**Primary mucinous adenocarcinoma of the orbit: a rare clinical entity**

**Key Clinical Message**

Primary mucinous adenocarcinoma is locally aggressive with a recurrence rate up to 40%, that’s why the mainstay of its treatment is a large local excision.

**Abstract**

Primary mucinous adenocarcinoma is an exceptionally rare neoplasm with a propensity for local recurrence and metastasis. We report the second case in the literature of a primary mucinous adenocarcinoma of the orbit in a 66-year-old male with its clinical, histological features, and management of this tumor.

**List of authors**

Kais Maamri 1, Rihab Ben Fredj 1, Nesrine Nessib 1, Mohamed Boukhit 1, Maher Hadhri 1, Ghassen Belkahla 1, Atef Ben Ncir 1, Mehdi Darmoul 1

1 Department of Neurosurgery, Fattouma Bourguiba University Hospital of Monastir, Tunisia.

**Correspondence**

Kais Maamri, Department of Neurosurgery , Fattouma Bourguiba University Hospital of Monastir, Tunisia.

Email: [Kais.maamri@gmail.com](mailto:Kais.maamri@gmail.com)

**Author’s contribution**

Kais Maamri treated the patient and writing the manuscript. Rihab ben fredj performed the acquisition , analysis and interpretation of data with support from Nesrine Nessib and Mohamed Boukhit . Maher hadhri did the conception and the design of the project, and Ghassen Belkahla prepared pathology figures and slides. Atef Ben Ncir and Mehdi Darmoul helped supervising the project. All authors discussed the results and contributed to the final manuscript.

# INTRODUCTION:

# Primary mucinous adenocarcinoma is an exceptionally rare neoplasm with a propensity for local recurrence and metastasis which may originate in the breast, gastrointestinal tract, the thyroid and from glands of the skin. Although rare, mucinous adenocarcinoma arising from the skin has a predilection for the eyelid.[1]

# This eyelid neoplasm has been widely reported in the ophthalmology literature, but not to our knowledge the intraconic localization.

# Only one case of infiltrating adenocarcinoma, with some features suggestive of mucoepidermoid carcinoma of the orbit have been reported in the literature.[2]

# We report the case of a primary mucinous adenocarcinoma of the orbit in a 66-year-old male with its clinical, histological features, and management of this tumor.

# CASE REPORT:

A 66-year-old man without significant medical history, presented to the Neurosurgery Department in Fattouma Bourguiba Hospital with complaints of pain, progressive protrusion of his left eye and a deep drop in vision on the left for several weeks.

There is neither diplopia nor periorbital swelling. There were no other systemic complaints.

External examination revealed significant propotosis with downward displacement of the left globe with no lagophthalmos. Limitation of abduction was noted.

Visual acuity without correction was 0/10 in the left eye whereas in right it was 10/10. No papillary oedema was revealed.

Intraocular pressures were 18 mm Hg in the right, and 16 mm Hg in the left.

Routine blood investigations were unremarkable.

A CT of the orbit with and without contrast showed intra- and extra-conical solid expansive process.

It is centered on the internal rectus muscle and has a large implantation base.

The lesion pushes the eyeball back and forth, responsible for exophthalmos with osteolysis (Fig1).

****

Fig.1 A :CT orbit without contrast, coronal cut



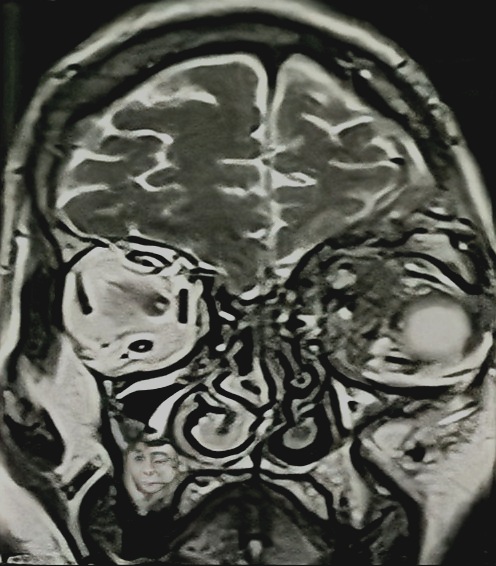
Fig.1 B : CT Orbit with contrast, axial cut



Fig.1 C : Cerebral CT showing the osteolysis

***Fig.1 : CT orbit demonstrating the large orbital mass surrounding and indenting the left globe with osteolysis***

An MRI of the orbit with and without contrast showed a process of the supero-internal angle of the left orbit, well limited, with an important enhancement after injection. This lesion is both intra and extra conal, exerting a mass effect on the internal rectus muscle and the optic nerve (Fig2).



