Primary BAP1-absent atypical meningioma arising from median nerve within infraclavicular brachial plexus: illustrative case

Adela Wu, MD,1,2 Adam C. Ring, MD,3 Jennifer Ziskin, MD, PhD,4 Tina Nguyen, MD,2 and Patrick Pezeshkian, MD1,2

1Department of Neurosurgery, Stanford University Medical Center, Stanford, California; Departments of 2Neurosurgery and 3Pathology, Kaiser Permanente Redwood City Medical Center, Redwood City, California; and 4Department of Vascular Surgery, Kaiser Permanente San Leandro Medical Center, San Leandro, California

BACKGROUND The authors present the only known case of a World Health Organization grade II ectopic meningioma occurring in the infraclavicular brachial plexus, causing pain within the axilla not associated with a primary malignant meningioma of the central nervous system. Peripheral nerve sheath tumors are rare entities, the majority of which are schwannomas or neurofibromas. Ectopic meningiomas only represent 1%–2% of all meningiomas. To date, there is one other published case specifically of a primary ectopic meningioma located in the brachial plexus.

OBSERVATIONS Following the dissection of the left axilla, a dominant rubbery tumor involving the median nerve was encountered. The tumor capsule contained areas of hemorrhage and a soft core with nerve fascicles coursing through, which were not compromised during internal tumor debulking. The tumor lacked a clear pseudocapsule that is characteristically seen in schwannomas. Histopathological studies confirmed an atypical epithelioid neoplasm with elevated numbers of mitotic figures and BAP1 gene deletion.

LESSONS Primary meningiomas arising outside the central nervous system are exceedingly rare. For this unusual higher-grade primary ectopic meningioma located in the distal brachial plexus, surgery with the goal of gross-total resection, adjuvant radiation, additional imaging, and genetics screening were recommended. Close follow-up is warranted.

Keywords: peripheral nerve sheath tumor; brachial plexus; meningioma; case report

Primary peripheral nerve sheath tumors (PNSTs) are rare entities, comprising about 5% of all soft tissue tumors.1 The majority are nerve sheath tumors, namely neurofibromas arising from nerve sheath connective tissue and schwannomas deriving from Schwann cells scattered in irregular connective tissue.2,3 Additional lesions, such as lipomas and desmoid tumors, have also been reported.3,4

Meningiomas that arise outside the central nervous system (CNS), termed “extracranial-extraspinal” or “ectopic,” are also unusual and comprise less than 1% of all tumors characterized as meningiomas.5,6 Many ectopic meningiomas are metastases to regions such as the mediastinum or liver from World Health Organization (WHO) grade III meningiomas based in the CNS.7 Only one prior account of a primary ectopic meningioma located in the brachial plexus has been published in detail.8 The patient was a 51-year-old female who had originally noted a rigid, fixed mass in the right supraclavicular area, which was diagnosed as a primary ectopic meningioma that has since recurred and required multiple resections. One comprehensive case series of 146 non–neural sheath tumors also included 2 benign meningiomas of the brachial plexus.9 In this context, we present our experience with a primary ectopic WHO grade II meningioma involving the median nerve within the infracavicular brachial plexus at the level of the axilla and not associated with a primary high-grade meningioma from the CNS.

Illustrative Case

History and Physical Examination

A 47-year-old male with a past medical history of diabetes and obesity presented with left arm pain for over a year. The patient described the pain as sharp and achy in quality, radiating from the left axilla toward the left biceps, and especially aggravated by any left arm movement, particularly arm adduction and extension. The patient had no other neurological deficits, including weakness, numbness, or paresthesia.
The patient was neurologically intact on physical examination other than experiencing severe pain. A firm mass could be palpated deep within the left axilla.

An electromyography (EMG) and nerve conduction study obtained in January 2023 showed electrodiagnostic evidence of left median neuropathy at the wrist without signs of ulnar neuropathy. Evidence of cervical radiculopathy was not specified in the report. Contrast-enhanced magnetic resonance imaging (MRI) of the left shoulder indicated a 4 × 3.1 × 4.9-cm homogeneously enhancing, well-circumscribed lesion with surrounding soft tissue invasion or edema (Fig. 1). Radiographically, the mass appeared consistent with a benign PNST within the left axilla.

**Operation and Observations**

The patient underwent surgical exploration of the left axilla and infraclavicular brachial plexus for tumor resection. The patient was positioned supine on the operating table with the left arm abducted by about 90° and positioned on an armrest. A gel roll was placed under the left shoulder to elevate the left axilla for better exposure. Ultrasound was used to confirm that the palpable mass was the tumor prior to planning a curvilinear incision along the anterior axillary line. Neuromonitoring of somatosensory evoked potentials (SEPs) of the bilateral median, left radial, and left ulnar nerves, as well as motor evoked potentials (MEPs) and spontaneous and triggered EMG of the left deltoid, biceps, triceps, brachioradialis, pronator teres, abductor pollicis brevis, first dorsal interosseous, and abductor digit minimi muscles and the right abductor pollicis brevis muscle was used (right median SEP and right abductor pollicis brevis MEPS served as controls). Of note, just prior to the incision, the left biceps MEPs decreased by more than 50%. However, the signals were maintained throughout the surgery and mildly augmented with higher blood pressure parameters. The change was ultimately attributed to positioning.

