

Malignant cutaneous adnexal neoplasms with distant brain metastasis: an aggressive behavior. Illustrative cases

John Vargas-Urbina, MD,^{1,2} Raúl Martínez-Silva, MD,¹ Giuseppe Rojas-Panta, MD,¹ Gabriel Ponce-Manrique, MD,¹
Jerson Flores-Castillo, MD,¹ and William Anicama-Lima, MD³

¹Department of Neurosurgery, Hospital Nacional Guillermo Almenara Irigoyen, La Victoria, Lima, Peru; ²Department of Neurosurgery, Clínica Internacional, San Borja, Lima, Peru; and ³Department of Anatomical Pathology, Hospital Nacional Guillermo Almenara Irigoyen, La Victoria, Lima, Peru

BACKGROUND Primary malignant cutaneous adnexal neoplasms are rare and can spread locally or to lymph nodes, and very infrequently to distant sites, such as the brain. Their management is poorly documented, and there are no established clinical practice guidelines for treatment.

OBSERVATIONS A 57-year-old male underwent surgery 2 years earlier for adenocarcinoma of the cutaneous adnexa of the right arm. He was admitted to the emergency department with a 15-day history of drowsiness, dysarthria, and signs consistent with frontal lobe involvement. Preoperative MRI revealed a heterogeneous left frontal lobe tumor with contrast enhancement of a solid mass. A craniotomy and complete tumor resection were performed. He then received radiosurgery (27 Gy). MRI studies at 1 and 6 months postoperatively showed complete resection. These tumors are rare and originate from hair follicles, sebaceous glands, or sweat glands. They have an overall 5-year survival rate of 78.2%, but the metastasis rate can range from 15% to 30%. The treatment approaches are not well described in the literature; combinations of surgery, chemotherapy, immunotherapy, targeted therapy, and radiotherapy are utilized.

LESSONS Malignant cutaneous adnexal neoplasms are rare conditions that need precise diagnosis and prompt multidisciplinary treatment.

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KEYWORDS neoplasms; adnexal and skin appendage; brain neoplasm; neoplasm metastasis; radiosurgery; survival

Malignant cutaneous adnexal neoplasms are a rare type of pathology in which metastasis occurs primarily due to local extension or to lymph nodes; however, they rarely lead to distant metastasis, especially to the brain.¹

The literature shows varying rates of local and distant metastasis, with 3 reported cases of brain metastasis resulting from local invasion.²⁻⁶ There is limited information on how to manage this condition, and no clinical practice guidelines are currently available to direct treatment.⁷

Therefore, we present the case of a patient with a malignant cutaneous adnexal neoplasm of the right arm that metastasized to the brain, managed with a multidisciplinary approach, and exhibited good clinical and neurological outcomes.

Illustrative Case

The patient was a 57-year-old male with a history of resection of adenocarcinoma of the cutaneous adnexa of the right arm 2 years earlier. The pathological examination shows that one of the lateral surgical margins is less than 1 mm from the neoplasm, and the deep margin

is 2 mm from the tumor (Fig. 1). Immunohistochemical analysis of the tumor is shown in Table 1.

The patient was admitted to the emergency department with a 15-day history of illness, presenting with hypersomnia, dysarthria, bradypsychia, and bradylalia. Full-body imaging and tumor markers showed no metastasis. Preoperative contrast-enhanced brain MRI showed a left frontal tumor measuring 6.51 × 5.17 × 4.90 cm (AP × T × CC), heterogeneous, with enhancement of the solid part. The membranes of the cystic areas also enhanced, with slight diffusion restriction in the solid part, no increased regional blood flow, a lipid peak on spectroscopy, subfalcine herniation, and moderate peripheral edema. The tumor was adjacent to the left middle cerebral artery and displaced both anterior cerebral arteries (Fig. 1). Mannitol and corticosteroid therapy were started, with gradual improvement.

