Analysis of the 3-Dimensional Fluid-Attenuated Inversion-Recovery (3D-FLAIR) Sequence in Idiopathic Sudden Sensorineural Hearing Loss

Stefano Berrettini, MD; Veronica Seccia, MD, PhD; Susanna Fortunato, MD; Francesca Forli, MD, PhD; Luca Bruschini, MD; Paolo Piaggi, PhD; Raffaello Canapicchi, MD

Importance: The unpredictability of idiopathic sudden sensorineural hearing loss (ISSNHL) presents a challenge to preventive care. Our study confirms the potentially important role of the 3-T magnetic resonance imaging (MRI), and in particular of the 3-dimensional fluid-attenuated inversion-recovery (3D-FLAIR) sequence, in the diagnosis and prognosis of ISSNHL to guide medical treatment.

Objective: To confirm the diagnostic, clinical, and prognostic role of 3D-FLAIR MRI in patients with idiopathic sudden sensorineural hearing loss (ISSNHL).

Design, Setting, and Patients: Retrospective study in a tertiary referral center with a consecutive sample of 23 patients diagnosed as having unilateral ISSNHL from January 2010 to March 2011.

Exposures: Patients underwent 3D-FLAIR MRI at 3 T to evaluate ISSNHL, and the MRI images were compared with those belonging to a random group of 20 age-matched healthy patients.

Main Outcomes and Measures: Precontrast and post-contrast high-intensity 3D-FLAIR MRI findings in patients with ISSNHL and the correlation with clinical findings.

Results: Thirteen patients showed high-intensity signals in the affected inner ear on precontrast and post-contrast 3D-FLAIR MRI (57%). From the analysis of different MRI sequences, we posited 3 radiologic patterns likely correlated with mild hemorrhage, acute inflammation, and presence or absence of blood-labyrinth or nerve barrier (BLB) breakdown. Hypersignal on 3D-FLAIR MRI was positively associated with pretreatment hearing loss (P = .04) and presence of vertigo (P = .04). A strict correlation also existed between distribution of the signal (vestibule, semicircular canals) and clinical features (vertigo) (P = .04).

Conclusions and Relevance: Use of 3D-FLAIR MRI at 3 T may contribute to the elucidation of pathologic conditions in the inner ears of patients with ISSNHL and provide new radiologic indicators (mild hemorrhage, acute inflammation, presence or absence of BLB breakdown) that might assume the role of prognostic factors.

Author Affiliations: Otolaryngology, Audiology, and Phoniatrics Unit, Department of Neuroscience (Drs Berrettini, Fortunato, Forli, and Bruschini), and Department of Energy and Systems Engineering (Dr Piaggi), University of Pisa, Italy; First Otorhinolaryngology Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa (Dr Seccia); and MR Laboratory “G. Monasterio” Foundation Tuscany Region, National Council of Research, Pisa (Dr Canapicchi).

Sudden sensorineural hearing loss (SSNHL) is an indirect sign of cochlear injury resulting from idiopathic causes (idiopathic ISSNHL [ISSNHL]). It is defined as a sensorineural hearing loss of 30 dB or more over at least 3 contiguous audiometric frequencies that develops over a period of a few hours to 3 days.

Despite efforts to clarify its pathophysiologic characteristics, the cause of ISSNHL remains unclear. The hypothesized causes include viral infection, vascular compromise, disruption of cochlear membranes, and the autoimmunity. However, detailed investigation based on medical and physical examination, audovestibular tests, blood examinations, and brain magnetic resonance imaging (MRI) studies with and without gadolinium administration shows a specific cause only in about 10% of patients.

The fluid-attenuated inversion-recovery (FLAIR) sequence is part of the routine protocol for MRI of the brain. There are emerging data in the scientific literature that the 3D-FLAIR sequence may provide diagnostic information in patients with ISSNHL, thus improving our possibility of detecting inner ear fluid anomalies by demonstrating alterations of the inner ear’s fluid protein composition, conditions that are difficult to identify on T1- and T2-weighted MRIs. However, the exact relationship between 3D-FLAIR findings and clinical signs is still unknown, and the role of 3D-FLAIR as an evaluative tool to discover prognostic indicators is only recently emerging. We
Therefore used the 3D-FLAIR MRI to investigate its diagnostic, clinical, and prognostic role in a selected population of patients affected by ISSNHL, and we compared our results with those of other centers.

