

## Intracranial multiple myeloma masquerading as subdural hematoma: illustrative cases

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**BACKGROUND** Intracranial involvement in multiple myeloma (MM) is a rare clinical presentation, often mimicking other conditions such as subdural hematoma (SDH) and resulting in poor prognosis.

**OBSERVATIONS** This case series highlights 2 older female patients, one with a prior diagnosis of MM, who developed subdural masses resembling SDH. Both cases were associated with significant cerebral edema and mass effect. Biopsies confirmed plasma cell neoplasms, and both patients underwent tailored treatment, including corticosteroids, radiation therapy, and systemic chemotherapy. The patients showed clinical and radiographic improvement posttreatment.

**LESSONS** These cases underscore the importance of maintaining a broad differential in patients with subdural collections, particularly if associated with significant vasogenic edema or in those with a history of MM. Nonoperative management is effective, despite mass effect.

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**KEYWORDS** multiple myeloma; central nervous system; plasmacytoma; subdural; radiation

Multiple myeloma (MM) is a hematological malignancy that primarily affects the bone and bone marrow, with extraosseous or extramedullary manifestations occurring in less than 5% of cases. These manifestations are typically associated with a more aggressive and undifferentiated form of the disease.<sup>1</sup> CNS involvement is particularly rare, reported in approximately 1% of MM patients, most often developing 6–18 months after the initial MM diagnosis with a median overall survival as low as 1.5 months.<sup>2</sup> CNS-MM may present as leptomeningeal myelomatosis, intraparenchymal masses, spinal lesions, and intracranial extra-axial dura-based masses, with subdural tumors being an exceptionally uncommon presentation.<sup>1,3–5</sup> We present 2 cases of older women, one with a history of MM, who both had biopsy-confirmed subdural plasmacytomas with significant mass effect and extensive cerebral edema. Despite the mass effect, both were effectively treated with nonsurgical management of radiation therapy, steroids, and systemic therapy. Finally, we provide a comprehensive review of the literature surrounding intracranial myeloma, focusing on the clinical presentation, treatment considerations, and associated outcomes.

### Illustrative Cases

#### Case 1

The first patient was a 79-year-old female with a history of asthma and right lung non–small cell adenocarcinoma for which she underwent a right middle lobectomy. A PET CT 2 years later revealed several areas of fluorodeoxyglucose (FDG)–avid osseous lesions. Biopsy of the right iliac wing lesion was consistent with kappa light chain–restricted plasma cell myeloma. Her initial myeloma treatment regimen consisted of lenalidomide 25 mg daily and dexamethasone 40 mg weekly. Over the next year, the dexamethasone was titrated down to 8 mg weekly. Afterward, she was switched to bortezomib and dexamethasone, but after failing 4 treatment cycles, she was switched to daratumumab/pomalidomide/dexamethasone. The dexamethasone was ultimately discontinued, and 6 months later she was switched to monthly daratumumab maintenance with a 3-week course of pomalidomide.

Eight months later, she presented with gait instability, frequent falls, and dizziness. Except for diminished hearing bilaterally, her neurological examination was normal. A noncontrast CT of the head (CTH)

**ABBREVIATIONS** ADC = apparent diffusion coefficient; CTH = CT of the head; DWI = diffusion-weighted imaging; FDG = fluorodeoxyglucose; IMRT = intensity-modulated radiation therapy; MLS = midline shift; MM = multiple myeloma; SDH = subdural hematoma; T1W = T1-weighted; WBRT = whole-brain radiation therapy.