A vascular surgeon assisted in gaining access and was available on standby, as preparative imaging indicated the axillary artery coursing beneath the tumor in close proximity (Fig. 1A). The axillary artery was not seen during the dissection, but the pulse could be palpated in the soft tissue just deep to the mass. Following fat and fascia dissection, a firm and well-circumscribed tumor was visualized. Grossly, the tumor was yellow-tan in color and contained areas of mottled hemorrhage and a soft core. We dissected through the tumor capsule in a focal region visually devoid of nerve components. Of note, the characteristic pseudocapsule layers often seen in schwannomas were not clearly present in this case. What then appeared to be median nerve fascicles (proven by direct stimulation of the fascicles causing median nerve–innervated EMG responses in the left pronator teres and abductor pollicis brevis) traversed the tumor, which was incised and internally debulked without cutting any nerve fibers. A second, smaller contiguous tumor nodule was also identified deep and medial to the original lesion. We used high-magnification surgical loupes and did not utilize the microscope for resection; multiple samples were sent for permanent pathological specimens.

Histopathology findings were notable for evidence of an epithelioid neoplasm with eosinophilic cytoplasm, vague whorls, and elevated numbers of mitotic figures up to 12 mitoses in 10 high-power fields (Fig. 2A). Additional studies demonstrated that the tumor stained positive for multiple markers, including epithelial membrane antigen (Fig. 2B), e-cadherin, D2-40, pancytokeratin (partial), CK7 (subset), Moc-31 (focal), Cam 5.2 (variable), SMA (partial), and SSTR2 (Fig. 2C). Based on the combined morphology and immunohistochemical features, this axillary distal brachial plexus mass was believed to be best classified as a WHO grade II atypical meningioma. Material was sent to Caris Life Sciences for whole-exome sequencing, whole-transcriptome sequencing, and protein evaluation. The whole-exome sequencing identified the presence of BAP1 deletion, which is common in various high-grade tumors including high-grade meningiomas. Immunohistochemical staining for BAP1 confirmed complete loss of staining in the tumor cells (Fig. 2D). Additionally, Caris Life Sciences calculated a genomic probability score based on the combined molecular testing, to predict

![Image](https://example.com/image1.png)

**FIG. 1.** A: MRI of the left axilla, T2 sequence, coronal view. The asterisk denotes the axillary artery deep to the tumor capsule. B: MRI of the left axilla, T2 sequence, coronal view. The arrow denotes the median nerve involved by the tumor. C: MRI of the left axilla, T1 postcontrast sequence, axial view. The asterisk denotes the axillary artery. D: Schematic of tumor nodule within the infraclavicular brachial plexus.

![Image](https://example.com/image2.png)

a most likely tissue of origin, and reported that the comparison to their
database showed a 92% match to meningioma and no match (0%) to
other tumor types in the database including mesothelioma. The com-
bined molecular results supported the classification of the tumor as a
meningioma.

Postoperative Course
The patient experienced moderate weakness (3/5 motor strength)
of the intrinsic hand muscles innervated by the left median nerve
and hand numbness in the distribution of the left median nerve. Postoperative MRI of the left axilla performed on the first postopera-
tive day showed gross-total resection (GTR) of the mass and expected
postsurgical changes. MRI of the brain and cervical, thoracic, and lumb-
bar spine without and with contrast did not show any other masses
or neoplastic abnormalities. Based on our regional tumor board rec-
ommendation, the patient was referred to neuro-oncology, radiation
oncology, and genetics consultation for adjuvant radiotherapy and
further treatment planning.

Patient Informed Consent
The necessary patient informed consent was obtained in this study.

Discussion
Observations
Consideration of both common and unusual etiologies is important
when assessing PNSTs. While the majority are schwannomas or neu-
rofibromas, occasionally other lesions are diagnosed with gross pathol-
ogy following resection. We present our experience with a peripheral
erve lesion, radiologically considered to be a benign-appearing
schwannoma, that was ultimately diagnosed as an atypical primary
ectopic meningioma of the distal brachial plexus within the axilla.

Extracranial-extraspinal meningiomas are typically metastases or
secondary extensions from other sites, such as extramedullary
meningiomas of the spine growing into the thoracic cavity and brachial
plexus. 10 Primary meningiomas in ectopic sites are highly unusual,
and there exist few published accounts of such lesions, including our
illustrative case, comprising 1%–2% of all meningiomas. 10-12 They are
thought to originate from an embryogenic anomaly trapping arachnoid
cells extradurally, metaplasia of mature nerve sheath cells, or ectopic
migration of arachnoid cells during peripheral nerve development. 8
These lesions can be found throughout the head and neck, peripheral
nerves, retroperitoneum, and lungs. 8,13,14

