Acute Interstitial Pneumonia in Siblings: A Case Report

Acute interstitial pneumonia (AIP) is a rapidly progressive condition of unknown cause that occurs in a previously healthy individual and produces the histologic findings of diffuse alveolar damage. Since the term AIP was first introduced in 1986, there have been very few case reports of AIP in children. Here we present a case of AIP in a 3-yr-old girl whose other two siblings showed similar radiologic findings. The patient was confirmed to have AIP from autopsy showing histologic findings of diffuse alveolar damage and proliferation of fibroblasts. Her 3-yr-old brother was also clinically and radiologically highly suspected as having AIP, and the other asymptomatic 8-yr-old sister was radiologically suspected as having AIP.

Key Words: Lung Diseases, Interstitial; Child; Siblings
ed. She presented with severe dyspnea and chest discomfort with pneumomediastinum and subcutaneous emphysema on chest radiograph. Pneumomediastinum was aggravated and resulted in pulmonary hemorrhage. Because of ongoing hypoxemia and decreased mentality, endotracheal intubation was performed at 13th hospital day. The patient died on the 14th day of admission after four times of cardiac arrest.

The patient underwent autopsy. The histopathologic findings on autopsy of the lungs revealed diffusely thickened alveolar septal interstitium by uniform, organizing loose fibrosis and foci of hyaline membranes as well as prominent interstitial and alveolar edema with focal hyperplasia of type II pneumocytes, which were indicative of organizing diffuse alveolar damage (DAD) and episodes of acute lung injuries (Fig. 2).

Her 2-yr-old brother showed a same clinical course with diffuse bilateral ground-glass opacities on his HRCT and also died after 4 weeks of intensive care due to respiratory

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**Fig. 1.** Chest CT shows symmetric ground glass opacities and consolidations in both upper (A) and lower (B) lobes.

**Fig. 2.** Hematoxylin and Eosin stain, × 100. (A) The alveolar septal interstitium is diffusely thickened by uniform, organizing loose fibrosis. (B) The lung shows involvement of hyaline membranes as well as prominent interstitial and alveolar edema. Focal type II pneumocyte hyperplasia is present.
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respiratory difficulty, but follow-up HRCT was not perform-
This study was performed at the beginning of the patient’s
consolidations with sparing zones in the peripheral portion
and chest HRCT showed diffuse ground-glass opacities and
lungs with peripheral sparing zones on chest radiograph,
traction bronchiectasis and cysts.

The histologic findings of AIP include the features of acute
and/or organizing phases of DAD. The exudative phase shows
dema, hyaline membranes, and interstitial acute inflam-
mation (7). In the organizing phase, organizing fibrin, loose
organizing fibrosis within alveolar lumens with incorpora-
tion within alveolar septa, and type II pneumocyte hyper-
plasia are seen (2). In this case, the patient underwent autops
y and histologic findings showed hyaline membrane with
interstitial edema and proliferation of interstitial fibroblasts
suggesting the presence of both acute exudative and late
organizing phases.

Treatment of AIP is usually supportive and initially con-
stitutes of oxygen supplement and noninvasive mechanical ven-
tilation, but mechanical ventilation with positive-end-expira-
tory pressure is required in most patients. Patients are often
treated with corticosteroids, which may improve the out-
come as in patients with adult respiratory distress syndrome
(ARDS) (1). Treatment with newer agents such as surfactant,
anti-cytokine antibodies, and inhaled nitric oxide traditionally
used for ARDS, might be beneficial but are largely untest-
ed (3). However, we did not use any newer agents other than
corticosteroids in this case. Even though corticosteroid was
not effective in two patients who died of AIP, it was effec-
tive in their asymptomatic older sister who had an inciden-
tal finding of ground-glass opacities on chest CT. Her chest
CT and PFT findings were improved after administration of
oral steroid agent.

Despite occurring in previously healthy persons, AIP is
associated with a poor prognosis (5). According to a review
of patient characteristics in the published series of AIP by
Bouros et al. in 2000, the mean 6-month mortality of patients
with AIP was 78% (range, 60-100%) (1). Olson et al. reported
a 41% survival rate from 29 patients (1), two other small
published series, total 2 of 13 patients survived (3, 9).

