Future ONCOLOGY

CASE REPORT

Single bone metastasis from adenocarcinoma of the lacrimal gland: a case report

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ABSTRACT Malignant tumors of the lacrimal gland are rare, and single bone metastases from lacrimal gland carcinoma are an exceptional event. We present the case of a 71-year-old man with a history of lumbar pain and left exophthalmos. Surgical resection of the lacrimal lesion and a bone biopsy gave a final histopathological diagnosis of primary ductal adenocarcinoma of the lacrimal gland with bone metastasis. The pathological tissue from both procedures was positive for androgen receptor expression. The patient underwent embolization and radiotherapy in association with total androgen blockade. After 20 months, the patient is still asymptomatic and has maintained the partial response at L1 with no progression to other sites. Our patient would appear to have a better prognosis and the disease a more indolent clinical course than the other cases of ductal adenocarcinoma of the lacrimal gland reported in the literature.

KEYWORDS
• androgen receptor
• androgen receptor blockade • bone metastasis
• ductal adenocarcinoma
• lacrimal gland tumor

Approximately 10% of lesions affecting the orbit are made up of inflammatory lesions, lymphoproliferative disorders and epithelial tumors [1]. Lacrimal gland tumors are represented, for the most part, by pleomorphic adenoma and adenoid cystic carcinoma. A small niche is also constituted by adenocarcinoma not otherwise specified [2,3]. We report the clinical, radiological, pathological and therapeutic features of a patient with a single bone metastasis from a primary ductal adenocarcinoma of the lacrimal gland.

Case report

A 71-year-old man was referred for evaluation of left lumbar pain that had been present for at least 3 years. In recent months, the pain had worsened, limiting his daily activities. The patient's medical history was uneventful apart from prostatic hypertrophy, which was being treated. MRI of the lumbar spine **(Figure 1)** showed an extensive osteolytic lesion in the left portion of L1 that extended into the ipsilateral lamina. The focal bone lesion was characterized by the presence of abundant

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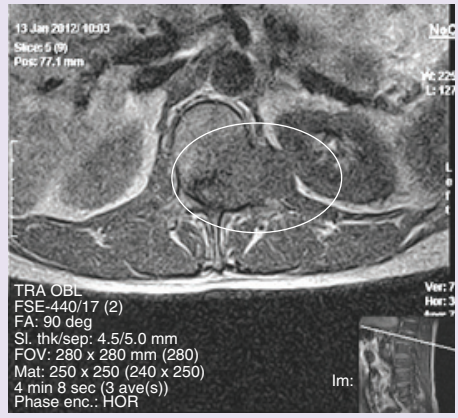

Figure 1. MRI of the lumbar spine (13 January 2012). Axial T1-weighted image: extended area of altered signal (hypointense on T1-weighted images) affecting the left portion of the soma of L1 and the ipsilateral lamina associated with pathological tissue that partly occupies the spinal canal, with moderate compression phenomena and minimum displacement to the right of the dural sac.

replacement pathological tissue that protruded beyond the vertebral body, medially and marginally occupying the spinal canal. The bone alteration showed hypointensity, characteristic of signal sequences in the dependent T1, and hyperintensity in the STIR sequence with the signal from fluids. An ^{18}F-fluorodeoxyglucose PET/computed tomography (CT) scan was performed, revealing a focal area of increased metabolism in the osteolytic lesion of the left hemibody of L1 extending into the lamina ipsilaterally (SUV_{max} = 5.40) (Figure 2).

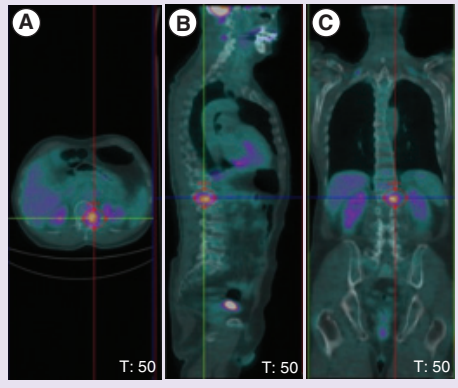

Figure 2. Computed tomography-PET (1 February 2012): area of increased focal metabolism at the site of the osteolytic lesion in the hemibody of L1 (SUV_{max} = 5.40).