The patient was taken to the operating room with a Glasgow Coma Scale score of 14, no motor or sensory deficits, isochoric and photo-reactive pupils, signs of frontalization, bradylalia, and no dysarthria. The patient underwent a left frontal craniotomy with fluorescein-guided resection of the left frontal tumor using a transulcal approach.

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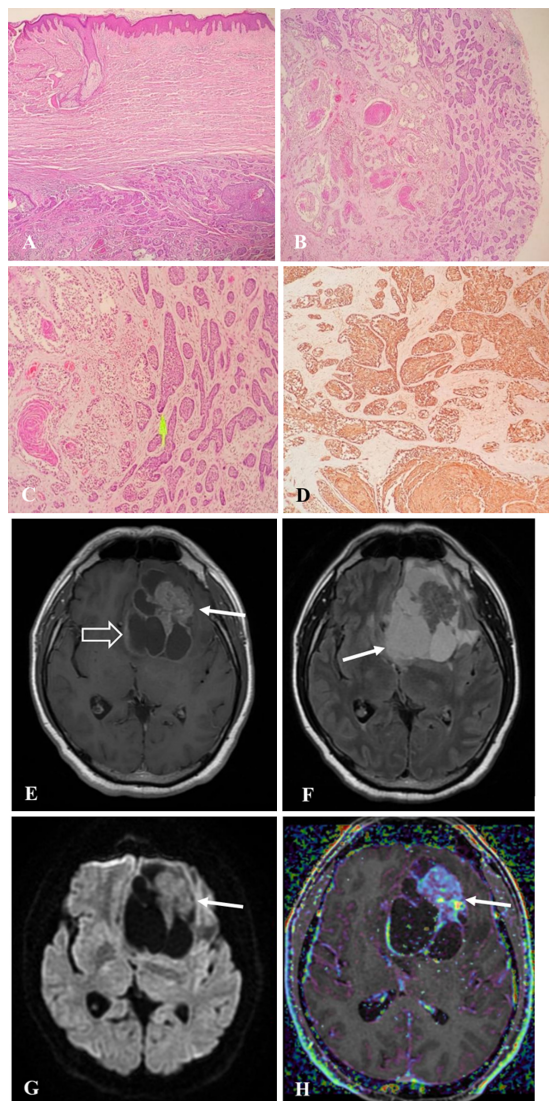


FIG. 1. A–D: Pathological anatomy study of the right arm tumor. **A:** Skin showing proliferation of epithelial-like neoplastic cells (*lower edge*). HE, original magnification $\times 10$. **B:** Neoplastic cells exhibit two patterns: solid nests with a geographical distribution (*right*) and others with a cystic appearance containing debris (*left*). HE, original magnification $\times 10$. **C:** Cells are arranged in a palisade pattern at the edge of the epithelial nests (*arrow*). HE, original magnification $\times 10$. **D:** Keratin. Immunohistochemistry, original magnification $\times 10$. **E–G:** Preoperative contrast-enhanced axial MR images of the brain. **E:** Contrast-enhanced T1-weighted sequence showing a heterogeneous tumor on the left frontal bone, with a solid part that avidly enhances (*arrow*) and another multicystic part with enhancing membranes (*empty arrow*). **F:** T2 FLAIR sequence showing the same tumor, where the multicystic part has high density, probably due to protein elevation (*arrow*). **G:** The diffusion-weighted sequence slightly restricts the solid part of the left frontal tumor (*arrow*). **H:** Perfusion-weighted sequence showing low relative cerebral blood volume (*arrow*) in the left frontal tumor.

The pathological study revealed primary metastatic adenocarcinoma of the cutaneous adnexa. The patient's cytomorphology showed

TABLE 1. Immunohistochemical results in tumor of right arm

Positive	Negative
Cytokeratin 7 (CK7)	Cytokeratin 20 (CK20)
Pankeratin	CEAm (X2)
High-molecular-weight keratin	CDX2
Epithelial membrane antigen (EMA)	S100
p63	
Actin	
p16: focal	
p53: 60%	
Ki-67: 10%	

carcinoma with features suggesting squamous cell differentiation, cellular degeneration, and necrosis.

