

Apraxia of speech with phonological alexia and agraphia following resection of the left middle precentral gyrus: illustrative case

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BACKGROUND Apraxia of speech is a disorder of speech-motor planning in which articulation is effortful and error-prone despite normal strength of the articulators. Phonological alexia and agraphia are disorders of reading and writing disproportionately affecting unfamiliar words. These disorders are almost always accompanied by aphasia.

OBSERVATIONS A 36-year-old woman underwent resection of a grade IV astrocytoma based in the left middle precentral gyrus, including a cortical site associated with speech arrest during electrocortical stimulation mapping. Following surgery, she exhibited moderate apraxia of speech and difficulty with reading and spelling, both of which improved but persisted 6 months after surgery. A battery of speech and language assessments was administered, revealing preserved comprehension, naming, cognition, and orofacial praxis, with largely isolated deficits in speech-motor planning and the spelling and reading of nonwords.

LESSONS This case describes a specific constellation of speech-motor and written language symptoms—apraxia of speech, phonological agraphia, and phonological alexia in the absence of aphasia—which the authors theorize may be attributable to disruption of a single process of “motor-phonological sequencing.” The middle precentral gyrus may play an important role in the planning of motorically complex phonological sequences for production, independent of output modality.

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KEYWORDS apraxia of speech; phonological alexia; phonological agraphia; precentral gyrus; area 55b; motor speech

Apraxia of speech (AOS) is a disorder of speech-motor planning characterized by difficulty initiating speech, articulatory groping, and trouble making transitions between syllables, despite normal strength in the articulators and preserved ability to perform non-speech orofacial movements.¹⁻⁴ AOS is regularly observed following left hemisphere stroke, and although early investigations of AOS often attributed this disorder to lesions in Broca's area (the left inferior frontal gyrus^{5,6}), more recent work has implicated more posterior frontal regions in ventral and middle portions of the precentral gyrus.^{2,7-9}

Another set of acquired language disorders, phonological alexia and agraphia, are also rare in their pure forms.¹⁰⁻¹² In these disorders, patients struggle to read or spell unfamiliar words and pseudo-words, even when they follow clear grapheme-phoneme rules (e.g., “andon”, “manver”¹³), while performing relatively well with familiar words with irregular spellings (e.g., “subtle”, “dough”). Many prior studies have attributed such phonological processes to supramarginal and/or ventral precentral substrates,¹⁴⁻¹⁸ although others have found the neural underpinnings of phonological processing during reading and spelling more difficult to localize.¹²

ABBREVIATIONS AOS = apraxia of speech; mPrCG = middle precentral gyrus; UCSF = University of California, San Francisco; WHO = World Health Organization.

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Here, we present a case of lasting AOS in the absence of aphasia with concurrent phonological alexia and agraphia following resection of the left middle precentral gyrus (mPrCG). For clinical reasons, this resected region included an area that elicited speech arrest during electrocortical stimulation mapping. We provide a detailed characterization of the patient's language, speech-motor, reading, and writing performance, revealing phonological and sequencing deficits that were analogous across spontaneous speech production, reading, and spelling. These findings may serve as evidence for a modality-independent "motor-phonological sequencing" stage of language production with bases in the left mPrCG, in line with recent work implicating this region as a hub for more abstract levels of speech production beyond direct motor control.^{9,19–22}

Illustrative Case

Patient Description

The patient is a high-functioning, left-handed female with a masters'-level education and no prior history of cognitive or neurological impairment. At the time of surgery, she was 36 years old and 27 weeks pregnant with her second child. The patient initially presented 6 weeks prior to surgery at an outside hospital with progressive right-sided facial weakness and difficulty with articulation before experiencing a seizure at 25 weeks of pregnancy. A $3.9 \times 3.7 \times 3.4$ -cm mass was identified in the left precentral gyrus (Fig. 1A and B); at this point, she was referred to the University of California, San Francisco (UCSF), for surgery.