***Fig 2: A: T2 weighted MRI, coronal cut; B: T2 weighted MRI , axial cut***

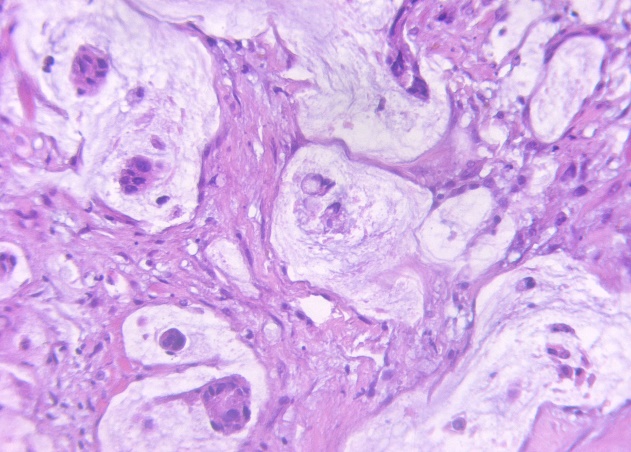
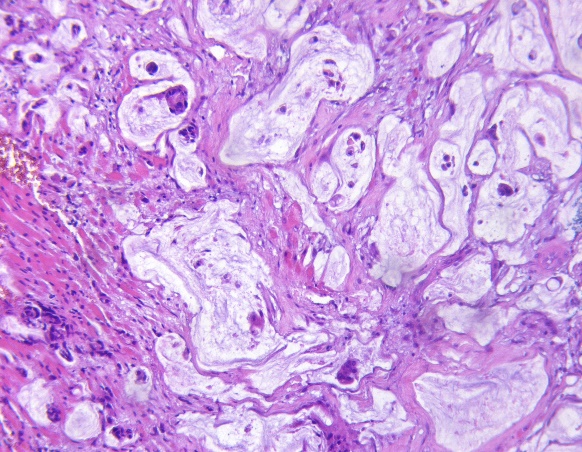
***Fig 2: T2 weighted MRI demonstrating the large orbital mass surrounding and indenting the left globe***

Our patient had a negative metastatic work-up for any primary malignancy elsewhere.

We completed with a thoraco-abdomino-pelvic CT scan and a colonoscopy which returned normal.

The patient was operated via a combined approach. Through a fronto orbito zygomatic approach, excision of a firm hard lesion infiltrating the eyeball as well as the optic nerve which motivated complete enucleation. We ended with a tarsorrhaphy.

A Total exeneration was ultimately performed and the surgical specimens were sent for histopathologic evaluation. The final pathologic diagnosis was mucinous adenocarcinoma of the orbit (Fig3).



***Fig 3: Carcinomatous proliferation made by patches of mucus in which tumor cells are bathed, often isolated or arranged in small clusters. These cells are of mucosecreting ring-like appearance with an eccentric nucleus, mild to moderate nuclear atypia and some mitosis.***

***The complementary imunohistochemical study showed an intense cytoplasmic staining of 20% of the tumor cells with the anti CK7 and an intense and cytoplasmic staining of rare cells (less than 20%) with the anti CK20.***

The postoperative neuroimaging showed a complete resection of the tumor. The patient is referred for adjuvant radiotherapy. A CT of the orbit was made 3 months postoperatively, and didn’t show any local recurrence.

# DISCUSSION :

Primary mucinous adenocarcinoma is uncommon, with no predisposing factors or etiology. **[1]**

# It can arise throughout the body especially the head and the neck. Mucinous adenocarcinoma arising from the skin has a predilection for the eyelid .The rate of occurrence of this tumor in the eyelid is between 30-45% according to several studies. [3]

# The average age of patients with primary mucinous adenocarcinoma is between the sixth and seventh decades. [3]

The age of the patient in our case was 66 years old wich is comparable with the previous studies.

