1 **Cerebrospinal Fluid Leaks from the Lateral Ventricle: A Case Series**

2 Running head: Lateral Ventricle CSF leaks

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1   **ABSTRACT**

2   **Objectives**: Describe the diagnosis and management of lateral skull base (LSB)

3   cerebrospinal fluid (CSF) leaks originating from the lateral ventricle.

4   **Study design:** Retrospective case review.

5   **Setting:** Tertiary referral academic center.

6   **Patients:** Patients with CSF leaks with direct communication to the lateral ventricle on

7   preoperative imaging.

8   **Intervention:** Surgical repair via the middle cranial fossa (MCF) approach.

9   **Main outcome measures:** CSF leak patient characteristics (age, sex, body mass index

10   [BMI]) and postoperative course (complications and CSF leak resolution) were collected.

11   **Results**: Three patients had CSF leaks from the lateral ventricle and all patients

12   demonstrated encephalomalacia of the temporal lobe on preoperative imaging.

13   Encephalomalacia resulted from trauma in one case (age 5) and neurodegeneration in two

14   cases (age 77 and 84). BMI ranged from 16.3 to 26.6 mg/kg^2 and follow-up ranged from 4-

15   21 months. Two patients presented with preoperative meningitis and all patients had

16   resolution of CSF leaks after MCF repair. With the exception of the higher rate of meningitis,

17   patient presentations did not differ from other spontaneous CSF leaks through middle fossa

18   defects. There were no minor or major postoperative complications.

19   **Conclusions**: CSF leaks from the lateral ventricle represent a rare subset of LSB CSF

20   leaks and can occur in non-obese patients secondary to temporal lobe encephalomalacia.

21   The MCF approach allows for repair of the dura and skull base in this cohort of patients with

22   high-flow CSF leaks and loss of brain parenchyma.

23   **Key Words**: Cerebrospinal Fluid Leak; Middle fossa craniotomy; encephalocele; lateral

24   ventricle; high flow; arachnoid granulation; temporal lobe encephalomalacia

INTRODUCTION:

Lateral skull base (LSB) cerebrospinal fluid (CSF) leaks are a relatively common condition encountered by the neurotologist. These most frequently occur in inherently thin portions of the LSB, including the tegmen mastoideum and tegmen tympani[1-5]. Clinical presentation is often vague and nonspecific, and symptoms may be overlooked given their intermittent nature[6]. Patients commonly report hearing loss, clear otorrhea if a tube/perforation is present, headaches[2,3,6,7], and/or aural fullness, while in some cases mastoiditis[8] or meningitis occur as the presenting symptoms[2,6,9].

CSF leaks of the lateral skull base have various etiologies, including trauma, neoplasm, cholesteatoma, and spontaneous etiology. Spontaneous CSF leaks (sCSF-L) are associated with obesity, female gender, and middle age[9]. In addition, recent literature demonstrates a strong association between sCSF-L and obesity-related conditions including obstructive sleep apnea (OSA) and idiopathic intracranial hypertension (IIH), which are known to transiently or chronically raise intracranial pressure (ICP), likely predisposing towards skull-base thinning and subsequent leak formation[2-4,9-28]. In addition, CSF leaks are often found in areas of the skull with higher densities of aberrant arachnoid granulations (AGs), which suggests that CSF pulsations may also play a role in bone erosion[7,29,30].

Unlike traumatic CSF leaks, spontaneous leaks rarely resolve on their own[9,31]. Surgical intervention is indicated in these patients to repair the defect given the risk of meningitis[1,2,4-9]. The standard surgical treatments for lateral temporal bone CSF leaks are either a middle cranial fossa (MCF) approach, a transmastoid (TM) approach, or a combination of the two[1,9,18,32,33]. The MCF approach has become the most commonly

48   used method[9]. While the TM approach avoids the need for a craniotomy, MCF allows

49   for better visualization of the tegmen mastoideum and tegmen tympani, which is

50   particularly useful in the case of multiple defects, and also avoids risks to the ossicular

51   chain[1,2,5,9,32].

52   Here we report three cases of LSB CSF leak through the tegmen via

53   communicating tracts from the lateral ventricle. None of the patients are obese. All three

54   demonstrated temporal lobe encephalomalacia (loss of brain parenchyma). Case 1 had

55   traumatic loss of cortical tissue, while cases 2 & 3 were elderly patients with

56   neurodegenerative changes of the temporal lobe. The authors hypothesize that

57   temporal lobe encephalomalacia in these patients facilitated propagation of a CSF tract

58   from the lateral ventricle to the tegmen. To our knowledge these are the first reported

59   cases of high-flow LSB CSF leaks with lateral ventricle involvement, which presented

60   unique considerations for surgical management. All three cases were successfully

61   repaired via the MCF approach.

62 **Methods:**

63   After obtaining Institutional Review Board approval (#1907071217), the electronic

64 medical record database was searched for all patients who underwent surgical repair of

65 CSF leaks by the senior author between January 1st, 2014 and January 31st, 2020.

66 Patients with CSF leaks emanating from the lateral ventricle were then selected for

67 further review. The medical records were evaluated for patient demographics,

68 comorbidities, body mass index (BMI), presenting symptoms, audiometric data

69 (including pure tone average (PTA) and speech discrimination scores), radiographic

70 data, intraoperative findings, and long-term outcomes. PTA was calculated by averaging

71 the hearing thresholds obtained at 500, 1000, 2000 and 3000 Hz. The clinical courses

72 of these patients were then compared with the published literature on lateral CSF leaks.

73   The institutional algorithm for LSB CSF leaks includes a surgical approach

74 catered to the defect size(s) and location(s); the MCF approach is most commonly used

75 at this institution to allow for a robust multilayer repair. In this specific cohort with lateral

76 ventricle involvement, given the lack of temporal lobe parenchyma it was not possible to

77 surgically limit the continued pulsatile nature of the lateral ventricle CSF onto the skull

78 base. Thus, the MCF was felt to be advantageous over a transmastoid approach and

79 allowed for a robust, multilayer closure with fascia and split calvarial bone or preferably

80 hydroxyapatite bone cement. Within our institutional algorithm, management of dural

81 defects depends on the location. Lateral dural defects resulting from bone flap elevation

82 should be repaired with intradural placement of Durarepair and Nurolon (Johnson &

83 Johnson, New Brunswick, NJ) suturing. Infratemporal dural defects from the CSF leak

84   do not require intradural repair since extradural repair provides excellent results.