Operation

The patient underwent awake left frontal craniotomy with speech and motor mapping. Electrocortical stimulation mapping was performed, identifying sites for right-hand flexion/forearm extension (sites 1–3); sensation in the mouth (site 4), tongue (sites 9–10), fingers (sites 5, 7–8), and thumb (site 6); and a single site for speech arrest (site A) near the center of the tumor in the mid-ventral precentral gyrus (Fig. 2A). Due to the size and rapid growth of the tumor, the circumstances of the pregnancy, and prior discussion with the patient regarding the relative risks of leaving residual tumor in place, it was determined that resection of the tumor should be

attempted despite the presence of a speech-arrest site. While monitoring her speech function, excision of the tumor began from the anterior margins of the tumor, and then proceeded posteriorly toward the speech-arrest site. No change to her speech was detected as the speech-arrest site was approached and slowly resected, and therefore resection continued as far as the posterior boundary of the tumor at the central sulcus. Speech difficulties were encountered toward the end of resection at the deep subcortical margin adjacent to the corticospinal tract and superior longitudinal fasciculus, and resection was stopped then. The patient went on to give birth to a healthy infant 2 months after the surgery.

Resection

The extent of resection was near total, with approximately 95% of tumor removed (Figs. 1A and 2B). Pathology showed a World Health Organization (WHO) grade IV isocitrate dehydrogenase-mutant astrocytoma. Per intersection of Montreal Neurological Institute–normalized postoperative images with a multimodal atlas,²² gray matter regions impacted by the resection primarily included the precentral gyrus and area 55b in the posterior middle frontal gyrus (Figs. 1A, 2B, and 3A). White matter tracts impacted primarily belonged to the superior longitudinal fasciculus (Fig. 3B–D).

Postoperative Motor Speech and Language Presentation

At 2 days postsurgery the patient exhibited marked expressive aphasia, AOS, and dysarthria. She also presented with numbness in the right hand and right-sided facial weakness. By 4 days postsurgery, all symptoms aside from the AOS had begun to resolve and by 3 months postsurgery were essentially absent; however, she continued to exhibit apraxic speech symptoms. The patient received speech and language therapy, where she received a formal diagnosis of moderate AOS at 1-month postsurgery that remained consistent throughout her 3 months of therapy. The patient's speech was characterized primarily by syllable segmentation, distorted substitutions, and slow rate (a strategy to improve articulation adopted and further honed in speech therapy). The patient also reported difficulty with spelling as one of her most bothersome postoperative symptoms, stating that, although she was

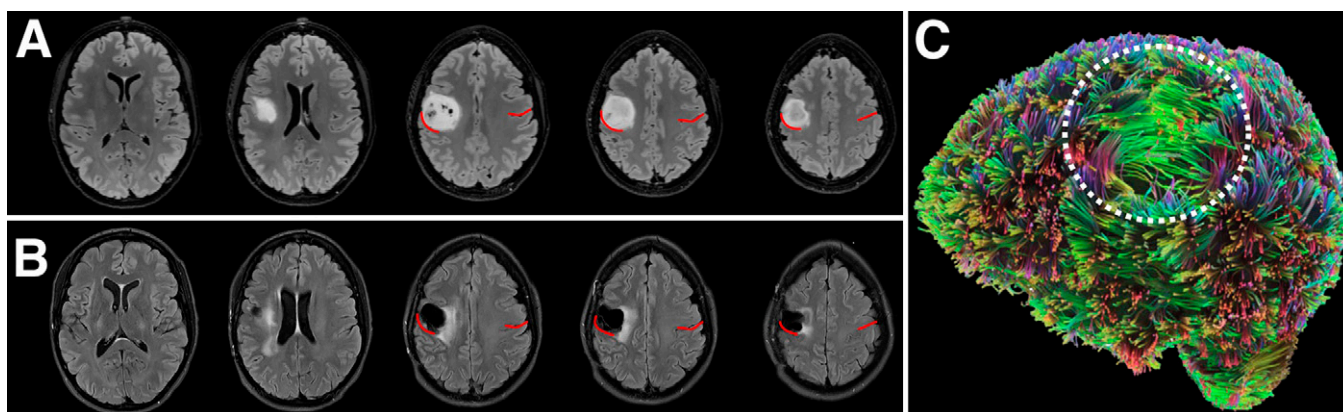


FIG. 1. Pre- and postoperative imaging of the patient's tumor and resection. **A:** Preoperative fluid-attenuated inversion recovery (FLAIR) imaging showing the patient's tumor prior to surgery (hyperintense/bright). Red lines indicate central sulcus. **B:** Eleven-month postoperative FLAIR imaging showing the patient's resection (hypointense/dark). Red lines indicate central sulcus. **C:** Diffusion tensor imaging of the patient's brain prior to surgery. Note the impact of the tumor on the fibers of the superior longitudinal fasciculus, circled in white.