The problem here is to distinguish whether it is a primary mucinous adenocarcinoma of the orbit or is it an orbital metastasis of a known adenocarcinoma. That’s why; many investigations should be done to determine the origin of this neoplasm.

Metastatic lesions involving the orbit are also rare, comprising between 1% and 13% of all orbital tumors. **[1]**

Orbital metastases are a rare manifestation of systemic malignancy which classically occurs late in the evolution of a known neoplasm, but in 42% to 61% of cases, the orbital symptoms precede detection of the primary tumor.

Prompt surgical intervention with biopsy enabled definitive diagnosis of a

mucinous adenocarcinoma, leading to the discovery of the primitive tumor. **[4]**

To our knowledge, there are only 6 known cases of metastatic mucinous adenocarcinoma in the orbit. Five arose from gastrointestinal primaries including rectal, esophageal, gastricand pancreatic, and the sixth represents orbital reoccurrence from a primary eyelid sweat-gland mucinous adenocarcinoma. **[4-8]**

Sometimes, ocular symptoms preceded the diagnosis of the primary lesion. This underscores the importance of a thorough investigation aiming to search for the primary neoplastic process. **[1,10]**

# In litterature, there is only one case of primary infiltrating adenocarcinoma of the orbit, with some features suggestive of mucoepidermoid carcinoma initially diagnosed as idiopathic sclerosing orbital inflammation.The tumor did not appear cytologically aggressive, but with infiltrative growth pattern suggestive of a high-grade tumor, T4N0M0. As demonstrated in that case, even though the biopsy concluded in benign lesion, the clinician must remain vigilant if he suspects signs of malignancy. This is particularly true in the presence of atypical presentation or signs of severity. [2]

Regardless of the orbital mass nature, clinically, these tumors usually present with symptoms such as proptosis which is due to the infiltration of fat and extraocular muscles by the tumor. Also, muscle involvement can produce diplopia. Pain is generally associated with periosteal and bone involvement. Pulsations are due to bone destruction or vascular tumors. Ptosis, a palpable mass, enophthalmos, or decreased vision are also described.**[9]**

There are no radiological specificities in this type of tumor compared to other orbital masses. The MRI of the orbit with and without contrast may show a heterogenous orbital process, well limited or infiltrating, with an important enhancement after injection. This lesion can be both intra and extra conal, and can exert a mass effect on rectus muscles and the optic nerve.

# A careful histopathological examination must be carried out for a definitive diagnosis of a mucinous adenocarcinoma. On gross examination, it shows a firm and white unencapsulated tumor mostly fixed to the dermis. [3]

Histologically, it may be very difficult to distinguish metastatic mucinous adenocarcinoma from primary entities. Orbit and eye mucinous adenocarcinoma closely resemble that of the ovary, breast, rectus, bronchus and colon. Characteristic round cuboidal cells with pale sialomucin-rich cytoplasm vacuoles, surrounded by extracellular mucin pools, positive for EMA, PAS, alcian blue, and mucicarmine histochemical staining are seen in both primary and metastatic lesions. The latter may show greater mitotic activity and pleomorphism on light microscopy. Stem cell origin studies may also be helpful to differentiate metastatic from primary mucinous adenocarcinomas. **[1]**

# The immunohistochemistry has greatly helped in differentiating primary mucinous adenocarcinomas from metastatic entities. The expression pattern of a CK panel is very helpful. The primary one is CK7 positive and CK20 negative, whereas metastatic adenocarcinoma from the gastrointestinal tract is CK7 negative and CK20 positive. Some other helpful immunohistochemical such as the carcinoembryonic antigen, the epithelial membrane antigen and CK AE1/E3 may be helpful markers which point its origin from a secretory lobule. Gross cystic disease fluid protein-15 (GCDFP-15), estrogen receptor (ER) and progesterone receptor (PR) are also helpuf markers to differentiate primary mucinous adenocarcinoma from a metastatic breast adenocarcinoma. Cytokeratin 5/6 and p63 are the recently added markers which also help. [3,11]

In our case, the histological examination have showed Carcinomatous proliferation made by patches of mucus in which tumor cells are bathed, often isolated or arranged in small clusters. These cells are of mucosecreting ring-like appearance with an eccentric nucleus, mild to moderate nuclear atypia and some mitosis.