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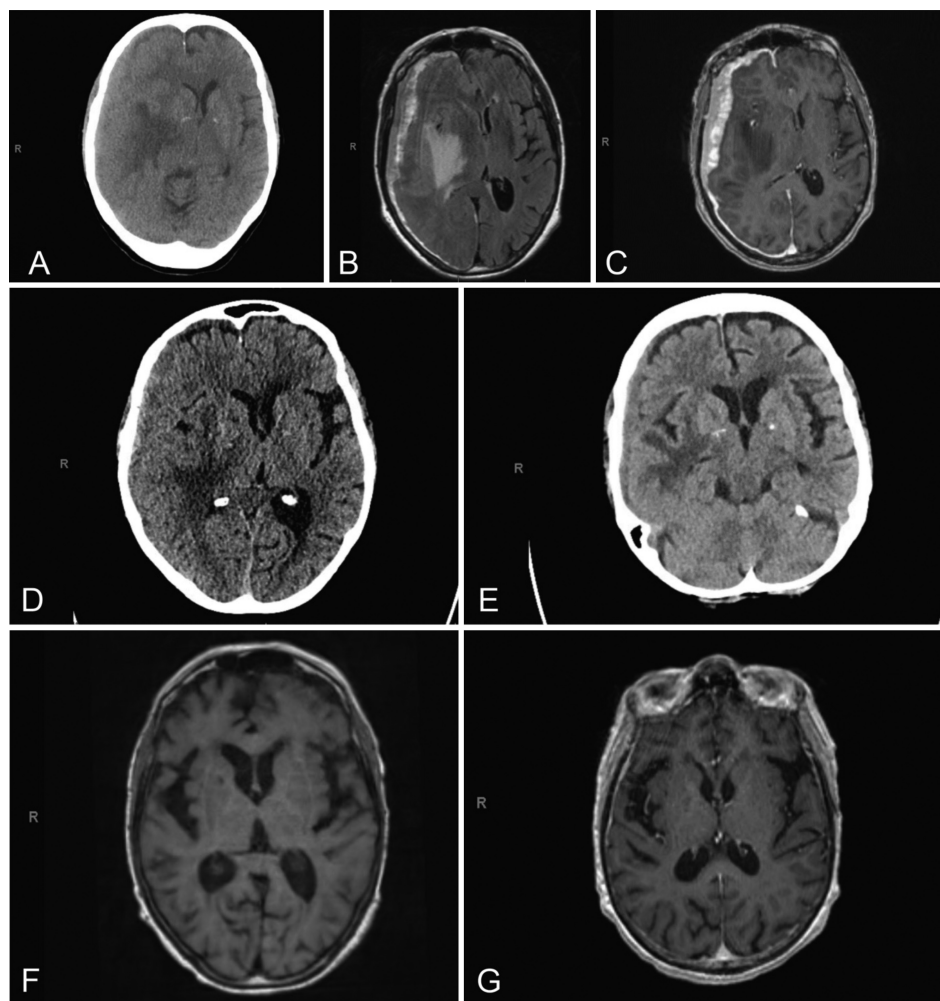
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revealed a 1.2-cm hyperdense right frontal temporal subdural collection with associated vasogenic edema and significant mass effect including 1.4 cm of midline shift (MLS) with trapping of the temporal horn and uncal herniation (Fig. 1). On her MRI, diffusion-weighted imaging (DWI) showed scattered areas of restricted diffusion within the lesion that lacked an apparent diffusion coefficient (ADC) correlate. Additionally, mild signal dropout on the susceptibility-weighted imaging sequence was observed, suggestive of hemorrhage. Biopsy of the dura-based mass was consistent with an IgG kappa-restricted plasma cell neoplasm (Fig. 2). The patient was started on dexamethasone as well as levetiracetam for seizure prophylaxis. Bone marrow biopsy was nondiagnostic for disease progression. Flow cytometry was unremarkable, and cytogenetics with chromosome analysis was normal. She was simulated for radiation therapy, but 1 day after starting whole-brain radiation therapy (WBRT), the patient became

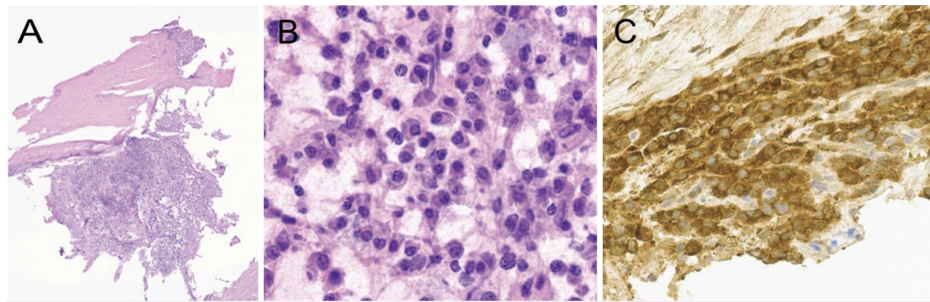
increasingly confused and stopped following commands. A repeat CTH showed marked progression of cerebral edema in the right hemisphere. WBRT was paused, and she received hyperosmolar therapy with good effect.