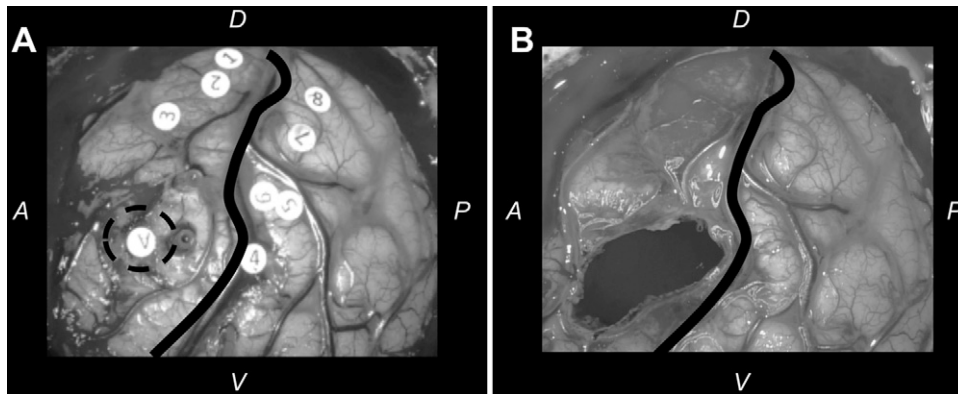


FIG. 2. Intraoperative photograph (A) showing eloquent sites identified during electrocortical stimulation. Sites correspond to functions as follows: right-hand flexion/forearm extension (sites 1–3), sensation in the mouth (site 4), sensation in the right-side fingers (sites 5, 7–8), sensation in the right thumb (site 6), and speech arrest (site A, circled). Sites 9–10 (not visible in image; ventral to site 4) correspond to sensation in the tongue. Intraoperative photograph (B) showing the resection cavity. Site A has been removed completely by the resection. Black lines indicate the central sulcus. A = anterior; D = dorsal; P = posterior; V = ventral.

often able to “identify that [her] writing [was] incorrect...,” she was not always able to “identify what the specific error may be.”

To summarize, the only persisting deficits following resection of a relatively circumscribed region in the left mPrCG were in the domains of speech-motor planning and phoneme-grapheme conversion.

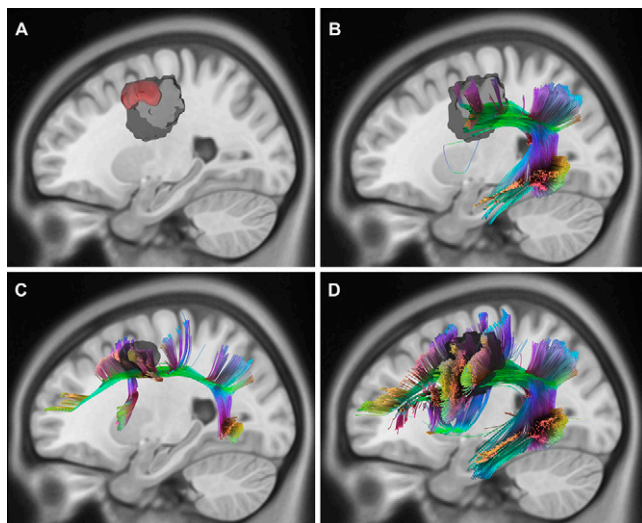


FIG. 3. White matter tract intersections with resection cavity registered to the Human Connectome Project (HCP) 1065 template. **A:** Overlay of area 55b²² (red) with the resection mask (gray). Primarily gray matter regions affected by the resection were in the left precentral gyrus, post-central gyrus, and area 55b. **B:** White matter tracts that originate in the posterior temporoparietal regions (inferior temporal gyrus, middle temporal gyrus, superior temporal gyrus, and angular gyrus) and terminate in the resection zone, consisting primarily of branches of the superior longitudinal fasciculus with terminals in the precentral gyrus and the inferior parietal lobe. **C:** Fiber tracts that intersect with area 55b. **D:** Fiber tracts that pass through the resection zone.