85   Lumbar drains are not routinely used during or after surgery.

86

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Results:

Three patients were determined to have a leak emanating from the lateral ventricle; two were spontaneous in etiology, while one was post-traumatic. Brief clinical vignettes of these three patients are presented below.

Case 1

A 5-year-old female patient presented with right-sided clear otorrhea of 2 weeks duration, following tympanostomy tube placement. Two and a half years prior to presentation, she had sustained a traumatic head injury and associated temporal bone fracture. At the time of the initial trauma, CT imaging had demonstrated complete disarticulation of the ossicles and a large temporal bone fracture extending from the tegmen mastoideum to the sigmoid/transverse junction. Repeat imaging at the time of presentation demonstrated improved healing of the temporal bone fracture but a residual large tegmen mastoideum defect. There was associated fluid in the middle ear and mastoid with complete disarticulation of the malleus and incus. The patient's BMI was normal at 16.3 mg/kg^2. MRI revealed a large area of temporal lobe encephalomalacia resulting in a large CSF communicating tract from the lateral ventricle to a meningocele within the mastoid (**Figure 1A-B**). This tract communicated with the large area of tegmen dehiscence on CT imaging (**Figure 1C**).

Further discussion revealed that the patient had been demonstrating concerning, but nonspecific, signs of meningitis over the past 24 to 48 hours prior to arrival in our clinic, including decreased appetite and deceased activity level. At this point she was not febrile and did not have any nuchal rigidity, nausea, vomiting, or altered mental status. Thus, rather than being admitted for lumbar puncture and further

111   workup/management of meningitis, the patient was prescribed a brief outpatient course

112   of antibiotics and then admitted for urgent CSF leak repair 3 days later via a right-sided

113   MCF approach. Intraoperatively, an encephalocele through a large oblique fracture line

114   within the mastoid tegmen was removed, and a meningocele was noted posteriorly. The

115   skull base defect was repaired with bone dust, split calvarial bone graft, temporalis

116   fascia, dura repair, and duraGen. The right ear tube was left in place for postoperative

117   monitoring for otorrhea. On postoperative day 3, the patient displayed signs of

118   meningitis including fever, malaise, and decreased interaction with parents and nursing

119   staff, prompting urgent lumbar puncture (LP) and infectious disease consultation;

120   meningitis was confirmed with CSF culture of *Pseudomonas* from this LP on

121   postoperative day 3. The patient was treated with 6 weeks of IV antibiotics and

122   demonstrated rapid improvement in meningitis symptoms. A post-operative pseudo-

123   meningocele, a collection of CSF under the skin flap between the temporalis muscle

124   and the craniotomy site, resolved without further surgical intervention. On routine follow-

125   up 10 months later there was no evidence of CSF leak recurrence. About 1.5 years after

126   the CSF leak repair, the patient underwent right tympanoplasty with ossicular chain

127   reconstruction. Preoperatively, her right PTA was 44 dB, and her postoperative hearing

128   improved by 25 dB to a PTA of 19 dB. The contralateral left ear was normal with a PTA

129   of 11 dB and both ears had normal word discrimination scores.

130

131   **Case 2**

132   A 77-year-old man presented to the clinic for evaluation of a possible right-sided

133   sCSF-L. He was not overweight (BMI was 22.9 mg/kg^2). He had a history of mild

134   dementia with temporal lobe atrophy and encephalomalacia noted on MRI imaging.

135   Prior to evaluation in our clinic, the patient had presented to another otolaryngologist

136   with a history of longstanding right-sided hearing loss and clear rhinorrhea. The hearing

137   loss had reportedly been present since childhood, and the patient had adapted to this

138   by learning to read lips very well. He had not obtained a formal audiogram until shortly

139   before his evaluation by a local otolaryngologist. A right myringotomy was performed,

140   resulting in a large amount of clear otorrhea. Shortly thereafter and prior to evaluation in

141   our clinic, the patient was hospitalized for meningitis and CT imaging at the time

142   showed a tegmen defect, while MRI demonstrated communication of CSF from the

143   lateral ventricle through the temporal lobe and into a defect within the skull base,

144   compatible with a high-flow CSF leak (**Figure 2 A-D**). The patient's meningitis resolved

145   with IV antibiotics over the next few weeks. He then presented to our clinic to discuss

146   CSF leak repair, and he additionally reported a history of obstructive sleep apnea which

147   had improved since losing 100 lbs 10 years prior. Due to the patient's high-flow CSF

148   leak, he underwent MCF craniotomy for CSF leak repair. Intraoperatively a large

149   encephalocele was removed from the mastoid, and a high-flow CSF leak was noted

150   from a dural defect. The skull base and dura were repaired with split calvarial bone

151   graft, bone cement along the entire MCF floor, temporalis fascia, dura repair, and

152   duraGen. The ear tube was left in place. On routine follow-up appointments at 3 weeks

153   and 4 months postoperatively, there has been no recurrence of rhinorrhea or otorrhea,

154   and the patient's mental status has been improving with ongoing cognitive behavioral

155   therapy. A postoperative audiogram has not yet been performed but will be obtained at

156   the next in-person appointment.