STUDY DESIGN AND PATIENTS

This retrospective clinical study involved 23 patients with unilateral ISSNHL (11 men and 12 women; mean [SD] age, 49.3 [18.5] years; age range, 20–78 years) who visited the Otolaryngology, Audiology, and Phoniatrics Unit of the University of Pisa between January 2010 and March 2011. The study was approved by the local ethics committee. Informed consent for the participation to the study was received from all patients.

The criteria used to define ISSNHL were the presence of a sensorineural hearing loss of 30 dB or more over at least 3 contiguous audiometric frequencies developed over a period of a few hours up to 3 days without obvious causes. We excluded patients with progressive or fluctuating hearing loss. All patients underwent a unified diagnostic protocol to exclude known causes of sudden sensorineural hearing loss (Table 1).

Medicare history was recorded for all patients, and all underwent physical and neurologic examinations and complete audiologic evaluations including otomicroscopy, impedance audiometry, speech audiometry, otoemissions, and auditory brainstem responses. Hearing levels were evaluated with pure-tone audiometry (Interacoustics; Amplifon) in a sound-isolated chamber. Hearing loss was defined by pure-tone average (PTA), calculated using thresholds at 0.5, 1.0, 2.0, and 4.0 KHz, following the standards of the National Institute on Deafness and Other Communication Disorders. Audiometric assessment was made at the time of diagnosis, every 2 days during treatment, and after 3 months; the 3-month findings were considered the definitive posttreatment result. Furthermore, the degree of recovery was evaluated according to the Siegel criteria.

Presence of vertigo, tinnitus, and time delay between ISSNHL onset and MRI were recorded. In cases of vertigo, patients underwent vestibular function evaluation with caloric test and videonystagmography (VNG). As far as therapy is concerned, all patients were treated with intravenous (IV) 6-methylprednisolone, 1 bolus/d for 3 days, followed by a 30-day course at 1 mg/kg/d, tapered every 2 days.

MAGNETIC RESONANCE IMAGING

Magnetic resonance scans were performed using a 3-T system (Excite HD; General Electric Medical) with an 8-element phased-array sensitivity-encoding head coil. All patients underwent MRI of the temporal bones using the following protocol:

1. Fast-inflow steady-state acquisition in 3 dimensions (3D FIESTA); repetition time (TR), 6.1 milliseconds; echo time (TE), 2.4 milliseconds; flip angle, 60°; isotropic voxel, 0.4 mm; slice thickness, 0.4 mm; acquisition time (TA) 10 minutes, 28 seconds; number of excitations (NEX), 2; bandwidth, 62.50 kHz; field of view (FOV), 14 cm, acquired in the axial plane to obtain high anatomic detail.

2. 3D-FLAIR; TR, 11.000 milliseconds; TE, 134 milliseconds; inversion time, 2581 milliseconds; bandwidth, 41.7 kHz; FOV, 25.6 cm; TA, 10 minutes 53 seconds; isotropic voxel, 1 mm using a 256 × 256 matrix (512 × 512 zip); echo train, 180°; parallel imaging; sagittal acquisition; fat-suppression pulse acquired in the sagittal plane covering the entire brain volume.

3. Both sequences (1) and (2) may be reformatted in all planes maintaining the same signal to noise ratio.

RESULTS

The characteristics of the 23 patients are summarized in Table 2. Thirteen of the 23 patients with ISSNHL showed high-intensity signals in the affected inner ear on precontrast 3D-FLAIR (57%), so we considered them 3D-FLAIR positive. In contrast, the group of 10 patients with no high-intensity signal in the affected ear was considered 3D-FLAIR negative. The 3D-FLAIR–negative group did not show any other signal alteration and/or postcontrast enhancement in any sequence. The side of the abnormal findings on 3D-FLAIR MRI correlated with the side of the affected ear in all patients.
No significant differences were observed between the 2 groups in age (P = .31), sex (P = .13), affected side (P = .16), and presence of tinnitus (P = .10). In contrast, at the onset of ISSNHL, the incidence of vertigo in the 3D-FLAIR–positive and 3D-FLAIR–negative groups differed significantly (8 of 13 [62%] and 2 of 10 [20%], respectively) (P = .04).

The period between the MRI study and the onset of ISSNHL was a mean (SD) of 17 (12) days, with no significant differences in the 3D-FLAIR–positive and 3D-FLAIR–negative groups (P = .06).