After resuming WBRT, she became encephalopathic and CTH showed increased left lateral ventricular dilation. She was found to be hyponatremic, was treated with normal saline and 3% hypertonic saline boluses, and tolerated the rest of her WBRT treatment thereafter. In total, she received 20 Gy in 10 fractions of WBRT (Fig. 1D) plus a boost to the macroscopic disease as 10 Gy in 5 fractions of intensity-modulated radiation therapy (IMRT) with good effect on serial head CT imaging (Fig. 1E). She was discharged to rehabilitation after a 37-day length of stay with a slow dexamethasone taper.

While at rehabilitation, she developed acute left hemiparesis, and CTH showed improvement of the right subdural mass but worsening



**FIG. 1.** Radiographic findings obtained in patient 1. **A:** Initial CT scan of the head without contrast, demonstrating a 1.2-cm hyperdense right frontal temporal subdural collection with associated vasogenic edema and significant mass effect, including 1.4 cm of MLS with ventricular trapping and uncal herniation. **B and C:** Follow-up FLAIR (B) and T1-weighted (T1W) (C) images with contrast, revealing that the subdural lesion is an enhancing mass and there is no parenchymal invasion. Also shown is resolution of the subdural lesion with nonoperative management. **D:** CT scan of the head without contrast after completion of WBRT. **E:** CT scan of the head without contrast after completion of WBRT + IMRT boost to the right convexity. **F:** T1W MR image without contrast 157 days after radiation therapy. **G:** T1W MR image with contrast 157 days after radiation therapy.

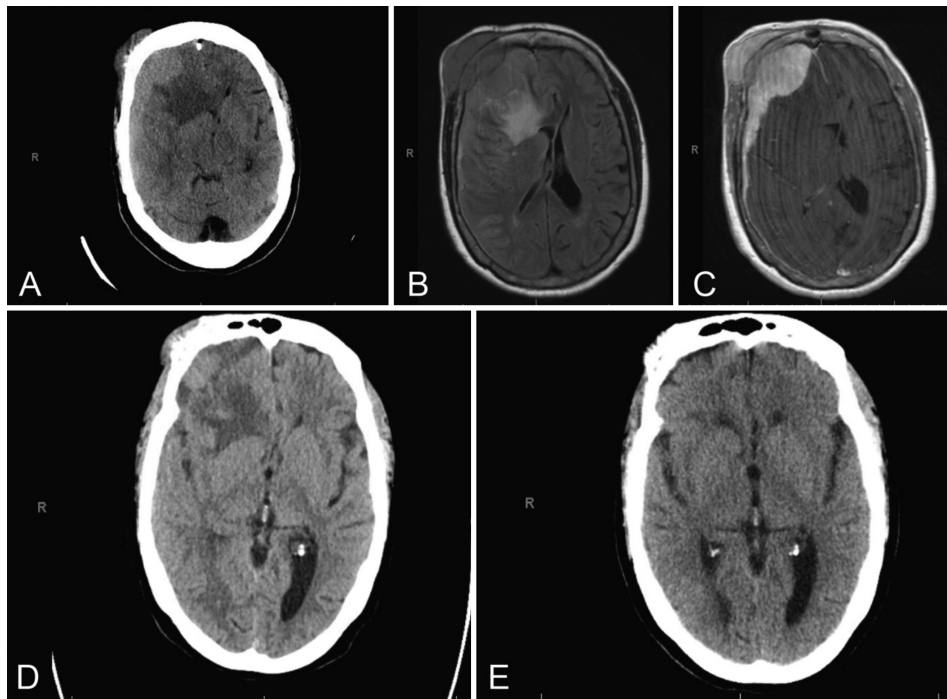


**FIG. 2.** Subdural biopsy results obtained in patient 1. **A:** Low-magnification micrograph of a hematoxylin and eosin-stained frozen section. The neoplasm is attached to dense fibrous tissue that is consistent with dura. **B:** High-magnification micrograph of a hematoxylin and eosin-stained frozen section, showing a dense plasma cell infiltrate. The majority of the plasma cells do not show atypical features; however, occasional forms display larger nuclear size, and binucleated cells are identified (not shown). **C:** An IgG kappa immunostain is positive for tumor cells. Original magnification  $\times 10$  (A),  $\times 40$  (B and C).

of right frontal edema. She was started on dexamethasone, and on completing the taper a few weeks later, she was started on venetoclax monotherapy. Overall, the patient made improvements in her strength and cognition and had complete resolution of the extra-axial convexity mass and associated mass effect (Fig. 1F and G). She had progression-free survival of her CNS-MM for 1 year but subsequently developed recurrence and died 3 months after that—1 year and 3 months after completing her radiation therapy.