Case 3

An 84-year-old man presented to the clinic with complaints of right otorrhea and otalgia. He was not obese (BMI was 26.6). He had a history of mild dementia with temporal lobe atrophy/encephalomalacia and bifrontal encephalomalacia and gliosis noted on prior imaging. He was initially treated with a course of antibiotics for presumed otitis externa infection. At 1-week follow up, the patient reported increased otorrhea and otalgia, and exam demonstrated clear fluid in the ear canal and a small spontaneous perforation in the tympanic membrane. Upon further questioning, the patient also reported a history of ventricular shunt placement 15 years prior; it was unclear why the prior shunt had been placed, as the patient did not know if this was for elevated ICP or for normal pressure hydrocephalus (NPH), and records were unavailable for further detailed review. He did however note progressive gait instability, confusion, and urinary incontinence, symptoms consistent with NPH. MRI imaging demonstrated hydrocephalus and temporal lobe encephalomalacia. CT demonstrated a tegmen defect over the mastoid, and repeat MRI redemonstrated evidence of numerous temporal lobe encephaloceles, along with a CSF leak from the lateral ventricle through the temporal lobe into the tegmen mastoideum **(Figure 3 A-D).** The contralateral tegmen was intact **(Figure 3E).** An X-Ray shunt series was obtained by the neurosurgery team and showed a right ventricular shunt with no tubing extending from the shunt to the neck, thorax, or abdomen (not functioning appropriately). The patient underwent revision right ventriculoperitoneal (VP) shunt placement and removal of the former right frontal ventricular catheter. Seven weeks later he continued to demonstrate CSF leak and underwent MCF craniotomy for repair. A large dural defect was repaired, as well as a

180 large encephalocele which was identified medially toward the petrous ridge, along with

181 two bony defects over the mastoid. The skull base was repaired with split calvarial bone

182 graft, bone cement along the entire MCF floor, temporalis fascia, dura repair, and

183 duraGen. At 1-month and 13-month follow up appointments, the patient has had a dry

184 ear with no evidence of ongoing CSF leak, and postoperative imaging has

185 demonstrated effective skull base reconstruction and an aerated mastoid **(Figure 3F).**

186 Preoperatively, his right PTA was 95 dB, and this improved to a PTA of 52.5 dB at 13-

187 months postoperatively, with complete closure of the air bone gap (of note, there was

188 persistent stable SNHL). The contralateral left ear has had stable SNHL with no air

189 bone gap. Hearing aids are being pursued by the patient.

Discussion:

190

191   Spontaneous CSF leaks have become increasingly prevalent in recent years, in

192 part related to changing population demographics[3]. Studies suggest that most sCSF-L

193 patients are middle-aged (mean 45-65 years), obese (average BMI = 35-38 kg/m^2)

194 females (female:male ratio = 70:30)[4,9,34]. In addition, over 80% of sCSF-L patients have

195 OSA[12], and OSA patients demonstrate thinning of the calvarium and skull-base

196 independent of BMI, age, and sex[11]. IIH, which is strongly correlated with sCSF-

197 L[10,16,35,36], has also been shown to cause calvarial thinning[10].

198   CSF leaks of all etiologies can lead to significant morbidity and mortality, making

199 them an important diagnosis to consider in patients presenting with otorrhea, aural

200 fullness, hearing loss, headaches, and pertinent history. A history of temporal bone

201 trauma should raise suspicion for post-traumatic CSF leak, as demonstrated by Case 1.

202 Conversely, a history of obesity, OSA and/or IIH should prompt further workup for

203 sCSF-L[2-4,9-14,16-28,37]. However, as demonstrated by cases 2 and 3, these demographic

204 features need not be present for a patient to develop a 'spontaneous' leak.

205   We present a series of three patients with high-flow CSF leaks emanating from

206 the lateral ventricle – one post-traumatic and two 'spontaneous'. All patients were non-

207 obese, and the two sCSF-L patients (cases 2 and 3) notably did not conform to

208 previously described demographic features of sCSF-L patients[9]. Instead, these patients

209 were elderly, male, non-obese, with a history of neurodegenerative changes (dementia).

210   Case 2 did endorse a remote history of obesity/OSA, but this had resolved a

211 decade prior to presentation and is unlikely to have caused his unilateral high-flow leak.

212 However, this history of obesity cannot be entirely dismissed, as it theoretically may

213   have been present for years and may have led to an insidious long-term spontaneous

214   CSF leak in this patient, which could be associated with his long-standing right-sided

215   hearing loss. Case 3 had symptoms of NPH requiring placement of a VP shunt, but had

216   no previous documentation of opening pressure, precluding assessment of elevated

217   ICP. This patient may have had long-term communicating hydrocephalus predisposing

218   him to CSF leak, but further history was limited regarding this. Of note, review of the

219   patient's imaging demonstrates an intact tegmen on the contralateral side **(Figure 3E)**,

220   which is not consistent with chronically elevated ICP[38].

221   Despite the potential aforementioned confounding variables, the authors argue

222   that temporal lobe encephalomalacia was likely causative of the high-flow CSF leaks in

223   this cohort, rather than elevated ICP or obesity. Case 1 had post-traumatic loss of

224   temporal lobe cortical tissue, while cases 2 & 3 were elderly and had underlying

225   neurodegenerative changes of the temporal lobe. In all three patients, loss of brain

226   parenchyma likely facilitated propagation of a CSF tract from the lateral ventricle down

227   to the tegmen, thereby transmitting CSF pulsations. These pulsations adjacent to the

228   thin bone of the tegmen likely led to bony erosion and dehiscence. The authors theorize

229   that, even in the absence of elevated ICP, the pulsatile nature of CSF adjacent to bone,

230   especially with a lateral ventricular source, can lead to bone erosion and CSF leak. This

231   suggests that, on a population level, the central location of the ventricles affords them a

232   cushioning parenchymal envelop which in turn provides an evolutionary advantage to

233   prevent skull erosion.

234   The notion that CSF pulsations can thin bone is supported by recent studies

235   examining arachnoid granulations. AGs are hypertrophied arachnoid villi, normally

236 involved in draining CSF into the venous system, which can aberrantly transmit CSF

237 pulsations to adjacent bone[39], leading to thinning and potentially sCSF-L[29]. Of note,

238 AGs have been found to occur more frequently with advancing age[29,30,40]. A review of

239 cadaveric temporal bone specimens from older adults found that AGs fully penetrated

240 dura and made contact with cortical surfaces in 13% of donor temporal bones[29]. Overall,

241 this lends support to the notion that CSF pulsations can lead to dura and bone erosion.