Based on imaging evidence alone, primary ectopic meningiomas
may be misdiagnosed as other entities, such as metastases or ham-
artomas. 13,15 Regarding a primary ectopic meningioma of the supra-
clavicular brachial plexus reported by Coons and Johnson, 9 the lesion
was initially deemed a schwannoma based on biopsy as well. Due to
involvement of brachial plexus components, that patient underwent a
subtotal resection. Then, due to rapid recurrence and tumor growth,
she required 3 additional tumor debulking procedures. In contrast to
our case, the meningioma presented by Coons and Johnson infiltrated
skelatal muscle and the connective tissue between epineurium, ren-
dering GTR challenging. 8

The management of primary ectopic meningiomas involves surgery
with the aim of GTR and adjuvant therapy, depending on the histo-
logical grade. Our patient’s tumor returned as WHO grade II or atypi-
cal meningioma due to an elevated number of mitotic figures. Atypical
meningiomas comprise 15%–20% of meningiomas and are more
likely to recur. Treatment for higher-grade meningiomas is currently
not standardized, as there is debate about the utility of adjuvant radia-
tion following GTR, while radiation is recommended following incom-
plete tumor resection. 10 One series investigated outcomes after GTR
and adjuvant radiation for atypical meningiomas. Receipt of radiation
therapy was associated with decreased local disease recurrence com-
pared to those without adjuvant therapy (hazard ratio 0.25, 95% confi-
dence interval: 0.07–0.96, p = 0.04). 10 The ability of adjuvant radiation
therapy to provide local disease control even after GTR, in addition to
improvements in restricted mean progression-free survival and overall
survival, has been shown in other studies. 10,13 Our patient has been
referred to radiation oncology and neuro-oncology specialists for addi-
tional treatment planning.

Individuals with certain genetic conditions, such as neurofibromato-
sis (NF) type 2, are at higher risk of developing multiple meningiomas,
in addition to other tumors, as about half of all patients with NF2 present
with meningioma. Our patient did not have a family history of NF2, nor
did he have any neurocutaneous stigmata. Albeit, he has not yet been
formally tested for NF1 or NF2. However, our patient’s tumor carried the
BAP1 deletion, a genetic alteration typically found in aggressive
cancers, such as mesothelioma, melanoma, and high-grade menin-
giomas. BAP1 is a tumor suppressor gene with a role in DNA repair
and cellular growth. BAP1-altered meningiomas tend to display more
aggressive behavior, can variably show rhabdoid features, and are
frequently graded as at least WHO grade II meningiomas. 21 BAP1-
absent meningiomas tend to have multiple recurrences and worse
survival outcomes. 21 Patients may require a genetics consultation to
evaluate for BAP1 cancer predisposition syndrome, as they may be
more susceptible to various familial cancers, such as cutaneous and
uveal melanoma and renal cell carcinoma. 23 Our patient underwent
comprehensive MRI screening for other lesions throughout his brain
and spine, which did not reveal other meningiomas or masses. He has
not yet presented for further genetics assessments.

Lessons
During dissection, care was taken to identify and preserve nerve
cascade integrity traversing through and around the tumor. While our
patient’s lesion did not have obvious pseudocapsule layers character-
istically seen in typical schwannomas, the tumor capsule was entered
at a site that was devoid of any obvious nerve fascicles, and the soft
core of the tumor was debulked to facilitate removal. During internal
tumor debulking, we did not transect any nerve fascicles, although it
is possible that small nerve fibers were stretched during the course,
resulting in our patient’s postoperative neurological deficits in a periph-
eral median nerve distribution. The tumor nodules did not appear to
infiltrate surrounding tissue, so we achieved GTR.

This case highlights lessons in the diagnosis and management of
PNSTs. These tumors present in diverse manners, depending on their
location, ranging from local swelling to pain and pronounced neurolog-
ic deficits. Numbness and weakness are unusual for benign PNSTs,
however, pain present at rest is common for malignant PNST, whereas
pain present at rest is common for malignant PNST, whereas
malignant PNSTs more frequently exhibit pain elicited with pressure. 24

The preoperative differential diagnosis included benign schwann-
oma based on tumor appearance on MRI and physical examination.
However, final pathology returned as primary ectopic atypical menin-
gioma, emphasizing the importance of histopathological confirmation.
In addition, comprehensive pathology testing revealed the presence
of BAP1 deletion, which prompts genetic testing for possible germ-
line deletion that can be associated with other rare and aggressive
cancers. Thus, our patient’s case was further discussed at the tumor board conference with recommendations for specialist referrals and adjuvant therapy.

References


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: Wu. Acquisition of data: all authors. Analysis and interpretation of data: Wu, Nguyen, Pezeshkian. Drafting the article: Wu, Nguyen, Pezeshkian. Critically revising the article: Ziskin, Pezeshkian. Reviewed submitted version of manuscript: Wu, Ring, Nguyen, Pezeshkian. Approved the final version of the manuscript on behalf of all authors: Wu. Administrative/technical/material support: Pezeshkian.

Correspondence

Adela Wu: Stanford Health Care, Stanford, CA. adelawu@stanford.edu.