The patient made a good neurological recovery and was discharged on the 4th postoperative day. A follow-up CT scan on the 1st postoperative day confirmed complete resection of the lesion (Fig. 2). The follow-up contrast-enhanced brain MRI 1 month after surgery showed complete resection, minimal bleeding in the surgical cavity, no abnormal contrast enhancement, and no diffusion restriction. At 3 months postoperatively, the patient underwent stereotactic radiosurgery in three sessions, receiving a total dose of 27 Gy. MRI at 6 months postsurgery, which was 3 months after radiotherapy, revealed complete resection with no abnormal contrast enhancement or diffusion restriction (Fig. 3). The patient continues regular outpatient follow-up and has been disease free for 8 months.

Informed Consent

The necessary informed consent was obtained in this study.

Discussion

Observations

Primary neoplasms of the cutaneous adnexa are usually benign; however, there are case reports of malignant neoplasms with local metastasis due to disease extension or distant metastasis to lymph nodes and, more rarely, to the brain, like in our patient.¹

These neoplasms can originate from any of the four skin appendages: hair follicles, apocrine glands, eccrine glands, and sebaceous glands.^{1,8,9} Additionally, Romeu et al. mentioned three types of cutaneous appendages: sweat glands (either apocrine or eccrine), hair follicles, and sebaceous glands.¹⁰

Sebaceous gland carcinoma is the most common malignant tumor of the skin appendages, primarily affecting the head and neck, and is classified into periocular and extraocular types.^{7,11,12} This tumor has an overall survival rate of 78.2% after 5 years and 61.72% after 10 years.⁷ It tends to recur locally, with 14.2% of cases in the extraocular type and 11.8% in the periocular type; however, there are also reports of distant metastasis.^{7,13}

Extraocular sebaceous carcinomas can occur sporadically or as part of Muir-Torre syndrome. They are usually asymptomatic and rarely metastasize. The literature reports fewer than 40 cases, with metastases typically reaching regional lymph nodes, viscera, or bone. The disease sometimes shows aggressive behavior, invading deeper structures such as muscle, bone, meninges, and even the brain. There are 3 case reports of brain metastasis, but all are due to local invasion; distant brain metastasis has not been documented, as is the case with our patient, whose primary tumor was located in the arm.^{4–6}