242   In addition to the potential etiology of these CSF leaks, the presenting symptoms

243 and demographics of this cohort are worth discussion. Notably, 2 of 3 patients

244 presented with meningitis, a much higher rate than that of LSB CSF-L patients

245 overall[2,6,9]. In a recent series, 16% of patients with spontaneous middle fossa CSF leaks

246 presented with meningitis as opposed to 100% of posterior fossa leaks[41]. One could

247 hypothesize that patients with encephalomalacia and a dehiscence communicating into

248 the lateral ventricle potentially have less of a physical barrier for intracranial spread of

249 infection (mirroring that of posterior fossa defects) than those that arise in association

250 with obesity/elevated intracranial pressure. However, due to small sample size, no

251 definitive conclusions can be drawn from this observation.

252   In addition, given that patients 2 and 3 were elderly with multiple comorbid

253 conditions, additional consideration for their care was warranted. Risks and benefits of

254 surgery were thoroughly discussed with the patients and their families, including

255 potential risks of craniotomy in the elderly. Ultimately, an MCF approach was pursued

256 as it afforded exposure of the entire involved skull base and dura, allowing for a more

257 definitive repair of the high-flow leaks and meningoencephaloceles in light of the

258 underlying loss of brain parenchyma and the known lateral ventricular involvement. The

259 repairs were successful and there have been no reports of leak recurrence on follow-up.

260 In addition, there have been no negative sequelae from performing a craniotomy in

261 these elderly patients thus far, consistent with prior studies that have demonstrated the

262 MCF approach to be a safe and effective method of repairing CSF leaks[32]. In patients

263 who are deemed to be poor candidates for an intracranial approach, an alternative that

264 could be considered is an extra-cranial repair with subtotal petrosectomy and fat graft

265 obliteration and closure of the ear canal[42].

266   Overall, CSF leaks from the lateral ventricle represent a rare subset of LSB

267 leaks. These likely occur secondary to temporal lobe encephalomalacia, which can

268 propagate a CSF tract from the lateral ventricle to the tegmen, allowing CSF pulsations

269 to occur adjacent to thin bone and potentially lead to defects and subsequent CSF leak.

270 In the CSF-leak patient with a history of severe head-trauma and/or dementia, or with

271 incidentally noted encephalomalacia or gliosis on prior head imaging, the authors

272 suggest consideration of high-resolution brain MRI to evaluate for ventricular

273 involvement. Neurosurgical consultation should be considered in patients with

274 ventriculomegaly for consideration of shunt placement, if indicated. These CSF leaks

275 are high-flow and represent unique considerations for surgical management. Due to the

276 high-volume leak and loss of brain parenchyma, robust repair likely requires a

277 craniotomy (MCF approach) with skull base repair from above. In our limited series, the

278 MCF approach has been successful in this patient population.

279   This study is limited by its retrospective nature, which in some instances led to

280 gaps in patient history which were unable to be fully delineated or objectively evaluated

281 (perioperative meningitis in case 1, long-term hearing loss in case 2, shunt history in

282 case 3). With regards to case 1, it is unclear if her perioperative meningitis was an

283 exacerbation of sub-clinical meningitis that was present prior to surgery, or if she

284 developed meningitis in the postoperative setting. A second limitation is the lack of long-

285 term follow up for all patients; Case 1 has followed up >1.5 years after MCF repair, case

286 3 just recently followed up 13-months after MCF repair, but case 2 has not had follow up

287 past 4 months. However, of note the patient in case 2 was contacted via phone >1 year

288 after MCF repair, and at that time denied any recurrent otorrhea. He will be following up

289 in person in the coming months. Finally, another limitation is that the lack of a

290 complication in this series doesn't mean that surgical complications will not occur in the

291 future.

292

293 **Conclusion:**

294 CSF leaks from the lateral ventricle represent a rare subset of LSB leaks. These occur

295 secondary to temporal lobe encephalomalacia. In patients being worked up for CSF

296 leak, a history consistent with neurodegenerative changes (elderly or post-traumatic)

297 should prompt providers to consider obtaining an MRI to evaluate for lateral ventricular

298 involvement. Due to the high-volume nature of these leaks and the loss of brain

299 parenchyma, robust repair likely requires a craniotomy (MCF approach) with skull base

300 repair from above, and this approach has been safe and effective in our cohort.

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411

Figure Legends

Figure 1: Case 1 – CT and MRI Findings. (**A**) T2 coronal MRI demonstrating a large CSF-communicating tract from the right lateral ventricle through a large area of temporal lobe encephalomalacia to the tegmen mastoideum. The white arrows outline the CSF tract. (**B**) T2 constructive interference in steady state (**CISS**) MRI further illustrating the right-sided CSF tract communicating through the tegmen, with some T2 signal present within the mastoid (white arrowhead). (**C**) Coronal CT IAC showing a large (>3 mm) right-sided tegmen defect (white arrow points to this) corresponding with the CSF tract shown in **A & B**.

Figure 2: Case 2 – CT and MRI Findings. (**A-C**) T2 coronal MRI demonstrating a large CSF-communicating tract from the right lateral ventricle through the temporal lobe to the tegmen mastoideum. The white arrows outline the CSF tract. (**D**) Coronal CT image showing a large (>3mm) tegmen defect (white arrow points to this) corresponding with the CSF tract shown in **A-C**.

Figure 3: Case 3 – CT and MRI Findings. (A) T1 coronal MRI demonstrating a large CSF-communicating tract from the right lateral ventricle through the temporal lobe, tracking towards the tegmen mastoideum. Note the presence of hydrocephalus. The white arrows flank the CSF tract. **(B&C)** T2 Coronal (**B**) and axial (**C**) CISS MRI sequences demonstrating ~~an encephalocele~~a meningocele off the lateral ventricle, tracking towards the tegmen. The white arrow points to the ~~encephalocele~~meningocele. (**D**) Coronal CT image showing a tegmen defect with fluid in the middle ear and

435   mastoid. The white arrow overlies the large tegmen defect. (**E**) Preoperative coronal CT

436   showing an intact contralateral tegmen with an aerated mastoid. (**F**) Postoperative

437   coronal CT image demonstrating skull base reconstruction with bone cement (white

438   arrow), with an aerated mastoid. The arrow overlies the repaired skull base.