# The complementary imunohistochemicalstudy showed an intense cytoplasmic staining of 20% of the tumor cells with the anti CK7 and CK20 negative.

# For the first case of primary mucinous adenocarcinoma of the orbit described in the litterature, additional surgery was suggested after biopsy, with or without radiation and chemotherapy. He ultimately decided to undergo adjuvant radiation therapy. Neuroimaging at six months post exenteration showed no signs of recurrence. [2]

The patient in our case received adjuvant radiotherapy after complete exenteration. A CT of the orbit was made 3 months postoperatively, and didn’t show any local recurrence.

# CONCLUSION:

# Primary mucinous adenocarcinoma of the orbit is an extremely rare neoplasm. Our case is the second case described in literature. A few cases of metastatic mucinous adenocarcinoma in the orbit have been described .It is important to remember that histological and immunohistochemical features are extremely helpful in the diagnosis of the primary etiology, but they surely cannot exclude the metastatic etiology.

# Primary mucinous adenocarcinoma is locally aggressive with a recurrence rate up to 40%, that’s why the mainstay of its treatment is a large local excision.

# These entities can be extremely difficult to diagnose. A work up must be done to look for a primary lesion in all patients with identified mucinous adenocarcinoma.

**Declaration of interest:**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

# REFERENCE :

# *Monson, B. K., Patel, B. C. K., & Kim, C. H. Metastatic Mucinous Adenocarcinoma of the Orbit. Orbit 2011 ; 30(1) :18–20.*

# *Reed D, Mehta A, Hayes B, Caldwell M, Scribbick F, Davies B. Primary adenocarcinoma of the orbit initially diagnosed as idiopathic sclerosing orbital inflammation. Am J Ophthalmol Case Rep 2019;16:100529.*

# *Albasri, A., Ansari, I., Aljohani, A., & Alhujaily, A. Primary mucinous adenocarcinoma of the eyelid. Saudi Medical Journal 2018 ; 39(9) :940–945.*

# *Yunker, J. J., Vicinanzo, M. G., Braswell, R. A., Read, R. W., Goldin, G. F., & Long, J.A.  Unusual Presentation of Gastric Adenocarcinoma Metastatic to the Orbit. Ophthalmic Plastic & Reconstructive Surgery 2006;22(6):490–491.*

# *Hisham, R. B., Thuaibah, H., & Gul, Y. A. Mucinous Adenocarcinoma of the Rectum with Breast and Ocular Metastases. Asian Journal of Surgery 2006; 29(2): 95–97.*

# *Chekrine, T., Hassouni, A., Hatime, M., Jouhadi, H., Benchakroun, N., Bouchbika, Z.,Benider, A. Métastase orbitaire d’un adénocarcinome mucineux du rectum. Journal Français d’Ophtalmologie 2013 ; 36(5) :73–75.*

# *Oh KT, Alford M, Kotula RJ, Nerad JA. Adenocarcinoma of the Esophagus Presenting as Orbital Cellulitis.*Arch Ophthalmol *2000;118(7):986–988.*

# *Holds JB, Haines JH, Mamalis N, Anderson RL, Wolin MJ. Mucinous adenocarcinoma of the orbit arising from a stable, benign-appearing eyelid nodule. Ophthalmic Surg 1990;21(3):163-6.*

# *Maheshwari, A., Finger, P.T. Cancers of the eye. Cancer Metastasis Rev 2018;37: 677–690.*

# *Patel V, Castell FA, Akinwunmi J, Francis I, Chandrasekharan L, Malhotra R. Prostatic adenocarcinoma presenting with metastatic frontal bone involvement and orbital invasion. Orbit. 2010 Aug;29(4):213-5.*

1. *Sanft DM, Zoroquiain P,Arthurs B, Burnier MN. Primary mucinous adenocarcinoma of the eyelid: A case-series. Human Pathology: Case Reports 2017;9:19-23.*