### Case 2

The second patient was a 75-year-old female who presented with right facial weakness, dysphagia, and dysarthria. Noncontrast CTH revealed an enlarging right frontal bone mass with an intracranial extra-axial component and  $> 1$  cm of MLS, edema, and uncal herniation (Fig. 3A–C). DWI showed two small areas of diffusion restriction in the right insular cortex and right corona radiata with associated hypointensity on ADC consistent with infarct. Her PET scan showed

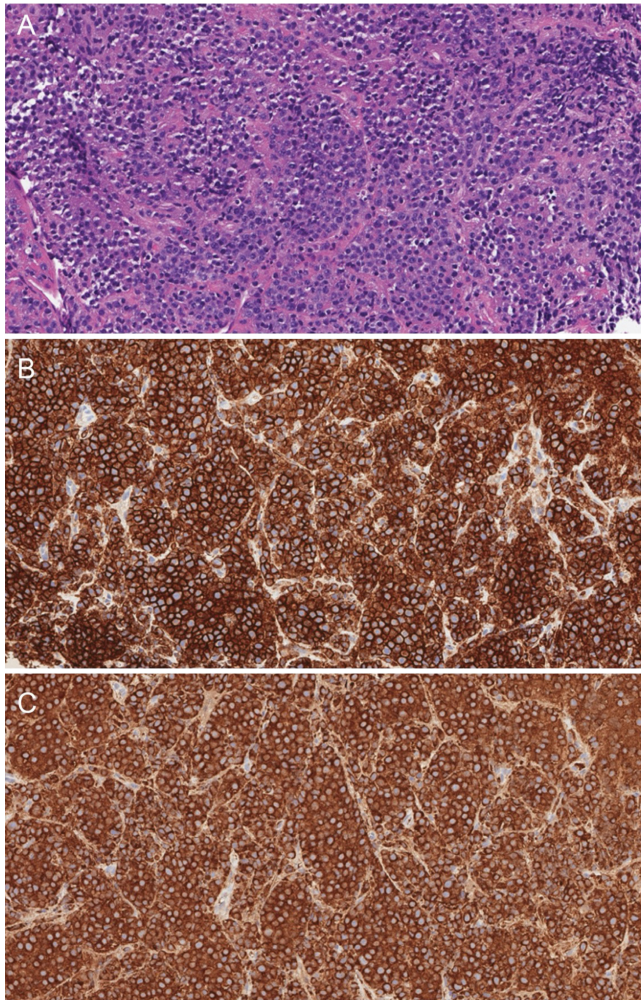


**FIG. 3.** Radiographic findings obtained in patient 2. **A:** CT scan of the head without contrast, showing a right frontal bone mass with both extra-cranial and intracranial extra-axial components, the latter of which are associated with  $> 1$  cm of MLS, edema, and uncal herniation. **B and C:** Follow-up FLAIR (B) and T1W (C) MR images with contrast, revealing that the lesion is enhancing and there is no parenchymal invasion. Also shown are the postradiation images. **D:** CT scan of the head without contrast 2 days after completing radiation therapy. **E:** CT scan of the head without contrast 31 days after completing radiation therapy.

many FDG-avid calvarial lesions and multiple osteolytic lesions throughout the axial and appendicular skeleton.

She was started on dexamethasone and mannitol for cerebral edema. Biopsy of the right forehead mass was consistent with lambda-restricted plasma cell neoplasm with plasmablastic features (Fig. 4). There was no evidence of lymphoproliferative or plasma cell neoplasm in blood or bone marrow, and flow cytometry and cytogenetic analysis were noncontributory due to a paucity of cells available for analysis. She received 8 Gy in 1 fraction to the right frontal skull mass and adjacent intracranial mass as well as external beam radiation therapy to skeletal lesions. She also completed a cycle of bortezomib and dexamethasone while admitted, followed by a planned 21-day cycle of a chemotherapy infusion of lenalidomide and bortezomib along with dexamethasone as an outpatient.