Regarding audiologic findings, mean (SD) pretreatment PTA for the whole group was 77.4 (21.2) dB, with a significantly worse value in the 3D-FLAIR–positive group (85.7 [23.1] dB) compared with the 3D-FLAIR–negative group (66.6 [12.5] dB) (P = .04). In contrast, no relevant differences between the 2 groups were observed in the posttreatment PTA values (P = .41) and the posttreatment gain (ΔPTA), calculated as the difference between pretreatment and posttreatment PTA values (P = .34). In the group of 23 patients, the 3-month outcome was not influenced by the presence of vertigo (P = .35) or tinnitus (P = .26).

For the 3D-FLAIR–positive group, the distribution of the MRI signal is summarized in Table 3. Of the 13 3D-FLAIR–positive patients, 7 (54%) showed multiple subsites of high-intensity signal, while 6 patients (46%) had only 1 subsite of hypersignal (5 cases in the cochlea only, and 1 case in the cochlear nerve) (Figure 1). In 3 patients (23%), there was high-intensity signal in T1-weighted MRI images; in 3 patients (23%), a high-intensity signal only in the 3D-FLAIR sequence; and in 7...

### Table 2. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>3D-FLAIR Positive</th>
<th>3D-FLAIR Negative</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>23</td>
<td>13</td>
<td>10</td>
<td>.13</td>
</tr>
<tr>
<td>Patient sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>5</td>
<td>7</td>
<td>.13</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>8</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>49.0 (19.0)</td>
<td>46.0 (20.0)</td>
<td>54.0 (16.0)</td>
<td>.31</td>
</tr>
<tr>
<td>Ear affected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>13</td>
<td>9</td>
<td>4</td>
<td>.16</td>
</tr>
<tr>
<td>Right</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Vertigo, No. (%)</td>
<td>10 (44)</td>
<td>8 (62)</td>
<td>2 (20)</td>
<td>.04</td>
</tr>
<tr>
<td>Tinnitus, No. (%)</td>
<td>20 (87)</td>
<td>13 (100)</td>
<td>8 (80)</td>
<td>.10</td>
</tr>
<tr>
<td>ISSNHL-MRI delay, mean (SD), d</td>
<td>17.0 (12.0)</td>
<td>13.0 (6.0)</td>
<td>22.0 (15.0)</td>
<td>.06</td>
</tr>
<tr>
<td>Pretreatment PTA, mean (SD)</td>
<td>77.4 (21.2)</td>
<td>85.7 (23.1)</td>
<td>66.6 (12.5)</td>
<td>.04</td>
</tr>
<tr>
<td>Posttreatment PTA, mean (SD)</td>
<td>63.0 (24.0)</td>
<td>68.0 (28.8)</td>
<td>57.5 (17.1)</td>
<td>.41</td>
</tr>
<tr>
<td>ΔPTA, mean (SD)</td>
<td>14.0 (14.0)</td>
<td>17.5 (15.4)</td>
<td>9.3 (11.6)</td>
<td>.34</td>
</tr>
<tr>
<td>No recovery, No. (%)</td>
<td>14 (61)</td>
<td>7 (54)</td>
<td>7 (70)</td>
<td></td>
</tr>
<tr>
<td>Slight improvement No. (%)</td>
<td>2 (9)</td>
<td>0</td>
<td>2 (15)</td>
<td></td>
</tr>
<tr>
<td>Partial recovery, No. (%)</td>
<td>6 (26)</td>
<td>3 (30)</td>
<td>3 (23)</td>
<td>.49</td>
</tr>
<tr>
<td>Complete recovery, No. (%)</td>
<td>1 (4)</td>
<td>0</td>
<td>1 (8)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ISSNHL, idiopathic sudden sensorineural hearing loss; MRI, magnetic resonance imaging; PTA, pure-tone audiometry; ΔPTA, posttreatment PTA gain.