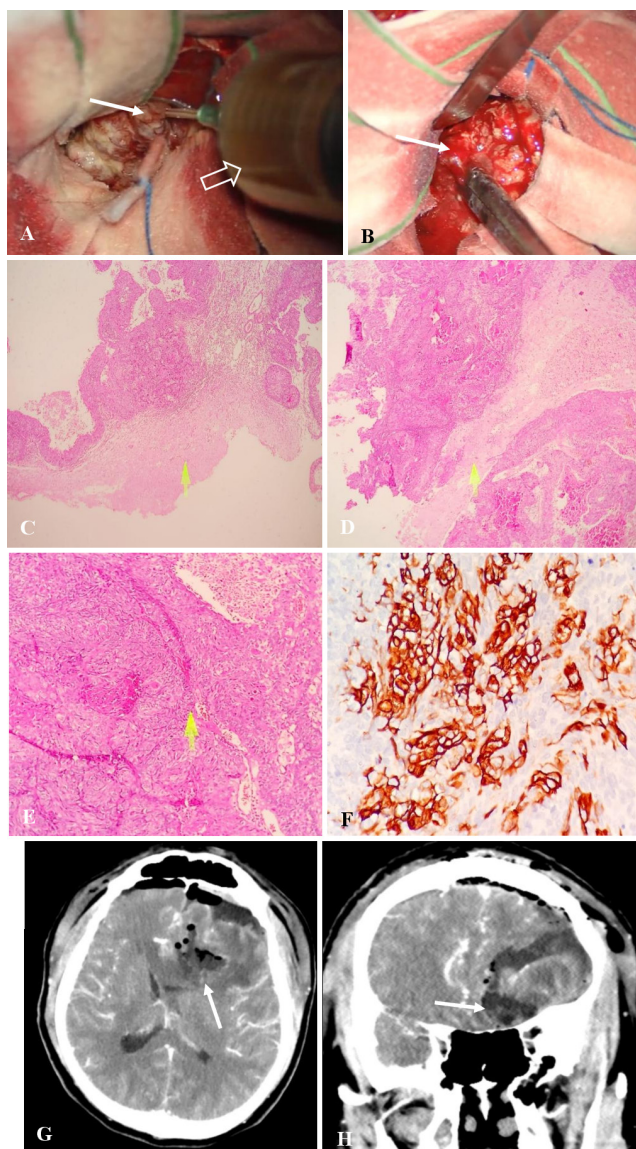


FIG. 2. A: Intraoperative image showing the puncture of the cystic part of the tumor (*arrow*), from which a greenish proteinaceous liquid is aspirated (*empty arrow*). **B:** Intraoperative image showing the solid part of the tumor (*arrow*), already separated from the healthy brain tissue with cotton patties. **C–F:** Pathological anatomy study of the brain tumor. **C:** Brain parenchyma (*arrow*) with the presence of solid-type neoplastic cell nests (*upper edge*). HE, original magnification $\times 4$. **D:** Another area with cystic-appearing neoplastic nests (*arrow*) containing debris. HE, original magnification $\times 10$. **E:** Presence of palisading cells (*arrow*) at the edges of the solid nests. HE, original magnification $\times 40$. **F:** Keratin. Immunohistochemistry, original magnification $\times 40$. **G and H:** Axial (G) and coronal (H) contrast-enhanced CT scans of the brain obtained on the 1st postoperative day, showing total resection of the tumor (*arrow*) without abnormal enhancement and with minimal bleeding in the surgical bed.