Diagnostic Assessments 6 Months Postsurgery

Speech and language testing was administered over Zoom by UCSF approximately 6 months after the patient’s surgery. Assessments consisted of a mix of formalized evaluations and nonstandard tasks (see references 1, 13, 23–33 and Supplementary Materials for further detail).

The patient’s performance on tasks assessing language, cognition, nonverbal praxis, nonspeech orofacial movement, and fine motor movements of the hands was overall excellent, suggesting no lingering aphasia, cognitive, or primary motor deficits. However, her performance on motor-speech tasks remained impaired in a manner consistent with AOS.^{34,35} Note that when the patient consciously slowed her speech, speech errors were ameliorated; for example, an attempt to say “prescription” (as transcribed in the International Phonetic Alphabet, /pɹɛskɹɪpʃən/) changed from a highly distorted and paraphasic pronunciation (/fɹɪpθɪv/) to a clearer and more appropriate pronunciation (/pɹɛs (.) kɹɪp (.) ʃn/ largely correct) with conscious slowing of her speech (Fig. 4A).

The patient’s reading and spelling of real words were also overall excellent; however, due to her strategy of spelling words orally simultaneously while writing, we were able to observe several instances in which the correct letter was said aloud while an anticipatory error (that is, the premature writing of a letter that occurred later in the word) was made in writing. These errors were always self-corrected (Fig. 4C). Additionally, the patient exhibited mild to moderate impairment in both the spelling and reading of nonwords of various lengths. Production was particularly impaired in the reading of 4-syllable nonwords, which were characterized by markedly more effortful production relative to 4-syllable real words. Note that the patient was later able to accurately verbally repeat the same 4-syllable nonwords that she struggled to read aloud, suggesting that pure motor-speech complexity of the nonwords was not the basis for these production errors. See Supplementary Materials for more detailed information on the patient’s task performance and the items administered.

Analysis of Reading and Spelling Errors

Each instance throughout the evaluation in which the patient was required to either spell or read a word or nonword, including in