### Table 3. Distribution of the Hypersignal in the 3D-FLAIR–Positive Group and Its Possible Diagnostic Interpretation

<table>
<thead>
<tr>
<th>Patient</th>
<th>No./Sex/Age, y</th>
<th>T1</th>
<th>T2</th>
<th>3D-FLAIR</th>
<th>Gd Enhancement</th>
<th>Subsites</th>
<th>Possible Radiologic Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochlea</td>
<td>Vestibule</td>
<td>Semicircular Canals</td>
<td>Vestibular Nerve</td>
<td>Cochlear Nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/M/78</td>
<td>1 0 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>ICH</td>
<td></td>
</tr>
<tr>
<td>2/M/21</td>
<td>1 0 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>ICH</td>
<td></td>
</tr>
<tr>
<td>3/M/60</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl with BLB-B</td>
<td></td>
</tr>
<tr>
<td>4/F/74</td>
<td>0 0 1 0</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl</td>
<td></td>
</tr>
<tr>
<td>5/M/39</td>
<td>1 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>ICH   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>6/F/20</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>ICH   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>7/M/54</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>ICH   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>8/M/64</td>
<td>0 0 1 0</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl</td>
<td></td>
</tr>
<tr>
<td>9/F/21</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>10/M/39</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>11/F/30</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>12/M/54</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl   with BLB-B</td>
<td></td>
</tr>
<tr>
<td>13/F/41</td>
<td>0 0 1 1</td>
<td>0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>Infl</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BLB-B, blood-labyrinth barrier breakdown; Gd, gadolinium; ICH, intracochlear hemorrhage; Infl, inflammation; 0, absent; 1, present; 3D-FLAIR, 3-dimensional fluid-attenuated inversion recovery imaging.

©2013 American Medical Association. All rights reserved.
of them (54%), there was a 3D-FLAIR hyperintensity associated with postcontrast enhancement.

From the combined analyses of T1 and FLAIR sequences, and from the findings of other researchers,7,9,12 we identified 3 possible radiologic patterns:

Pattern 1: presence of high-intensity signal in the T1-weighted sequence, owing to the presence of intracellular and extracellular methemoglobin, and in 3D-FLAIR images, owing to the increased protein content in the membranous fluid secondary to the presence of methemoglobin (Figure 2), potentially consistent with intra-cochlear hemorrhage.

Pattern 2: presence of high-intensity signal in 3D-FLAIR images, owing to the increased protein content in the membranous fluid secondary to the presence of a protein exudate, while FIESTA and T1 sequences did not show any signal alteration (Figure 3), potentially consistent with acute inflammatory process.

Pattern 3: contrast enhancement after gadolinium injection is currently considered a result of a breakdown of the blood-labyrinth barrier (BLB); it can be associated with either of the diagnoses from pattern 1 and pattern 2, and it is expressed by high-intensity signal on T1 images and enhancement of the high-intensity signal on the 3D-FLAIR images (Figure 4). This pattern may be consistent with breakdown of the BLB.

We therefore studied, by means of the independent samples t test, whether some of the 3D-FLAIR–related

---

Figure 1. Patient imaging studies from the present series. A and B, Contiguous, axial, T1 fat-suppression post gadolinium images with no enhancement in the left internal acoustic canal. C-F, Axial (C and D) and oblique sagittal (E and F) reformatted 3D-FLAIR (3-dimensional fluid-attenuated inversion-recovery) images before (C and E) and after (D and F) gadolinium administration showing enhancement of the left cochlear nerve consistent with blood-nervous barrier breakdown after gadolinium administration (white arrows).
factors could influence the outcome and if they could be considered prognostic. From our statistical analysis, we concluded that the 3D-FLAIR diagnosis of a possible acute inflammatory process or intracochlear hemorrhage does not influence patient outcome, measured as ∆PTA, in a statistically significant way ($P = .26$), nor does the diagnosis of BLB breakdown ($P = .47$).

Figure 2. Patient imaging studies from the present series. A and B, Fast-spin echo T1 axial images before (A) and after (B) gadolinium administration with fat suppression showing mild hyperintense signal of the middle gyrus of the left cochlea without enhancement after gadolinium administration owing to methemoglobin deposition from hemorrhage. C and D, Three-dimensional FLAIR (fluid-attenuated inversion-recovery) axial images before (C) and after (D) gadolinium administration showing diffuse, nonhomogeneous hyperintense signal within the middle and apical gyrus of the cochlea on the left, without enhancement.