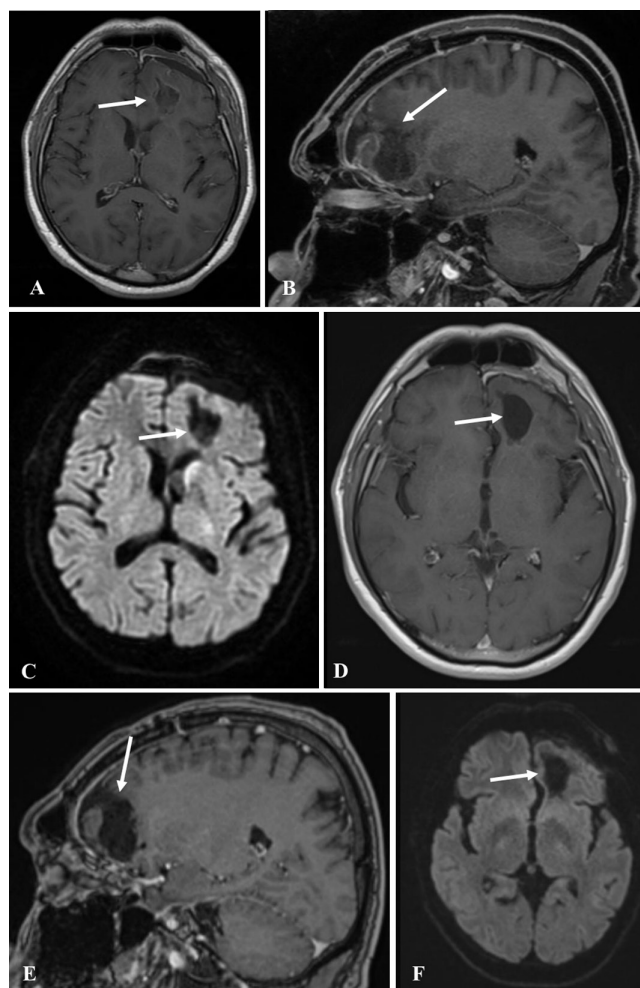


FIG. 3. A–C: Contrast-enhanced MR images of the brain obtained in the 1st postoperative month. **A:** Axial T1-weighted image showing only postsurgical changes without residual tumor (*arrow*). **B:** Sagittal T1-weighted image showing postsurgical changes without residual tumor (*arrow*). **C:** Diffusion-weighted image with no evidence of restriction foci in the surgical area (*arrow*). **D–F:** Contrast-enhanced brain images of the brain obtained in the 6th postoperative month (3rd month after radiotherapy). **D:** Axial T1-weighted image showing no abnormal contrast enhancement, tumor recurrence, or residual tumor (*arrow*). **E:** Sagittal T1-weighted image showing abnormal contrast uptake, but no residual tumor or tumor recurrence (*arrow*). **F:** Diffusion-weighted image showing no restriction in the surgical cavity (*arrow*).

gastrointestinal neoplasm, the most common origin of metastatic adenocarcinomas.^{1,2,14,15} These markers were identified in our patient, leading to a definitive diagnosis.

Systemic therapy for metastatic tumors of the cutaneous adnexa is not well described, and options may include conventional chemotherapy, targeted therapy, or immunotherapy.⁷ Sometimes, this includes chemotherapy based on platinum-based agents, taxanes, anthracyclines, adriamycin, and bleomycin.^{2,7} However, it is known that most adenocarcinomas are very aggressive and often resistant to chemotherapy, so only targeted therapy can potentially improve survival.²

Adjuvant radiotherapy is beneficial in high-risk cases, such as those with large tumors greater than 5 cm, positive surgical margins less

Regarding the immunohistochemical results that may be present in a neoplasm of the cutaneous adnexa, a summary is given in Table 2. Its main differential is gastrointestinal neoplasia, when the absence of CK7 and the positivity of CK20 and CDX2 indicate a

TABLE 2. Immunohistochemical results in cutaneous adnexal tumors

Positive	Negative
CK7	CK20
Low-molecular-weight keratin	CDX2
High-molecular-weight keratin	
EMA	
Carcinoembryonic antigen (CEA)	
S100 protein	
Smooth muscle actin (SMA)	
p63	
Calponin	
Cytokeratin 14 (CK14)	
B-cell lymphoma 2 (BCL-2) protein	

than 1 cm, poor or moderate histological differentiation, or lymphovascular invasion. Radiotherapy to involved lymph nodes is recommended when there is extranodal extension or more than four nodes are involved. Whole-brain radiotherapy or radiosurgery has been used for brain metastases, but generally indicates a poor prognosis.^{2,16–18} This therapy was chosen for our patient and had favorable results during the follow-up period.

Lessons

Malignant neoplasms of the cutaneous adnexa are rare, and their distant metastasis, especially to the brain, is even more uncommon. However, pathological assessment, including immunohistochemistry, helps establish an accurate diagnosis and enables timely, multidisciplinary treatment.

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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: Vargas-Urbina, Ponce-Manrique. Acquisition of data: Vargas-Urbina, Martinez-Silva, Ponce-Manrique, Anicama-Lima. Analysis and interpretation of data: Vargas-Urbina, Martinez-Silva, Rojas-Panta, Ponce-Manrique, Anicama-Lima. Drafting the article: Vargas-Urbina, Martinez-Silva, Rojas-Panta, Ponce-Manrique. Critically revising the article: all authors. Reviewed submitted version of manuscript: Vargas-Urbina, Martinez-Silva, Ponce-Manrique, Anicama-Lima. Approved the final version of the manuscript on behalf of all authors: Vargas-Urbina. Statistical analysis: Vargas-Urbina, Ponce-Manrique. Administrative/technical/material support: Ponce-Manrique. Study supervision: Ponce-Manrique, Flores-Castillo.

Correspondence

John Vargas-Urbina: Hospital Nacional Guillermo Almenara Irigoyen, La Victoria, Lima, Peru. johnkilin27@hotmail.com; jvargas.jvu@gmail.com.