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Nothing to Spit at

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Dr. Adesina

A 59-year-old Hispanic man initially came to medical attention via an emergency room visit for a painful, neurologically isolated, pupil-sparing right third nerve palsy that spontaneously resolved. This was thought to be a microvascular palsy, as his past medical history, in addition to a tubular adenoma of the colon, included hypertension, diabetes mellitus type II complicated by diabetic nephropathy, and nonproliferative diabetic retinopathy. He was admitted by the neurology service, at the time of his third nerve palsy, and neuroimaging and lumbar puncture were obtained.

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Dr. Supsupin

Contrast-enhanced magnetic resonance imaging (MRI) was unremarkable except for an abnormality of the posterior right sphenoid sinus that is consistent with arrested pneumatization (Fig 1). Magnetic resonance angiography (not shown) was unremarkable.

Dr. Adesina

Lumbar puncture showed a normal opening pressure. Cerebrospinal fluid analysis revealed a protein concentration of 111 mg/dL (normal: 15–45 mg/dL) with a normal glucose level and normal white blood cell count. C-reactive protein, erythrocyte sedimentation rate, thyroid stimulating hormone, and angiotensin converting enzyme levels were normal. Antinuclear, Lyme, and Sjögren antibody assays were negative.

The patient was evaluated in the neuro-ophthalmology clinic 4 months later complaining of 1 month of progressive blurry vision in his right eye. Visual acuity was counting fingers, right eye, and 20/20, left eye. Pupils were isocoric and there was a right relative afferent pupillary defect. Ocular motility was intact and while the left fundus was normal there was right optic disc pallor. The patient underwent repeat neuroimaging.

Dr. Supsupin

Contrast-enhanced MRI of the brain and orbits performed 6 months after his initial presentation showed interval development of an expansile 3.2 cm × 3.8 cm × 2.1 cm central skull base mass with involvement of the clivus, partially encasing the right cavernous internal carotid artery. The mass displaced the optic chiasm and extended into the orbital apex, compressing the right optic nerve (Figs 2A, 2B). In retrospect, this mass corresponded to the lesion that was initially thought to represent arrested pneumatization of the right sphenoid sinus. Maxillofacial computed tomography (CT) showed a predominantly hyperdense mass that infiltrated the central skull base and sphenoid sinus and extended anteriorly into the ethmoid sinuses on both sides, right more than left (Fig 2C). The bulk of the lesion demonstrated an appearance consistent with a bony matrix. There was a soft tissue density in the right sphenoid sinus and the left ethmoid air cells, consistent with either a soft tissue component of the mass or changes related to obstruction. Overall, the findings were most concerning for a malignant neoplasm, either primary, originating from the sphenoid sinus or nasopharynx and invading the skull base, or secondary, from metastasis from a distant site.

Dr. Adesina

The patient was referred to the otolaryngology service and underwent nasal endoscopy with partial resection of the right superior turbinate, sphenoidotomy, and biopsy of the sphenoid sinus mass.

Dr. Billah

Microscopic examination of the surgical specimen revealed bony trabeculae with an infiltrate of neoplastic cells within the marrow. Architecturally, the tumor consisted of glands and solid sheets of intermediate-sized cells with abundant cytoplasm and bland nuclei. Occasional prominent nucleoli were seen. Rare cells with intracytoplasmic mucin also were present (Fig 3A).

Immunohistochemical stains with appropriate controls showed that the tumor cells were positive for cytokeratin AE1/AE3, CAM 5.2, androgen receptor, prostate-specific antigen (PSA), and prostate-specific acid phosphatase (PSAP) and negative for vimentin, CD31, CD34, PAX-8, TTF-1, p63, S100 proteins, cytokeratin 5/6, chromogranin, and synaptophysin (Figures 3B, 3C). Cytokeratin 7 staining was focally positive. Ki-67 showed a moderate proliferative index within tumor cells.