The patient underwent a CT-guided bone biopsy, revealing a lesion composed of glandular, duct-like structures surrounded by dense fibrous tissue. Epithelial cells showed abundant eosinophilic cytoplasm and large nucleoli with features of apocrine metaplasia. Necrotic foci and mucus secretion were present. Cells were positive for cytokeratin 7, GCDFP-15 and androgen receptors, but negative for TTF-1, cytokeratin 20, CDX2, prostate-specific antigen and estrogen and progesterone receptors (Figure 3). These finding were suggestive of bone metastasis from breast, salivary gland or biliary tract cancer.

Breast and neck ultrasound scans and blood tests including TSH, thyroglobulin, calcitonin, CA15.3, CA19.9 and α-fetoprotein were thus performed, but all were negative. As there was slight exophthalmos of the patient's right eye, which had been present for several years, an ophthalmic examination was carried out, with no remarkable findings and normal visual acuity. It was decided to proceed with a facial CT scan (Figure 4) that revealed a solid hypodense lesion (23 × 17 mm) with some contextual calcifications and marked contrastographic impregnation in the upper outer portion of the right orbit. The lesion was not clearly separable from the lateral rectus muscle and in some points came into contact with the eyeball and the superior rectus muscle. There were no evident osteoblastic alterations in the orbital walls. These findings were strongly suggestive of a primary tumor of the lacrimal gland.

To confirm the malignant nature of the orbital lesion, fine-needle aspiration of the mass was performed and cytological examination revealed the presence of malignant epithelial cells attributable to poorly differentiated carcinoma, positive for cytokeratin AE1–AE3 (Figures 5 & 6). The L1 biopsy slides were sent for a second evaluation to external pathologists who diagnosed poorly differentiated adenocarcinoma exhibiting cribriform aspects of undefined primitivity. Tumor cells were positive for cytokeratin 7 and androgen receptors, but negative for TTF1 and cdx-2 (Figure 6). On the basis of this information, a definitive diagnosis of primary adenocarcinoma of the lacrimal gland with bone metastasis was made. Arterial embolization of the lesion in L1 was performed because of severe lumbar pain, resulting in a

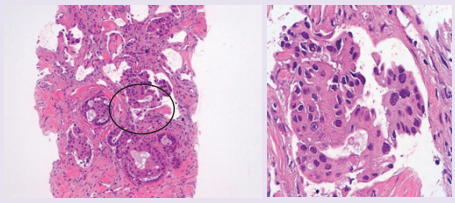

Figure 3. Computed tomography-guided bone biopsy showing infiltrating adenocarcinoma with mucus secretion and scattered mitotic figures.

marked decrease in pathological vertebral tissue and a net reduction in clinical symptoms (Figure 7). The patient refused surgery on the single bone metastasis.

A contrast-enhanced MRI of the brain and orbits was carried out to rule out infiltration of the rectus muscles and surgery was performed in which a soft tissue fragment (4 × 3.5 × 1 cm) with adherent bone fragment (1.7 × 1 cm) was removed. The tissue was compatible with adenocarcinoma of the lacrimal gland. The immunophenotype of the neoplastic population was positive for androgen receptors and intense membrane immunoreactivity for Her-2 neu was observed in 40% of the neoplastic cells. Margins were tumor free.

Radiotherapy consisting of 8 Gy in one fraction was delivered with tomotherapy. Total androgen blockade treatment with leuprorelin and cyproterone was also started. The patient refused therapy with intravenous zoledronic acid and was thus prescribed clodronate 200 mg i.m. every 2 weeks with colecalciferol supplementation.