1   **ABSTRACT**

2   **Objectives**: Describe the diagnosis and management of lateral skull base (LSB)

3   cerebrospinal fluid (CSF) leaks originating from the lateral ventricle.

4   **Study design:** Retrospective case review.

5   **Setting:** Tertiary referral academic center.

6   **Patients:** Patients with CSF leaks with direct communication to the lateral ventricle on

7   preoperative imaging.

8   **Intervention:** Surgical repair via the middle cranial fossa (MCF) approach.

9   **Main outcome measures:** CSF leak patient characteristics (age, sex, body mass index

10   [BMI]) and postoperative course (complications and CSF leak resolution) were collected.

11   **Results**: Three patients had CSF leaks from the lateral ventricle and all patients

12   demonstrated encephalomalacia of the temporal lobe on preoperative imaging.

13   Encephalomalacia resulted from trauma in one case (age 5) and neurodegeneration in two

14   cases (age 77 and 84). BMI ranged from 16.3 to 26.6 mg/kg^2 and follow-up ranged from 4-

15   21 months. Two patients presented with preoperative meningitis and all patients had

16   resolution of CSF leaks after MCF repair. With the exception of the higher rate of meningitis,

17   patient presentations did not differ from other spontaneous CSF leaks through middle fossa

18   defects. There were no minor or major postoperative complications.

19   **Conclusions**: CSF leaks from the lateral ventricle represent a rare subset of LSB CSF

20   leaks and can occur in non-obese patients secondary to temporal lobe encephalomalacia.

21   The MCF approach allows for repair of the dura and skull base in this cohort of patients with

22   high-flow CSF leaks and loss of brain parenchyma.

23   **Key Words**: Cerebrospinal Fluid Leak; Middle fossa craniotomy; encephalocele; lateral

24   ventricle; high flow; arachnoid granulation; temporal lobe encephalomalacia

INTRODUCTION:

Lateral skull base (LSB) cerebrospinal fluid (CSF) leaks are a relatively common condition encountered by the neurotologist. These most frequently occur in inherently thin portions of the LSB, including the tegmen mastoideum and tegmen tympani[1-5]. Clinical presentation is often vague and nonspecific, and symptoms may be overlooked given their intermittent nature[6]. Patients commonly report hearing loss, clear otorrhea if a tube/perforation is present, headaches[2,3,6,7], and/or aural fullness, while in some cases mastoiditis[8] or meningitis occur as the presenting symptoms[2,6,9].

CSF leaks of the lateral skull base have various etiologies, including trauma, neoplasm, cholesteatoma, and spontaneous etiology. Spontaneous CSF leaks (sCSF-L) are associated with obesity, female gender, and middle age[9]. In addition, recent literature demonstrates a strong association between sCSF-L and obesity-related conditions including obstructive sleep apnea (OSA) and idiopathic intracranial hypertension (IIH), which are known to transiently or chronically raise intracranial pressure (ICP), likely predisposing towards skull-base thinning and subsequent leak formation[2-4,9-28]. In addition, CSF leaks are often found in areas of the skull with higher densities of aberrant arachnoid granulations (AGs), which suggests that CSF pulsations may also play a role in bone erosion[7,29,30].

Unlike traumatic CSF leaks, spontaneous leaks rarely resolve on their own[9,31]. Surgical intervention is indicated in these patients to repair the defect given the risk of meningitis[1,2,4-9]. The standard surgical treatments for lateral temporal bone CSF leaks are either a middle cranial fossa (MCF) approach, a transmastoid (TM) approach, or a combination of the two[1,9,18,32,33]. The MCF approach has become the most commonly

48   used method[9]. While the TM approach avoids the need for a craniotomy, MCF allows

49   for better visualization of the tegmen mastoideum and tegmen tympani, which is

50   particularly useful in the case of multiple defects, and also avoids risks to the ossicular

51   chain[1,2,5,9,32].

52   Here we report three cases of LSB CSF leak through the tegmen via

53   communicating tracts from the lateral ventricle. None of the patients are obese. All three

54   demonstrated temporal lobe encephalomalacia (loss of brain parenchyma). Case 1 had

55   traumatic loss of cortical tissue, while cases 2 & 3 were elderly patients with

56   neurodegenerative changes of the temporal lobe. The authors hypothesize that

57   temporal lobe encephalomalacia in these patients facilitated propagation of a CSF tract

58   from the lateral ventricle to the tegmen. To our knowledge these are the first reported

59   cases of high-flow LSB CSF leaks with lateral ventricle involvement, which presented

60   unique considerations for surgical management. All three cases were successfully

61   repaired via the MCF approach.

Methods:

62

63   After obtaining Institutional Review Board approval (#1907071217), the electronic

64 medical record database was searched for all patients who underwent surgical repair of

65 CSF leaks by the senior author between January 1st, 2014 and January 31st, 2020.

66 Patients with CSF leaks emanating from the lateral ventricle were then selected for

67 further review. The medical records were evaluated for patient demographics,

68 comorbidities, body mass index (BMI), presenting symptoms, audiometric data

69 (including pure tone average (PTA) and speech discrimination scores), radiographic

70 data, intraoperative findings, and long-term outcomes. PTA was calculated by averaging

71 the hearing thresholds obtained at 500, 1000, 2000 and 3000 Hz. The clinical courses

72 of these patients were then compared with the published literature on lateral CSF leaks.

73   The institutional algorithm for LSB CSF leaks includes a surgical approach

74 catered to the defect size(s) and location(s); the MCF approach is most commonly used

75 at this institution to allow for a robust multilayer repair. In this specific cohort with lateral

76 ventricle involvement, given the lack of temporal lobe parenchyma it was not possible to

77 surgically limit the continued pulsatile nature of the lateral ventricle CSF onto the skull

78 base. Thus, the MCF was felt to be advantageous over a transmastoid approach and

79 allowed for a robust, multilayer closure with fascia and split calvarial bone or preferably

80 hydroxyapatite bone cement. Within our institutional algorithm, management of dural

81 defects depends on the location. Lateral dural defects resulting from bone flap elevation

82 should be repaired with intradural placement of Durarepair and Nurolon (Johnson &

83 Johnson, New Brunswick, NJ) suturing. Infratemporal dural defects from the CSF leak

84   do not require intradural repair since extradural repair provides excellent results.