Dr. Adesina

Given the finding of positive prostate markers, the patient's clinical picture at this time was thought to be most consistent with metastatic prostate cancer. He, therefore, was referred to urology and oncology for further workup. Clinical prostate examination revealed a gland of 35 grams without nodularity. His PSA was normal at 3.54 ng/ml (normal < 4.0 ng/ml). Oncology workup with CT and positron emission tomography (PET/CT) showed diffuse hypermetabolic osteoblastic metastatic disease with the largest and most fluorodeoxyglucose (FDG)-avid lesion in the central skull base with maximum standardized uptake values of 5 (Fig 4). There were no soft tissue lesions or masses seen to suggest a primary source of malignancy, including the prostate. The urology service did not think that the patient's clinical picture was consistent with a primary prostate tumor and did not pursue a biopsy. His case was presented to a multidisciplinary tumor board where, despite staining positively for prostate markers, the tumor was thought to be an adenocarcinoma of minor salivary gland origin, arising primarily from the sphenoid sinus.

Dr. Billah

The morphologic and immunohistochemical features were consistent with either salivary gland or prostate origin. Although PSA and PSAP are commonly seen in prostatic adenocarcinoma, they also may be expressed in salivary duct carcinoma. The CK7 positivity also favors salivary gland carcinoma over prostate adenocarcinoma, which tends to be negative for CK7 (1). In all, the pathologic features were insufficient to differentiate confidently between these 2 sites, and the determination of tumor origin relied heavily on the clinical picture. The negative prostate exam, low PSA, and dominant sphenoid sinus mass supported a primary salivary gland tumor (2–4).

Final diagnosis

Adenocarcinoma of minor salivary gland origin, arising from the sphenoid sinus, stage T4dN0M1 (5) causing compressive optic neuropathy.

Dr. Adesina

Minor salivary glands, from which malignant tumors can arise, are found throughout the paranasal sinuses. On initial imaging, the sphenoid mass appeared small and nonaggressive, mimicking a benign fibro-osseous lesion. Thus, the correct diagnosis was delayed, resulting in tumor growth and optic nerve compression. Histopathologic evaluation initially favored a prostate origin; however, no prostate abnormality was found clinically or radiographically. Salivary duct tumors are known to stain with androgen and prostate markers, thus mimicking prostate carcinoma. Further review of the literature (3, 6) showed that positive CK7 staining favored a salivary gland primary over metastatic prostate disease and that the overall clinical picture supported the diagnosis of an aggressive primary salivary duct tumor.

The prognosis for minor salivary gland malignancies depend on histologic subtype, tumor site and grade at diagnosis, stage at time of diagnosis, age at diagnosis, and surgical intervention (7). Overall, neoplasms located in the larynx and nasal/paranasal sinuses, age over 75, and no surgical intervention portend a dimmer prognosis. In a large review of survival rates of patients with minor salivary gland tumors, 5- and 10- year cause specific survival for patients with regional disease were 74.9% and 63.4%, respectively; for those with distant disease, 44.8% and 28.8%, respectively. A site in the nasal cavity and/or paranasal sinus carried a worse cause-specific survival (CSS) across all histologic subtypes. Given our patient's sphenoid sinus primary and evidence of distance metastasis, he unfortunately has a poor prognosis for long-term survival (7).

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Figure 1.

Brain MRI at presentation. Postcontrast axial T1 image demonstrates an abnormality of the right posterior sphenoid sinus (arrow). Given its location and relatively non-expansile appearance, the abnormality is most consistent with arrested pneumatization of the sinus, although the differential diagnosis included other benign fibro-osseous lesions.

Figure 2.

Follow-up MRI 6 months after initial presentation. Postcontrast axial (A) and coronal (B) T1 images with fat suppression show a large, heterogeneously enhancing mass invading the central skull base and extending into the posterior ethmoid air cells. Note dural enhancement (arrows). C. Non-contrast computed tomographic scan shows an expansile skull-based mass with partial effacement of the right orbital apex.

Figure 3.

Sphenoid sinus biopsy. A. Mass is composed of intermediate sized cells, some containing intracytoplasmic mucin(arrows) (hematoxylin and eosin, x 10). B. Immunohistochemistry using pan-keratin confirms the carcinomatous nature of the tumor. [3,3'-Diaminobenzidine (DAB) chromogen, pan-keratin antibody x 40]. C. Immunohistochemistry using androgen receptor (AR) is positive in nuclei of tumor cells. [3,3'-Diaminobenzidine (DAB) chromogen, AR antibody, x 40].

Figure 4. Position emission tomography (PET)/computed tomography (CT). A. PET/CT shows avid fluorodeoxyglucose (FDG) uptake in the central skull base mass (arrow). B. Bony metastases with multiple foci of increased FDG uptake are present in the spine (bracket), scapula (arrows), and proximal femur (arrowhead).