The patient continues to be still asymptomatic 20 months after diagnosis and has maintained the partial response at L1, with no disease progression to other sites (Figure 8).

Discussion

Very few cases of ductal adenocarcinoma of the lacrimal gland have been reported in the literature [4–6]. A highly aggressive disease occurring mainly in males around 50 years of age, it represents 9% of all epithelial tumors of the eye and 5% of all orbital cancers [5–7]. These tumors do not have their own histological categorization because of their very low incidence and are aligned with the WHO classification of salivary gland tumors because of the similarity between the two malignancies [8]. Histological subtypes

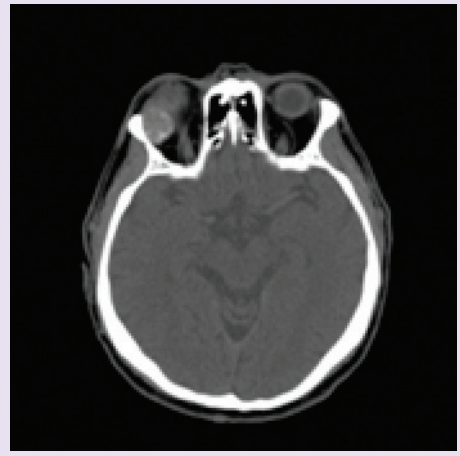

Figure 4. CT scan: contrast-enhanced total-body CT scan showing solid hypodense lesion (23 × 17 mm) with some contextual calcifications and marked contrastographic impregnation in the upper outer portion of the right orbit.

of lacrimal gland tumors are mainly adenocarcinoma, adenoid cystic carcinoma (more frequent and more aggressive) and pleomorphic adenoma, all showing positivity for cytokeratin 7, 18, 19, CEA, EMA and androgen receptors. The clinical presentation of this tumor is frequently an asymptomatic palpable mass with displacement of the globe. This tumor generally has slow growth and a low percentage of local recurrence. However, distant metastases to the lung and liver, GI tract and, more rarely, to the bone and skin, have also been reported [5–7].

There is still no well-defined treatment for adenocarcinoma of the lacrimal gland because

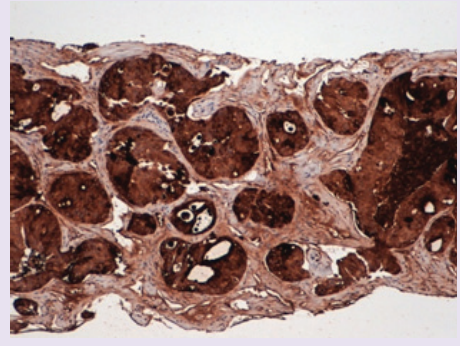

Figure 5. Immunohistochemistry for cytokeratin 7 showing strong diffuse cytoplasmic positivity

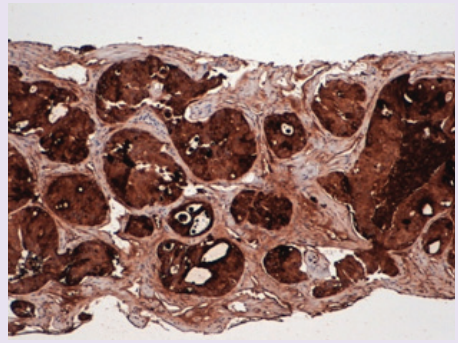

Figure 6. Immunohistochemistry for GCDFP-15 showing cytoplasmic positivity.

of its very low incidence rate. The standard approach is resection of the primary tumor followed by radiation therapy. Surgery consists in orbital exenteration, but the few works published on this topic suggest that there is no difference between extensive or conservative treatment in terms of overall survival [9]. In cases of single local recurrences or single distant metastases, the most widely used treatment is surgical resection [10–12].