85   Lumbar drains are not routinely used during or after surgery.

86

87

88   **Results:**

89   Three patients were determined to have a leak emanating from the lateral

90   ventricle; two were spontaneous in etiology, while one was post-traumatic. Brief clinical

91   vignettes of these three patients are presented below.

92   **Case 1**

93   A 5-year-old female patient presented with right-sided clear otorrhea of 2 weeks

94   duration, following tympanostomy tube placement. Two and a half years prior to

95   presentation, she had sustained a traumatic head injury and associated temporal bone

96   fracture. At the time of the initial trauma, CT imaging had demonstrated complete

97   disarticulation of the ossicles and a large temporal bone fracture extending from the

98   tegmen mastoideum to the sigmoid/transverse junction. Repeat imaging at the time of

99   presentation demonstrated improved healing of the temporal bone fracture but a

100   residual large tegmen mastoideum defect. There was associated fluid in the middle ear

101   and mastoid with complete disarticulation of the malleus and incus. The patient's BMI

102   was normal at 16.3 mg/kg^2. MRI revealed a large area of temporal lobe

103   encephalomalacia resulting in a large CSF communicating tract from the lateral ventricle

104   to a meningocele within the mastoid (**Figure 1A-B**). This tract communicated with the

105   large area of tegmen dehiscence on CT imaging (**Figure 1C**).

106   Further discussion revealed that the patient had been demonstrating concerning,

107   but nonspecific, signs of meningitis over the past 24 to 48 hours prior to arrival in our

108   clinic, including decreased appetite and deceased activity level. At this point she was

109   not febrile and did not have any nuchal rigidity, nausea, vomiting, or altered mental

110   status. Thus, rather than being admitted for lumbar puncture and further

111 workup/management of meningitis, the patient was prescribed a brief outpatient course

112 of antibiotics and then admitted for urgent CSF leak repair 3 days later via a right-sided

113 MCF approach. Intraoperatively, an encephalocele through a large oblique fracture line

114 within the mastoid tegmen was removed, and a meningocele was noted posteriorly. The

115 skull base defect was repaired with bone dust, split calvarial bone graft, temporalis

116 fascia, dura repair, and duraGen. The right ear tube was left in place for postoperative

117 monitoring for otorrhea. On postoperative day 3, the patient displayed signs of

118 meningitis including fever, malaise, and decreased interaction with parents and nursing

119 staff, prompting urgent lumbar puncture (LP) and infectious disease consultation;

120 meningitis was confirmed with CSF culture of *Pseudomonas* from this LP on

121 postoperative day 3. The patient was treated with 6 weeks of IV antibiotics and

122 demonstrated rapid improvement in meningitis symptoms. A post-operative pseudo-

123 meningocele, a collection of CSF under the skin flap between the temporalis muscle

124 and the craniotomy site, resolved without further surgical intervention. On routine follow-

125 up 10 months later there was no evidence of CSF leak recurrence. About 1.5 years after

126 the CSF leak repair, the patient underwent right tympanoplasty with ossicular chain

127 reconstruction. Preoperatively, her right PTA was 44 dB, and her postoperative hearing

128 improved by 25 dB to a PTA of 19 dB. The contralateral left ear was normal with a PTA

129 of 11 dB and both ears had normal word discrimination scores.

130

131 **Case 2**

132   A 77-year-old man presented to the clinic for evaluation of a possible right-sided

133 sCSF-L. He was not overweight (BMI was 22.9 mg/kg^2). He had a history of mild

134 dementia with temporal lobe atrophy and encephalomalacia noted on MRI imaging.

135 Prior to evaluation in our clinic, the patient had presented to another otolaryngologist

136 with a history of longstanding right-sided hearing loss and clear rhinorrhea. The hearing

137 loss had reportedly been present since childhood, and the patient had adapted to this

138 by learning to read lips very well. He had not obtained a formal audiogram until shortly

139 before his evaluation by a local otolaryngologist. A right myringotomy was performed,

140 resulting in a large amount of clear otorrhea. Shortly thereafter and prior to evaluation in

141 our clinic, the patient was hospitalized for meningitis and CT imaging at the time

142 showed a tegmen defect, while MRI demonstrated communication of CSF from the

143 lateral ventricle through the temporal lobe and into a defect within the skull base,

144 compatible with a high-flow CSF leak (**Figure 2 A-D**). The patient's meningitis resolved

145 with IV antibiotics over the next few weeks. He then presented to our clinic to discuss

146 CSF leak repair, and he additionally reported a history of obstructive sleep apnea which

147 had improved since losing 100 lbs 10 years prior. Due to the patient's high-flow CSF

148 leak, he underwent MCF craniotomy for CSF leak repair. Intraoperatively a large

149 encephalocele was removed from the mastoid, and a high-flow CSF leak was noted

150 from a dural defect. The skull base and dura were repaired with split calvarial bone

151 graft, bone cement along the entire MCF floor, temporalis fascia, dura repair, and

152 duraGen. The ear tube was left in place. On routine follow-up appointments at 3 weeks

153 and 4 months postoperatively, there has been no recurrence of rhinorrhea or otorrhea,

154 and the patient's mental status has been improving with ongoing cognitive behavioral

155 therapy. A postoperative audiogram has not yet been performed but will be obtained at

156 the next in-person appointment.