Figure 3. Patient imaging studies from the present series. A and B, Fast-spin echo T1 axial images before (A) and after (B) gadolinium administration with fat suppression showing normal signal of labyrinthine fluid without enhancement. C and D, Three-dimensional FLAIR (fluid-attenuated inversion-recovery) axial images before (C) and after (D) gadolinium administration showing mild hyperintense signal of the middle and apical gyri of the cochlea on the left without enhancement after gadolinium administration.
The correlations among some clinical features, such as vertigo and tinnitus, and the site of the hypersignal at 3D-FLAIR MRI were evaluated in all 3D-FLAIR–positive subjects, and we found that a 3D-FLAIR hyperintense signal in the vestibule or in the semicircular canals was related to vertigo in a statistically significant way ($P = .04$ or $P = .01$, respectively) (Table 4). Such correlations could not be done for tinnitus, as all 3D-FLAIR–positive patients had it.

The intensity range of the hypersignal, expressed as the number of subsites with 3D-FLAIR hyperintensity, was not related to the initial hearing level ($P = .16$) nor to the final outcome indicated as $\Delta$PTA ($P = .95$).

### DISCUSSION

The most controversial aspect of ISSNHL is the complete lack of unequivocal diagnostic and pathogenetic elements in the patients’ history. An improvement of our knowledge is urgently needed, especially when considering that there is an ongoing discussion about better treat-
Hypersignal 4 (100) 6 (75)
Hypersignal 0 1 (13)
Hypersignal 0 2 (25)

Hypersignal 0 6 (75)
Hypersignal 0 5 (63)

Normal signal 4 (100) 6 (75)
Normal signal 0 3 (38)
Normal signal 0 2 (25)

Normal signal 4 (100) 6 (75)
Normal signal 0 3 (38)
Normal signal 0 2 (25)

Normal signal 4 (100) 7 (88)
Normal signal 0 1 (13)
Normal signal 0 2 (25)

The $t$ test was used for independent samples.
Statistically significant difference.

Table 4. Statistical Correlation Between Distribution of Hypersignal on 3D-FLAIR MRI and Vertigoa

<table>
<thead>
<tr>
<th>Subsite</th>
<th>No Vertigo (n = 4)</th>
<th>Vertigo (n = 8)</th>
<th>$P$ Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochlea</td>
<td>Normal signal</td>
<td>0</td>
<td>2 (25)</td>
</tr>
<tr>
<td></td>
<td>Hypersignal</td>
<td>4 (100)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Vestibule</td>
<td>Normal signal</td>
<td>4 (100)</td>
<td>3 (38)</td>
</tr>
<tr>
<td></td>
<td>Hypersignal</td>
<td>0</td>
<td>2 (25)</td>
</tr>
<tr>
<td>SC</td>
<td>Normal signal</td>
<td>4 (100)</td>
<td>5 (63)</td>
</tr>
<tr>
<td></td>
<td>Hypersignal</td>
<td>0</td>
<td>6 (75)</td>
</tr>
<tr>
<td>VN</td>
<td>Normal signal</td>
<td>4 (100)</td>
<td>5 (63)</td>
</tr>
<tr>
<td></td>
<td>Hypersignal</td>
<td>0</td>
<td>1 (13)</td>
</tr>
<tr>
<td>CN</td>
<td>Normal signal</td>
<td>4 (100)</td>
<td>6 (75)</td>
</tr>
<tr>
<td></td>
<td>Hypersignal</td>
<td>0</td>
<td>2 (25)</td>
</tr>
</tbody>
</table>

Abbreviations: 3D-FLAIR MRI, 3-dimensional fluid-attenuated inversion recovery magnetic resonance imaging; CN, cochlear nerve; NA, not applicable; SC, semicircular canals; VN, vestibular nerve.

aUnless otherwise indicated, data are reported as number (percentage) of patients.
bThe $t$ test was used for independent samples.

ment of ISSNHL (intratympanic vs systemic therapy) that still necessitates more information to be guided.

The 3D-FLAIR 3-T MRI sequence may potentially be a tool for improving diagnostic accuracy, for guiding therapeutic decisions, and for serving as a prognostic factor in ISSNHL. Being insensitive to flux artifacts, it causes signal nulling of the cerebrospinal fluid and normal endolymphatic fluid, as we noticed in the control group, which has physicochemical composition similar to it. In our patients, it seems plausible to assume that the endolymphatic fluid creates a hyperintense signal when its composition changes due to pathologic conditions like hemorrhage (pattern 1) or inflammatory exudate (pattern 2). Thus, 3D-FLAIR hyperintensity indicates the modification of the inner ear protein composition that can be ascribed to a minor hemorrhage or to an acute inflammatory process. Also, 3D-FLAIR imaging can detect the BLB breakdown as the enhancement of the endolymphatic fluid signal and/or nerve signal after gado
dolinium injection owing to its high sensitivity to magnetic susceptibility. In our experience 3D-FLAIR imaging is more sensitive to hemolabyrinthic and hematon
ergious barrier breakdown than T1 imaging, with fat suppression increasing the diagnosis accuracy.

