolar and partly interstitial infiltration of macrophages loaded with foamy storage material.

Abbreviations: EM: electron microscopy; LAN: lymphadenopathy; LM: light microscopy; OLBx: open lung biopsy; PA: pulmonary artery; PMN: polymorphonuclear; TBBx: transbronchial biopsy.

with only a single instance reported (37). The radiographical differential diagnosis may include diseases involving the lung bases predominantly, with an interstitial pattern such as idiopathic pulmonary fibrosis and asbestosis. Other (non-pulmonary) radiographic features of NPD may include hepatosplenomegaly, metacarpal widening, osteoporosis and expansion of the marrow cavity of long bones (40).

PULMONARY PHYSIOLOGY

As in the present case, pulmonary function tests (Table 2) usually reveal normal lung volumes with a decreased diffusion capacity for carbon monoxide (DLCO) (7). Niggeman *et al.* (35) reported normal body plethysmographic lung volumes and exercise test results in one 13-year-old patient. Ferretti *et al.* (36) reported normal lung volumes and flows [FVC 3·72 (95% predicted), FEV_1 3·4 (95% predicted)] and a decreased DLCO (56% predicted) with normal arterial blood gases. Long *et al.* (7) reported pulmonary function tests in two patients. One patient had normal lung volumes and flow rates with a transfer factor below predicted (11·0 ml $CO\,min^{-1}\,mm\,Hg^{-1}$; predicted 20·1) while the other patient demonstrated hyperinflation with a transfer factor less than half the predicted value (11·8 ml $CO\,min^{-1}\,mm\,Hg^{-1}$; predicted 24·0). As suggested by decreased values of FVC in several patients [Table 2 (9,10,30,41)], restrictive changes can occur. Other physiological features can include decreased maximal breathing capacity (24) and exercise desaturation (24).

HISTOPATHOLOGY OF PULMONARY INVOLVEMENT

As reported in one patient by Niggeman *et al.* (35), bronchoscopic findings included 'remarkably rugged appearing mucosa' which can bleed easily. In available reports, cultures of aspirated secretions were negative and BAL fluid showed 'foam cells' of PAS and Sudan black B staining (35,41).

Histopathological features (Table 3) include diffuse infiltration of the lymphatics, subpleural spaces, alveolar walls and alveoli with 'foamy histiocytes'. In a post-mortem series of 11 patients, Crocker and Farber (6) found Niemann–Pick cells in alveolar septa; tracheal and bronchiolar walls and pleura in 58% of patients. The underlying pulmonary architecture is usually preserved (26). Inflammation and fibrosis are generally not features of this disease (36), although a few authors have described 'sclerotic' alveolar septae (21) and increased connective tissue around the bronchi and vessels (16).

NATURAL HISTORY

The natural history of NPD varies among the six described variants (A–F) (4,35). As a general rule, pulmonary involvement is rare in the adult variants of NPD but is more common in the infantile forms. Specifically, the clinical course of type A NPD is dominated by storage retinopathy, visceromegaly and neuronal involvement presenting in early infancy and causing rapid deterioration and a poor outcome. In contrast, the course of type B NPD, or the chronic visceral form, is more slowly progressive and does not involve the central nervous system. The diagnosis of type B NPD may be made at the time of traumatic rupture of an enlarged spleen or, infrequently, at post-mortem examination. Lung involvement may be noted incidentally on chest radiography, or during evaluation of cough, dyspnea, or recurrent pulmonary infections. The prognosis of type B NPD is more favorable than for type A disease, with most patients surviving into adulthood. Type C NPD is characterized by progressive visceral and neurological involvement with a subacute disease course and variable age at onset. Type D NPD (Nova Scotian) represents a juvenile form of the disease with normal early development. Neurological deterioration occurs in childhood and most patients die by 20 years of age. Patients with adult type E NPD develop generalized organ involvement (including lungs, liver, spleen and the central nervous system), but too few cases have been reported to allow a systematic description.

Definitive diagnosis and distinction from other interstitial diseases may require a biopsy showing characteristic Pick cell organ infiltration. The current case extends the available experience by presenting the 32nd reported patient with type B disease and pulmonary involvement. Like others, our patient demonstrated basilar interstitial infiltrates with a decreased diffusing capacity, exercise desaturation, but preserved spirometric flow rates and normal lung volumes.

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