After her first discharge, follow-up serial scans showed improvement in both size and mass effect of the lesion (Fig. 3D and E). On day 10 of her chemotherapy infusion of lenalidomide, bortezomib,



**FIG. 4.** Subdural biopsy results obtained in patient 2. **A:** Hematoxylin and eosin–stained section showing a diffuse infiltrate of plasma cells in a background of loose sclerosis. Many of the cells show immature, plasmablastic features. **B:** A CD138 immunostain is diffusely and strongly positive for tumor cells. **C:** The plasma cells express lambda immunoglobulin light chain. Original magnification  $\times 20$  (A–C).

and dexamethasone, she developed constitutional symptoms and was admitted for septic shock with *Escherichia coli* bacteremia from a urinary source. Additionally, a workup of altered mental status with head CT demonstrated resolution of her subdural plasmacytoma, but revealed an incidental trace parafalcine subdural hematoma (SDH), likely secondary to chemotherapy-induced thrombocytopenia, which was managed conservatively. After her second discharge, the patient moved out of state to be closer to family and was lost to follow-up. Prior to her move, she had at least 1 month of documented progression-free survival of her CNS-MM.

## Informed Consent

The necessary informed consent was obtained in this study.

## Discussion

### Observations

We present 2 cases of CNS-MM initially diagnosed as SDH. While the first patient had a history of MM, the second patient had primary CNS-MM, a presentation seen in only 22% of CNS-MM patients according to one study, highlighting the variability of this condition.<sup>6</sup> In both cases, these older women exhibited hyperdense subdural masses with significant vasogenic edema and MLS on initial CT imaging, prompting neurosurgical consultation for SDH. Subsequent contrast-enhanced MRI and biopsy revealed CNS-MM, with plasma cell neoplasms confirmed in both cases. Both cases responded completely to nonoperative management with concurrent radiation therapy, hyperosmolar therapy, and chemotherapy. Notably, the first patient represents the first documented case of CNS-MM treated with venetoclax, with clinical and radiographic improvement suggesting CNS penetration of the drug.<sup>7,8</sup> Although previous reports have described CNS involvement in MM, subdural plasmacytomas remain exceedingly rare and diagnostically challenging. To identify relevant cases, we performed a search of the PubMed database using the terms “multiple myeloma” AND “subdural,” which returned 19 results from 1967 to 2025. Filtering for studies involving human subjects yielded 14 articles, among which only 5 reported presentations of MM with subdural involvement confirmed as plasmacytoma (Table 1).<sup>1,3–5,10</sup>

### Diagnosis of CNS-MM

Subdural presentations of MM and other hematological malignancies can masquerade as SDHs on noncontrast CT imaging and share overlapping epidemiology of older patients.<sup>11</sup> In patients who are suspected to have CNS-MM due to prior history or because of unusual cerebral edema, MRI of the brain with and without contrast can provide clarifying information, including enhancement of the extra-axial mass (Figs. 1B, 1C, 3B, and 3C). PET imaging may also be helpful, as it can identify extracranial sites of active disease. Biopsy remains the gold standard for definitive diagnosis.<sup>6,12–14</sup>

### Treatment Considerations

There are currently no established treatment guidelines for CNS-MM. However, systemic therapy, intrathecal therapy, cranial or cranial-spinal irradiation, and stem cell transplant have shown success.<sup>6,12</sup> Both patients in this report responded well to radiation therapy, demonstrating that surgery for mass resection may be avoided entirely if CNS-MM is not mistaken for SDH. Previous reports have described cases in which surgery was pursued, yet nonsurgical approaches can achieve comparable outcomes while minimizing surgical risks.<sup>14–16</sup> Our findings suggest that biopsy followed by targeted