157 **Case 3**

158   An 84-year-old man presented to the clinic with complaints of right otorrhea and

159 otalgia. He was not obese (BMI was 26.6). He had a history of mild dementia with

160 temporal lobe atrophy/encephalomalacia and bifrontal encephalomalacia and gliosis

161 noted on prior imaging. He was initially treated with a course of antibiotics for presumed

162 otitis externa infection. At 1-week follow up, the patient reported increased otorrhea and

163 otalgia, and exam demonstrated clear fluid in the ear canal and a small spontaneous

164 perforation in the tympanic membrane. Upon further questioning, the patient also

165 reported a history of ventricular shunt placement 15 years prior; it was unclear why the

166 prior shunt had been placed, as the patient did not know if this was for elevated ICP or

167 for normal pressure hydrocephalus (NPH), and records were unavailable for further

168 detailed review. He did however note progressive gait instability, confusion, and urinary

169 incontinence, symptoms consistent with NPH. MRI imaging demonstrated

170 hydrocephalus and temporal lobe encephalomalacia. CT demonstrated a tegmen defect

171 over the mastoid, and repeat MRI redemonstrated evidence of numerous temporal lobe

172 encephaloceles, along with a CSF leak from the lateral ventricle through the temporal

173 lobe into the tegmen mastoideum **(Figure 3 A-D).** The contralateral tegmen was intact

174 **(Figure 3E).** An X-Ray shunt series was obtained by the neurosurgery team and

175 showed a right ventricular shunt with no tubing extending from the shunt to the neck,

176 thorax, or abdomen (not functioning appropriately). The patient underwent revision right

177 ventriculoperitoneal (VP) shunt placement and removal of the former right frontal

178 ventricular catheter. Seven weeks later he continued to demonstrate CSF leak and

179 underwent MCF craniotomy for repair. A large dural defect was repaired, as well as a

180 large encephalocele which was identified medially toward the petrous ridge, along with

181 two bony defects over the mastoid. The skull base was repaired with split calvarial bone

182 graft, bone cement along the entire MCF floor, temporalis fascia, dura repair, and

183 duraGen. At 1-month and 13-month follow up appointments, the patient has had a dry

184 ear with no evidence of ongoing CSF leak, and postoperative imaging has

185 demonstrated effective skull base reconstruction and an aerated mastoid **(Figure 3F).**

186 Preoperatively, his right PTA was 95 dB, and this improved to a PTA of 52.5 dB at 13-

187 months postoperatively, with complete closure of the air bone gap (of note, there was

188 persistent stable SNHL). The contralateral left ear has had stable SNHL with no air

189 bone gap. Hearing aids are being pursued by the patient.

Discussion:

190

191 Spontaneous CSF leaks have become increasingly prevalent in recent years, in

192 part related to changing population demographics[3]. Studies suggest that most sCSF-L

193 patients are middle-aged (mean 45-65 years), obese (average BMI = 35-38 kg/m^2)

194 females (female:male ratio = 70:30)[4,9,34]. In addition, over 80% of sCSF-L patients have

195 OSA[12], and OSA patients demonstrate thinning of the calvarium and skull-base

196 independent of BMI, age, and sex[11]. IIH, which is strongly correlated with sCSF-

197 L[10,16,35,36], has also been shown to cause calvarial thinning[10].

198 CSF leaks of all etiologies can lead to significant morbidity and mortality, making

199 them an important diagnosis to consider in patients presenting with otorrhea, aural

200 fullness, hearing loss, headaches, and pertinent history. A history of temporal bone

201 trauma should raise suspicion for post-traumatic CSF leak, as demonstrated by Case 1.

202 Conversely, a history of obesity, OSA and/or IIH should prompt further workup for

203 sCSF-L[2-4,9-14,16-28,37]. However, as demonstrated by cases 2 and 3, these demographic

204 features need not be present for a patient to develop a 'spontaneous' leak.

205 We present a series of three patients with high-flow CSF leaks emanating from

206 the lateral ventricle – one post-traumatic and two 'spontaneous'. All patients were non-

207 obese, and the two sCSF-L patients (cases 2 and 3) notably did not conform to

208 previously described demographic features of sCSF-L patients[9]. Instead, these patients

209 were elderly, male, non-obese, with a history of neurodegenerative changes (dementia).

210 Case 2 did endorse a remote history of obesity/OSA, but this had resolved a

211 decade prior to presentation and is unlikely to have caused his unilateral high-flow leak.

212 However, this history of obesity cannot be entirely dismissed, as it theoretically may

213 have been present for years and may have led to an insidious long-term spontaneous

214 CSF leak in this patient, which could be associated with his long-standing right-sided

215 hearing loss. Case 3 had symptoms of NPH requiring placement of a VP shunt, but had

216 no previous documentation of opening pressure, precluding assessment of elevated

217 ICP. This patient may have had long-term communicating hydrocephalus predisposing

218 him to CSF leak, but further history was limited regarding this. Of note, review of the

219 patient's imaging demonstrates an intact tegmen on the contralateral side **(Figure 3E)**,

220 which is not consistent with chronically elevated ICP[38].

221   Despite the potential aforementioned confounding variables, the authors argue

222 that temporal lobe encephalomalacia was likely causative of the high-flow CSF leaks in

223 this cohort, rather than elevated ICP or obesity. Case 1 had post-traumatic loss of

224 temporal lobe cortical tissue, while cases 2 & 3 were elderly and had underlying

225 neurodegenerative changes of the temporal lobe. In all three patients, loss of brain

226 parenchyma likely facilitated propagation of a CSF tract from the lateral ventricle down

227 to the tegmen, thereby transmitting CSF pulsations. These pulsations adjacent to the

228 thin bone of the tegmen likely led to bony erosion and dehiscence. The authors theorize

229 that, even in the absence of elevated ICP, the pulsatile nature of CSF adjacent to bone,

230 especially with a lateral ventricular source, can lead to bone erosion and CSF leak. This

231 suggests that, on a population level, the central location of the ventricles affords them a

232 cushioning parenchymal envelop which in turn provides an evolutionary advantage to

233 prevent skull erosion.

234   The notion that CSF pulsations can thin bone is supported by recent studies

235 examining arachnoid granulations. AGs are hypertrophied arachnoid villi, normally

236   involved in draining CSF into the venous system, which can aberrantly transmit CSF

237   pulsations to adjacent bone[39], leading to thinning and potentially sCSF-L[29]. Of note,

238   AGs have been found to occur more frequently with advancing age[29,30,40]. A review of

239   cadaveric temporal bone specimens from older adults found that AGs fully penetrated

240   dura and made contact with cortical surfaces in 13% of donor temporal bones[29]. Overall,

241   this lends support to the notion that CSF pulsations can lead to dura and bone erosion.