Although there is no proven effective chemotherapy for the treatment of metastatic tumors of the lacrimal gland, radiotherapy is recommended for local disease control in unresectable salivary ductal carcinoma [9]. While recent works have reported that salivary ductal carcinoma shares similarities with ductal breast cancer with

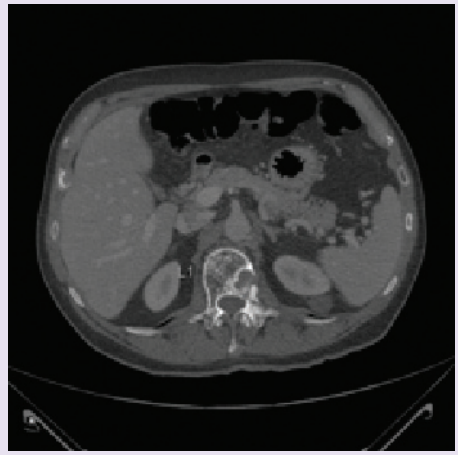

Figure 8. CT scan (16 October 2012) showing a further reduction in the amount of pathological tissue and the appearance of sclerosis in the bone lesion.

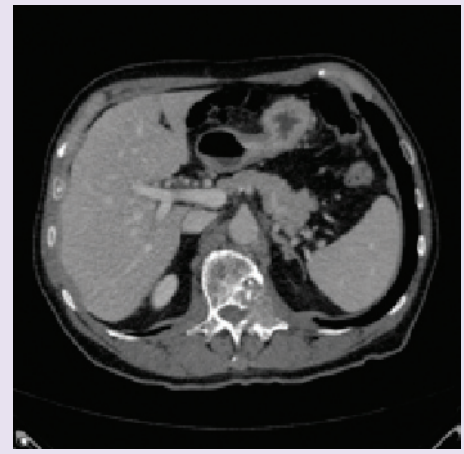

Figure 7. CT scan (17 May 2012) showing a reduction in the osteolytic soft tissue lesion.

atypical ER expression, it also shows androgen receptor positivity, as found in prostate cancer [10–14]. Recently, there have been cases showing complete remission of adenocarcinoma of the parotid gland or a partial response of cerebral metastases using combination treatment with triptorelin and bicalutamide [15,16]. Although some cases of salivary gland tumors treated with androgen blockade have been reported in the literature [13], this is the first time that a patient with a single bone metastasis from a tumor of the lacrimal gland has been treated with the above combination.

In conclusion, we presented a very rare case of a single bone metastasis from primary adenocarcinoma of the lacrimal gland treated with surgical excision, embolization, radiotherapy and androgen blockade. A total of 20 months after diagnosis and 10 months after the start of medical treatment, the patient continues to show a partial remission of the disease at L1, is asymptomatic and has no evidence of other metastatic disease apart from that of the bone.

Conclusion & future perspective

We describe our experience of a patient with a single bone metastasis from lacrimal gland carcinoma treated with a multimodality approach including, for the first time, androgen blockade. Although prognosis of metastatic disease is normally poor, our patient obtained an optimal objective long-term response with disease control, symptom resolution and good quality of life. Further studies are needed to confirm this new therapeutic option.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Informed consent disclosure

The authors state that they have obtained verbal and written informed consent from the patient/patients for the inclusion of their medical and treatment history within this case report.

EXECUTIVE SUMMARY

- Ductal adendocarcinoma of the lacrimal gland is an extremely aggressive disease occurring mainly in males around 50 years of age. The tumor represent 9% of all epithelial tumors of the eye and 5% of all orbital cancers.
- There is still no well-defined treatment for adenocarcinoma of the lacrimal gland because of its very low incidence.
- Although the standard approach is resection of the primary tumor followed by radiation therapy, there are no approved therapeutic options for metastatic disease.
- Very few cases of salivary gland tumors treated with androgen blockade have been reported in the literature.
- Using androgen blockade and a multimodality approach, our patient obtained an optimal objective long-term response with disease control, symptom resolution and good quality of life.

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