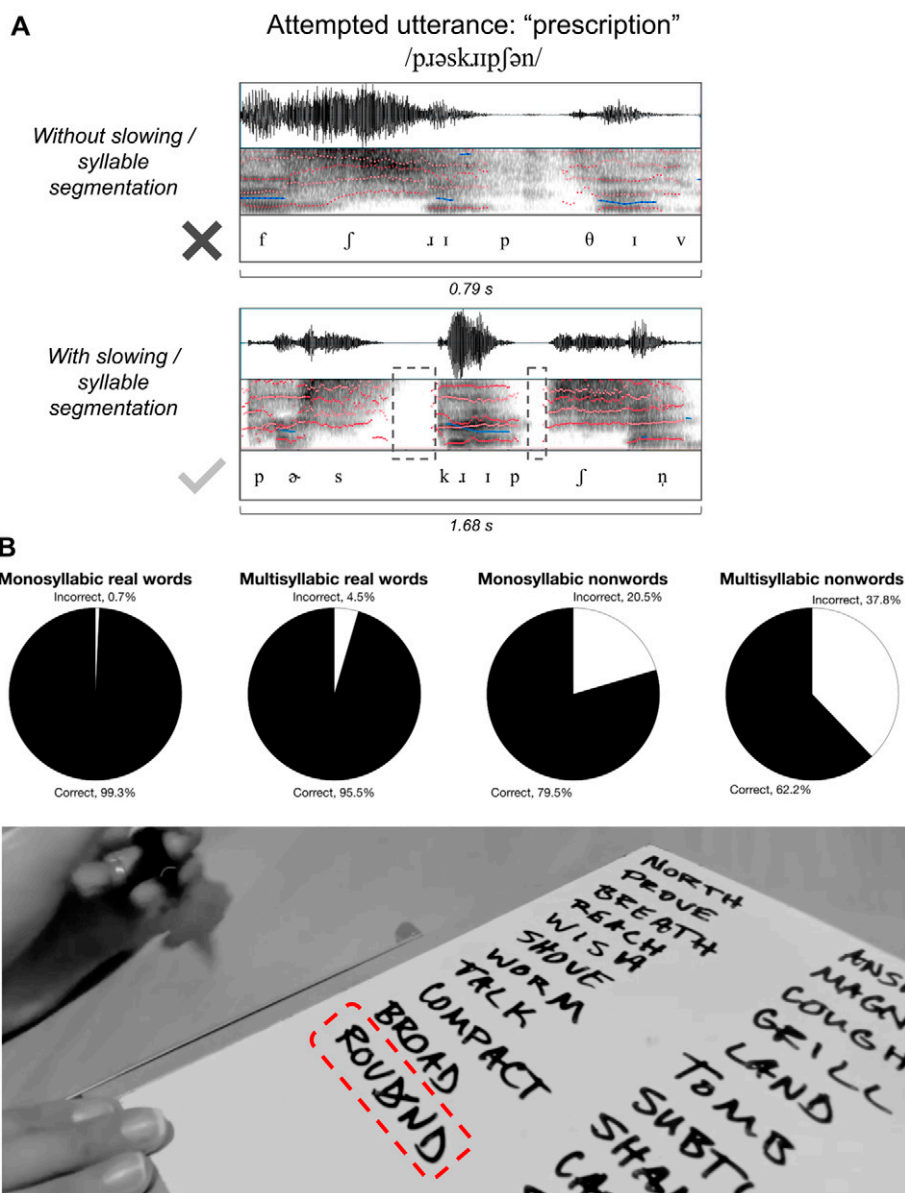


FIG. 4. Errors mediated by phonology and sequencing complexity in spontaneous speech and reading/spelling. **A:** Patient's attempt to say the word "prescription" (International Phonetic Alphabet transcription: /pɹɛskɹɪpʃən/) in spontaneous speech (*upper*); highly distorted and with phonemic errors. Patient's attempt to say the word "prescription" using the effective self-monitoring strategy of slowed production (*lower*); note greater accuracy, longer duration, and increased syllable segregation (*dashed rectangles*). **B:** Patterns of correct/incorrect productions combined across reading and spelling tasks for (left to right) monosyllabic real words, multisyllabic real words, monosyllabic nonwords, and multisyllabic nonwords. Note that more errors were made on both nonwords and multisyllabic words, suggesting that both number of syllables and degree of unfamiliarity may increase load on the resected region. No significant difference in error patterns in reading versus spelling tasks was observed, and thus data are collapsed across these tasks. **C:** Still frame from an evaluation video showing a sample anticipatory spelling error in an attempt to spell the word "round," self-corrected (*dashed red rectangle*).

the context of sentences, was coded for (1) whether or not it was a nonword (labeled "nonword"), (2) whether it was monosyllabic or multisyllabic (labeled "multi"), and (3) whether the relevant task was spelling or reading (labeled "task"). A multinomial logistic regression

was then used to predict from these variables, plus the interaction term of word status with syllable number, whether each word was produced accurately. This analysis revealed that word status and syllable number were significant predictors of errors in production,

such that both nonwords status and multisyllabic stimuli increased the likelihood of making an error ($\beta_{\text{nonword}} = 3.59$, $p < 0.001$; $\beta_{\text{multi}} = 1.89$, $p = 0.03$). No interaction of word status and syllable number ($\beta_{\text{nonword} \times \text{multi}} = -1.06$, $p = 0.29$) or effect of task (i.e., difference in accuracy for spelling versus reading) was observed ($\beta_{\text{task}} = 0.21$, $p = 0.61$). See Fig. 4B for performance summary.

Summary of Results

To summarize, following resection of the mPrCG and surrounding regions impacting white matter tracts, the patient exhibited a pattern of deficits—moderate AOS and mild phonological alexia/agraphia—consistent with simultaneous damage to systems involved in motor-speech and phonological processing relevant for reading and writing. The pattern of deficits observed may be explained in 1 of 2 ways: first, as an injury to 2 distinct but neighboring systems, 1 in the mid-superior precentral gyrus supporting motor-speech function^{2,7–9} and 1 in the ventral precentral gyrus supporting phonological function^{14,15} (here referred to as the “adjacent deficits hypothesis”); or second, as an injury to a single system underlying the ability to take intended phonological sequences and convert them efficiently and fluently into ordered, abstract motor plans, regardless of the articulators required for motor execution, with its basis in the mPrCG (here referred to as the “motor-phonological sequencing hypothesis”).

