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

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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.

https://thejns.org/doi/abs/10.3171/CASE24226

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 infraclavicular 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 aching 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. Neuroradiographic evaluation demonstrated the tumor capsule clearly was separated from the axillary artery. The axillary artery was not seen during the dissection, but the pulse could be palpated in the popliteal fossa 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. Neuroradiographic evaluation demonstrated the tumor capsule clearly was separated from the axillary artery. The axillary artery was not seen during the dissection, but the pulse could be palpated in the popliteal fossa 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. Neuroradiographic evaluation demonstrated the tumor capsule clearly was separated from the axillary artery.

A vascular surgeon assisted in gaining access and was available on standby, as preoperative imaging indicated the axillary artery coursing along the anterior axillary line. 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...
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 combined 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 postoperative day showed gross-total resection (GTR) of the mass and expected postsurgical changes. MRI of the brain and cervical, thoracic, and lumbar spine without and with contrast did not show any other masses or neoplastic abnormalities. Based on our regional tumor board recommendation, 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 neurofibromas, occasionally other lesions are diagnosed with gross pathology following resection. We present our experience with a peripheral nerve 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 extradural meningiomas of the spine growing into the thoracic cavity and brachial plexus. 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. 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. These lesions can be found throughout the head and neck, peripheral nerves, retroperitoneum, and lungs. Based on imaging evidence alone, primary ectopic meningiomas may be misdiagnosed as other entities, such as metastases or hamartomas. Regarding a primary ectopic meningioma of the supravclavicular brachial plexus reported by Coons and Johnson, 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 skeletal muscle and the connective tissue between epineurium, rendering GTR challenging.

The management of primary ectopic meningiomas involves surgery with the aim of GTR and adjuvant therapy, depending on the histological grade. Our patient’s tumor returned as WHO grade II or atypical 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 radiation following GTR, while radiation is recommended following incomplete tumor resection. One series investigated outcomes after GTR and adjuvant radiation for atypical meningiomas. Receipt of radiation therapy was associated with decreased local disease recurrence compared to those without adjuvant therapy (hazard ratio 0.25, 95% confidence interval: 0.07–0.96, p = 0.04). 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. Our patient has been referred to radiation oncology and neuro-oncology specialists for additional treatment planning.

Individuals with certain genetic conditions, such as neurofibromatosis 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 meningiomas. 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. BAP1-absent meningiomas tend to have multiple recurrences and worse survival outcomes. 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. 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 fascicle integrity traversing through and around the tumor. While our patient’s lesion did not have obvious pseudocapsule layers characteristically 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 peripheral 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 neurological deficits. Numbsness and weakness are unusual for benign PNSTs, while any degree of neurological deficit predicts malignancy. Symptoms of pain are associated with approximately 75% of PNSTs. However, pain present at rest is common for malignant PNST, whereas benign PNSTs more frequently exhibit pain elicited with pressure.

The preoperative differential diagnosis included benign schwannoma based on tumor appearance on MRI and physical examination. However, final pathology returned as primary ectopic atypical meningioma, 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. Critically revising the article: Ziskin, Pezeshkian. Drafting the article: Wu, Pezeshkian. Conception and design: Wu. Acquisition of data: all authors. Analysis and interpretation of data: Wu, Nguyen, Pezeshkian. Drafting the article: Wu, Nguyen, 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.

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