The aim of our study was to provide a correct interpretation of the 3D-FLAIR MRI findings, to correlate the findings with the patients’ clinical features, and to find out if they have some prognostic value of clinical interest.

First, our experience confirms the high clinical value of the 3D-FLAIR findings: there was a 100% correlation between the affected site and the hypersignal, and we never found a contralateral alteration and/or a hypersignal in the control group. This confirms the high reliability of the 3D-FLAIR pulse sequence. Furthermore, the 3D-FLAIR sequence proved to be more sensitive than the T1-weighted sequence in pointing out BLB breakdown. Moreover, high diagnostic specificity was obtained in association with the T1 sequence, which reveals the presence of methemoglobin within the labyrinth due to hemorrhage.

In our group, the initial PTA had a good correlation with 3D-FLAIR MRI findings, while a statistically significant association in the 3D-FLAIR–positive group ($P = .04$). We observed a worse initial PTA together with a hy-

of Cadoni et al,9 Yoshida et al,14 Sone et al,15 Ishida et al,16 Tanigawa et al,17 and Lee et al.7 Our mean (SD) delay between ISSNHL onset and 3D-FLAIR MRI (17 days [12]; range, 1-60 days) was similar to that already reported in literature, and in particular similar to the findings of Sugita et al12 (14.8 [5.4] days), Yoshida et al14 (15 [12] days), Tanigawa et al17 (24-98 days), and Cadoni et al9 (3-20 days).

However, this time interval was not consistently reported by all authors, and in particular, data are not available in the studies by Sone et al15 and Lee et al.7 The time factor may be an element that significantly affects 3D

-FLAIR MRI findings, which may be negative within 90-150 days after the onset of ISSNHL. Moreover, we have to consider that some minor findings, such as a slight 3D

-FLAIR hyperintensity, may be masked by steroid therapy, which in our group, as in those of other researchers, is initiated at ISSNHL diagnosis and not after the execution of the MRI. In fact, as Ramos et al16 suggest, a certain number of normal-appearing MRIs might provide better information if they were performed before the start of steroid therapy. If the diagnostic and prognostic value of 3D-FLAIR MRI in ISSNHL is to be further confirmed and validated, the interval between the onset of ISSNHL, the execution of the MRI, and the beginning of the therapy must be reduced to a minimum. This should happen very soon and at an organizational level.

Herein, we introduce what we believe are 3 new radiologic patterns to better delineate the significance of the generic term of hypersignal found in other authors’ works.7,9 Our definitions are easily understandable, reproducible, and easily applicable to future studies. In our group, for the moment, those patterns have no prognostic value, but we think that larger samples may provide a more interesting interpretation. In particular, we will be able to confirm or disconfirm that BLB breakdown can be considered an unfavorable prognostic factor, as previously suggested.12 For the moment, this is nothing more than an impression because it is drawn on the basis of the clinical course of 1 patient belonging to a small group sample ($N = 8$).12
persignal on 3D-FLAIR can be interpreted as an indirect expression of major damage to inner ear structures. Such correlation can be valid also for the accompanying symptoms: for vertigo, it can be present in up to 30% of patients with ISSNHL and is considered a poor prognostic factor for hearing recovery.\textsuperscript{7} In fact, it is suspected that vertigo in ISSNHL is an indirect sign of more extensive damage to the inner ear structures, therefore making ISSNHL more difficult to recover. At the onset of ISSNHL, our group showed vertigo in 44% of cases (n = 10) and it was significantly more common in 3D-FLAIR–positive than in 3D-FLAIR–negative patients. Therefore, if vertigo means more significant damage to the inner ear, and if patients with vertigo have a hypersignal in 3D-FLAIR sequences more frequently, we can presume that the 3D-FLAIR hypersignal is an indirect sign of more extensive damage to the inner ear, thus demonstrating a link between radiologic and clinical features. Our impression is consistent with the reported experiences of Ryu et al,\textsuperscript{8} who found not only a statistically significant correlation between 3D-FLAIR hypersignal and vertigo, but also a directly proportional link between the intensity of the signal and the severity of the nystagmus.