**TABLE 1. Summary of published cases of subdural plasmacytoma associated with MM**

Authors & Year	Age (yrs)/ Sex	Radiographic Appearance	Treatment	Immunophenotype/Lab Results	Survival
Tabuchi et al., 1993 <sup>10</sup>	53/M	Plain skull radiograph showed lt frontal destruction; CT showed compressive mass extending from subcutaneous to subdural space; MRI was isointense on T1, homogeneously enhanced w/ gadolinium	Surgery followed by unspecified combined therapy	IgA lambda paraproteinemia; hypergammaglobulinemia	Died of interstitial pneumonia ~10 mos after symptom onset
De Blay et al., 2000 <sup>1</sup>	79/F	Mixed-density lt convexity subdural mass w/ mass effect, MLS, & transtentorial herniation on CT	Emergency lt frontal craniotomy; RT postop	IgA lambda paraproteinemia; hypergammaglobulinemia	Died of pneumonia 1 mo postop
Tsang et al., 2006 <sup>3</sup>	61/M	Lt subdural collection w/ significant mass effect; CT initially misread as chronic SDH	Emergency burr holes	Lambda light chain–restricted plasmacytoma	Died 1 wk postop
Prajsnar-Borak et al., 2017 <sup>4</sup>	62/F	Rt frontoparietal extra-axial hyperdense mass on CT w/ MLS; initially diagnosed as acute SDH	Emergency craniotomy w/ near-total resection; chemo & RT started postop	CD138+, CD20–, lambda-restricted, Ki-67 proliferation index 80%–90%	Died 2 mos postop due to CMV pneumonia
Tanaka et al., 2020 <sup>5</sup>	64/M	Rt frontal convexity subdural extramedullary mass, hyperdense on CT, low T1/T2/DWI/FLAIR on MRI w/ perifocal edema	Rt frontal craniotomy to remove tumor	IgG4+/IgG ratio ~50%, polyclonal plasma cells, no light chain restriction ( $\kappa/\lambda = 1.5$ ), elevated serum IgG4	Survived w/ no recurrence 7 yrs postop, including 4 yrs off steroids

CMV = cytomegalovirus; RT = radiation therapy;  $\kappa/\lambda$  = kappa/lambda light chain ratio.

nonsurgical interventions may be a preferable strategy in appropriately selected patients.

Our cases also underscore the importance of vigilant monitoring during treatment. Cerebral edema associated with CNS-MM may worsen with WBRT, requiring a hiatus from treatment and treatment with corticosteroids and hyperosmolar therapy. Monitoring and expedited workup for opportunistic infections in this immunocompromised patient is critical, especially when they are also placed on steroids. For example, the second patient developed *E. coli* urosepsis, and there are other reports describing fatal opportunistic infections, such as cytomegalovirus pneumonia.<sup>1</sup> These findings highlight the need for a multidisciplinary approach to manage complications and optimize outcomes for this rare clinical entity.

### Risk Factors and Prognostic Markers

Although the mechanisms underlying the development of CNS-MM are not well understood, deletion of chromosome 17p13.1 has been more frequently observed in CNS-MM patients than in MM patients without CNS involvement.<sup>17</sup> Also, the downregulation of CD56 may play a role in CNS-MM pathogenesis.<sup>12,18,19</sup> In this case series, the first patient had normal flow cytometry and cytogenetics, which may reflect a less aggressive disease phenotype. Furthermore, novel MM therapies such as thalidomide, lenalidomide, and bortezomib that do not cross the blood-brain barrier prolong the time to CNS involvement but do not improve the prognosis of CNS-MM.<sup>19–21</sup>

### Lessons

The 2 cases presented here underscore the diagnostic and therapeutic challenges of managing intracranial MM, particularly when it mimics SDH on initial CTH. While CNS-MM is often associated with poor prognosis, these cases demonstrate that nonsurgical management with radiation therapy, hyperosmolar therapy, and chemotherapy

can achieve excellent outcomes. CNS-MM is rare, and additional study is essential to improve patient outcomes. Comprehensive yet expedient workup, including advanced imaging and biopsy, is critical for guiding appropriate radiotherapy and systemic therapy to achieve local tumor control and extend survival. Finally, prior systemic therapy that lacks CNS penetration may lead to relapses in the CNS as a sanctuary site.

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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: Hong. Acquisition of data: Hong, Ihezic, Zanzazi. Analysis and interpretation of data: Hong, Ihezic, Zanzazi, PonnammReddy, Lansigan. Drafting the article: Hong, Ihezic, Natarajan. Critically revising the article: all authors. Reviewed submitted version of manuscript: Hong, Ihezic, Natarajan, PonnammReddy, Lansigan, Evans. Approved the final version of the manuscript on behalf of all authors: Hong. Administrative/technical/material support: Hong. Study supervision: Hong.

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