242   In addition to the potential etiology of these CSF leaks, the presenting symptoms

243   and demographics of this cohort are worth discussion. Notably, 2 of 3 patients

244   presented with meningitis, a much higher rate than that of LSB CSF-L patients

245   overall[2,6,9]. In a recent series, 16% of patients with spontaneous middle fossa CSF leaks

246   presented with meningitis as opposed to 100% of posterior fossa leaks[41]. One could

247   hypothesize that patients with encephalomalacia and a dehiscence communicating into

248   the lateral ventricle potentially have less of a physical barrier for intracranial spread of

249   infection (mirroring that of posterior fossa defects) than those that arise in association

250   with obesity/elevated intracranial pressure. However, due to small sample size, no

251   definitive conclusions can be drawn from this observation.

252   In addition, given that patients 2 and 3 were elderly with multiple comorbid

253   conditions, additional consideration for their care was warranted. Risks and benefits of

254   surgery were thoroughly discussed with the patients and their families, including

255   potential risks of craniotomy in the elderly. Ultimately, an MCF approach was pursued

256   as it afforded exposure of the entire involved skull base and dura, allowing for a more

257   definitive repair of the high-flow leaks and meningoencephaloceles in light of the

258   underlying loss of brain parenchyma and the known lateral ventricular involvement. The

259 repairs were successful and there have been no reports of leak recurrence on follow-up.

260 In addition, there have been no negative sequelae from performing a craniotomy in

261 these elderly patients thus far, consistent with prior studies that have demonstrated the

262 MCF approach to be a safe and effective method of repairing CSF leaks[32]. In patients

263 who are deemed to be poor candidates for an intracranial approach, an alternative that

264 could be considered is an extra-cranial repair with subtotal petrosectomy and fat graft

265 obliteration and closure of the ear canal[42].

266 Overall, CSF leaks from the lateral ventricle represent a rare subset of LSB

267 leaks. These likely occur secondary to temporal lobe encephalomalacia, which can

268 propagate a CSF tract from the lateral ventricle to the tegmen, allowing CSF pulsations

269 to occur adjacent to thin bone and potentially lead to defects and subsequent CSF leak.

270 In the CSF-leak patient with a history of severe head-trauma and/or dementia, or with

271 incidentally noted encephalomalacia or gliosis on prior head imaging, the authors

272 suggest consideration of high-resolution brain MRI to evaluate for ventricular

273 involvement. Neurosurgical consultation should be considered in patients with

274 ventriculomegaly for consideration of shunt placement, if indicated. These CSF leaks

275 are high-flow and represent unique considerations for surgical management. Due to the

276 high-volume leak and loss of brain parenchyma, robust repair likely requires a

277 craniotomy (MCF approach) with skull base repair from above. In our limited series, the

278 MCF approach has been successful in this patient population.

279 This study is limited by its retrospective nature, which in some instances led to

280 gaps in patient history which were unable to be fully delineated or objectively evaluated

281 (perioperative meningitis in case 1, long-term hearing loss in case 2, shunt history in

282 case 3). With regards to case 1, it is unclear if her perioperative meningitis was an

283 exacerbation of sub-clinical meningitis that was present prior to surgery, or if she

284 developed meningitis in the postoperative setting. A second limitation is the lack of long-

285 term follow up for all patients; Case 1 has followed up >1.5 years after MCF repair, case

286 3 just recently followed up 13-months after MCF repair, but case 2 has not had follow up

287 past 4 months. However, of note the patient in case 2 was contacted via phone >1 year

288 after MCF repair, and at that time denied any recurrent otorrhea. He will be following up

289 in person in the coming months. Finally, another limitation is that the lack of a

290 complication in this series doesn't mean that surgical complications will not occur in the

291 future.

292

Conclusion:

CSF leaks from the lateral ventricle represent a rare subset of LSB leaks. These occur

secondary to temporal lobe encephalomalacia. In patients being worked up for CSF

leak, a history consistent with neurodegenerative changes (elderly or post-traumatic)

should prompt providers to consider obtaining an MRI to evaluate for lateral ventricular

involvement. Due to the high-volume nature of these leaks and the loss of brain

parenchyma, robust repair likely requires a craniotomy (MCF approach) with skull base

repair from above, and this approach has been safe and effective in our cohort.

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411

Figure Legends

Figure 1: Case 1 – CT and MRI Findings. (**A**) T2 coronal MRI demonstrating a large

CSF-communicating tract from the right lateral ventricle through a large area of

temporal lobe encephalomalacia to the tegmen mastoideum. The white arrows outline

the CSF tract. (**B**) T2 constructive interference in steady state (**CISS**) MRI further

illustrating the right-sided CSF tract communicating through the tegmen, with some T2

signal present within the mastoid (white arrowhead). (**C**) Coronal CT IAC showing a

large (>3 mm) right-sided tegmen defect (white arrow points to this) corresponding with

the CSF tract shown in **A & B**.

Figure 2: Case 2 – CT and MRI Findings. (**A-C**) T2 coronal MRI demonstrating a large

CSF-communicating tract from the right lateral ventricle through the temporal lobe to the

tegmen mastoideum. The white arrows outline the CSF tract. (**D**) Coronal CT image

showing a large (>3mm) tegmen defect (white arrow points to this) corresponding with

the CSF tract shown in **A-C**.

Figure 3: Case 3 – CT and MRI Findings. (A) T1 coronal MRI demonstrating a large

CSF-communicating tract from the right lateral ventricle through the temporal lobe,

tracking towards the tegmen mastoideum. Note the presence of hydrocephalus. The

white arrows flank the CSF tract. **(B&C**) T2 Coronal (**B**) and axial (**C**) CISS MRI

sequences demonstrating a meningocele off the lateral ventricle, tracking towards the

tegmen. The white arrow points to the meningocele. (**D**) Coronal CT image showing a

tegmen defect with fluid in the middle ear and mastoid. The white arrow overlies the

435   large tegmen defect. (**E**) Preoperative coronal CT showing an intact contralateral

436   tegmen with an aerated mastoid. (**F**) Postoperative coronal CT image demonstrating

437   skull base reconstruction with bone cement (white arrow), with an aerated mastoid. The

438   arrow overlies the repaired skull base.

Figure 1

Figure 2

Figure 3