Discussion

Observations

We report a case of resection in the left mPrCG that resulted in pure AOS concurrent with phonological alexia and agraphia in the absence of aphasia. Errors were more pronounced on nonwords than real words, as well as multisyllabic more than monosyllabic words, in both the spoken and written modality. These results support our view that this mPrCG region may independently play a key role in the preparation of complex motor-phonological sequences for execution, regardless of the output modality through which these sequences are executed (the motor-phonological sequencing hypothesis). These results add important new information and specificity to our understanding of the mPrCG region.

A recent case study⁹ described a case of severe AOS following resection of area 55b,²² a posterior middle frontal gyrus region that partially overlaps with the mPrCG. Although the 2 sets of findings are similar in principle, the AOS presentation was much more severe in the earlier case, and reading and spelling were not assessed in detail. However, many errors observed in the earlier case are consistent with an underlying phonological and/or sequencing deficit—for example, the presence of clear phonemic substitutions, the preserved ability to read irregular words such as “dough,” and increased difficulty on longer items (see text and supplementary materials in reference 9).

The extent to which AOS is a pure motor-planning disorder versus a linguistic disorder has long been a subject of debate.^{3,4,36–39} Similarly, prior work using functional magnetic resonance imaging and lesion-symptom mapping has debated the extent to which phonological processes are shared versus distinct across reading, writing, and speaking.^{12,36,40} Relatively little work has focused on the neural bases of spelling, particularly through a neurosurgical lens (but see reference 41 for an exception). While we do not claim that the mPrCG region is the sole seat of phonological processing, it does appear to play a crucial enough role that removing it impacts

the ability to convert from phonological information to properly sequenced motor plans across various modalities (i.e., speaking, reading, and writing) and in various directions (e.g., orthography → phonology → speech, as in reading aloud, and phonology → orthography → writing, as in spelling). Our diffusion tensor imaging findings, showing that the resection impacted white matter tracts densely connected to posterior temporal and parietal regions relevant for phonology,^{14,36} also suggest that these deficits may result from disconnection of a distributed phonological system.

While speech-arrest sites are commonly believed to be critical for language function, they have been observed bilaterally in areas where resections are tolerated well (e.g., the pars opercularis, precentral gyrus, and supplementary motor area^{42–44}). To maximize the extent of resection, and as discussed with the patient prior to surgery, the clinical team made the decision to slowly remove the speech-arrest area during continuous speech monitoring and to stop only when abnormal speech was encountered. This did not occur until the deep subcortical margin of the tumor was reached.

Due to the presence of a tumor in the resected region, it is possible that some reorganization of the language system may have taken place prior to surgery, limiting generalizability of our findings. However, the late age of symptom onset (36 years old) and the tumor’s rapid rate of growth (WHO grade IV) speak against the notion that this patient’s brain was atypically organized from birth; recent work has also demonstrated that reorganization of the language system appears to be relatively infrequent even within clinical populations.⁴⁵

Lessons

In conclusion, we report a unique case in which resection of the left mPrCG resulted in a deficit specific to phonological sequencing for production but not specific to output modality, manifesting as pure apraxia of speech with mild phonological alexia and agraphia. The observed effect of word length and presence of anticipatory errors in both oral speech and written spelling suggest that this region may perform sequencing of phonologically informed motor plans for production, independently of the articulators in question. This work provides a clearer understanding of complex, speech-relevant functions in what is often considered to be a purely motor region, the middle precentral gyrus.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Chang, Levy, Scott. Acquisition of data: Chang, Levy. Analysis and interpretation of data: Chang, Levy, Silva, Scott, Liu, Harper, Zhao, Hullett, Kurteff, Wilson. Drafting of the article: Chang, Levy, Silva. Critically revising the article: Chang, Levy, Silva, Liu, Harper, Zhao, Kurteff, Wilson, Leonard. Reviewed submitted version of the manuscript: Chang, Silva, Scott, Liu, Harper, Zhao, Hullett, Kurteff, Wilson, Leonard. Approved the final version of the manuscript on behalf of all authors:

Chang. Statistical analysis: Levy, Silva, Harper. Administrative/technical/material support: Silva. Study supervision: Chang.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Materials. <https://thejns.org/doi/suppl/10.3171/CASE22504>.

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