Our study, in agreement with Sugiura et al\textsuperscript{12} and Ryu et al,\textsuperscript{8} revealed that high-intensity signals in the vestibule and/or in the semicircular canals are consistent with the occurrence of vertigo, thus confirming once more the clinical reliability of 3D-FLAIR in ISSNHL. In our opinion, this evidence is strong enough to support the important association of 3D-FLAIR MRI findings with relevant clinical features. It is natural to ask whether these features could, in the future, influence the choice of the therapy protocol and in particular, if we are still justifying in proposing a trans tympanic therapy to a patient who shows a hypersignal located in the vestibular or cochlear nerve. Maybe it is too soon to draw any conclusions, but it is surely an interesting practical aspect to investigate further.

Some authors consider tinnitus in ISSNHL as a favorable sign because it may suggest survival of cell function and repair of a damaged auditory system.\textsuperscript{19} In our study, tinnitus was present in 87% of cases (n = 20), with no significant differences in 3D-FLAIR–positive and 3D-FLAIR–negative groups, and no statistical link to hearing recovery. This aspect is in line with the findings of Lee et al\textsuperscript{7} and Ryu et al.\textsuperscript{8} In our group, owing to the distribution in the 3D-FLAIR–positive population (100%), it was not possible to determine an association with 3D-FLAIR findings.

Yoshida et al\textsuperscript{14} and others\textsuperscript{7,8} affirm that precontrast high-intensity signal on 3D-FLAIR images may be a new prognostic factor in ISSNHL because hearing improvement in patients with high-intensity signals in the affected inner ear on precontrast 3D-FLAIR imaging was significantly worse than that in patients with no signal. However, in our study, 3D-FLAIR MRI findings could not be considered a prognostic factor for hearing recovery; in fact, there were no significant differences in posttreatment PTA (P = .41), ΔPTA (P = .34), or Siegel criteria\textsuperscript{11} (P = .43) between the 2 groups. Moreover, our study failed to demonstrate a correlation between the extent of the distribution of the hypersignal and ISSNHL severity, while Ryu et al\textsuperscript{8} found that both initial and follow-up hearing levels were worse in patients with a multiple-location hypersignal (cochlea plus vestibule) than in patients with a single-subsite hypersignal (only cochlea). Maybe further and more extensive experience will help us understand this aspect.

In conclusion, our study of 23 patients confirms the potentially important role of 3-T MRI, and in particular of the 3D-FLAIR sequence, in the diagnosis of ISSNHL. High-intensity signal in the affected ear on 3D-FLAIR MRI closely correlates with the severity of the hearing loss and with the clinical features (vertigo). In addition, 3-T MRI can provide new radiologic elements to consider: we identified 3 new radiologic patterns (presumably consistent with mild hemorrhage, acute inflammation, and BLB breakdown) that could potentially assume the role of prognostic factors. In the future, the information deriving from 3D-FLAIR sequences may have an impact on the choice of the most appropriate treatment in ISSNHL, which today is still assigned to insufficiently rigorous and reproducible elements of randomization.

Submitted for Publication: August 29, 2012; final revision received January 5, 2013; accepted February 4, 2013.

Correspondence: Stefano Berrettini, MD, Otolaryngology, Audiology, and Phoniatrics Unit, Azienda Ospedaliero-Universitaria Pisana, Via Paradisa n2, 56124, Pisa, Italy (s.berrettini@med.unipi.it).

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Berrettini and Canapicchi. Acquisition of data: Seccia, Fortunato, and Bruschini. Analysis and interpretation of data: Forli and Piaggi. Drafting of the manuscript: Fortunato and Piaggi. Critical revision of the manuscript for important intellectual content: Berrettini, Seccia, Forli, Bruschini, and Canapicchi. Statistical analysis: Piaggi. Study supervision: Berrettini.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank Diana Elizabeth Hearn, MISS, for her help in translation and revising the manuscript.

REFERENCES


Announcement

Clinical Problem Solving: Pathology Temporarily Closed to New Submissions

Due to a recent dramatic increase in the number of submissions for the monthly Pathology Quiz section, JAMA Otolaryngology–Head & Neck Surgery has temporarily stopped accepting new submissions for this feature. Submissions will resume in July 2013.