The prevalence of AIP in childhood is rare, and only two
cases of AIP have been previously reported; one of them sur-
vived after intravenous antibiotics and corticosteroid treat-
ment (8), and the other died on 40th day of admission (5).
In this case, the patient showed the same clinical course and
radiologic, histologic findings as the previously reported AIP
cases in adults. Notably, two other siblings, her 2-yr-old broth
and 8-yr-old sister, also showed the similar radiologic
findings indicative of AIP, even though they had some

DISCUSSION

In 1944, Hamman and Rich initially described four pre-
viously healthy patients with fatal fulminant lung disease
that, on autopsy, was characterized as extensive pulmonary fibrosis (8). In 1986, Katzenstein and coworkers introduced
the term “AIP” to describe eight patients characterized by
idiopathic interstitial lung disease causing a rapid onset of
respiratory failure, which was distinguished from other chronic forms of interstitial pneumonia (3). Since then, some reports
have reviewed the cases of AIP (4-8), but among them, there
were only 2 pediatric cases reports (4, 8) showing a much
lower incidence then in adult.

Clinical manifestation of AIP usually begins with prodromal ‘flu-like’ upper respiratory infection symptoms, followed
by rapid progression of dyspnea and respiratory failure that
requires mechanical ventilation. In our case, the patient presented the same clinical course as in the previously reviewed
cases; beginning with mild cough and rhinorrhea, which
was aggravated into respiratory failure requiring mechanical ventilation.

Most of the cases reported as AIP had extensive bilateral
air-space opacification with sparing of costophrenic angles
on their chest radiograph. As AIP moves from exudative to
organizing stage, the radiograph shows less consolidation and
presents a ground-glass appearance with irregular linear opacities (7). The most common CT findings in AIP patients
are diffuse ground-glass attenuation with a mosaic pattern and
consolidation (often in the dependent regions of the lungs) (2). In the early exudative phase, the lung shows areas of
ground-glass attenuation that are most often bilateral and
patchy, with areas of focal sparing of lung lobules giving a
geographic appearance. The later, organizing stage of AIP is
associated with distortion of bronchovascular bundles and
traction bronchiectasis and cysts.

In our case, there was bilateral diffuse consolidation of
lungs with peripheral sparing zones on chest radiograph,
and chest HRCT showed diffuse ground-glass opacities and
consolidations with sparing zones in the peripheral portion
of each lobe, suggesting the early exudative phase of AIP.
This study was performed at the beginning of the patient’s
respiratory difficulty, but follow-up HRCT was not perform-
ed due to the patients critical condition. Even though we
could not undergo another follow-up HRCT, her chest radi-
ograph showed an increase of bilateral haziness and findings
of spontaneous pneumomediastinum and subcutaneous em-
physema with bronchiectatic changes, suggesting a progress-
ion into the late organizing phase. Her 2-yr-old brother also
showed same findings on chest CT, which was aggravated
into bronchiectatic changes and pneumomediastinum on
his chest radiograph. Their 8-yr-old sister who did not have
any symptoms only showed a mild degree of bilateral ground-
glass opacities without progression to bronchiectatic changes
of lung parenchyma.

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radiologic, histologic findings as the previously reported AIP
cases in adults. Notably, two other siblings, her 2-yr-old broth
and 8-yr-old sister, also showed the similar radiologic
findings indicative of AIP, even though they had some
different degrees of symptoms and destruction of lung parenchyma.

Considering the coincidence in three children, we speculated that any genetic deficit or infectious attack might have been involved. However, we did not perform any genetic studies such as surfactant protein B and C. On the other hand, we could not exclude the possibility of an infectious origin, although the studies for infection were all negative.

In summary, this rare case of AIP in children gave us a chance to review the clinical course, radiologic and pathologic findings of AIP in children, which showed no significant difference from those of adult cases in the literature. Furthermore, we first experienced three different phases of AIP in one family: one clinically, radiologically, and histologically confirmed AIP; another clinically and radiologically highly suspected as having AIP; and the other only radiologically suspected as having AIP.

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