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Case Report

Paediatric painless proptosis-not always benign: A case of adenoid cystic carcinoma of the lacrimal gland in a child treated with globe sparing surgery and proton beam radiation

Maneksha Velu[1], Aparna K S[1,*], Kavya Shetty[1], Jeyapriya T[1]

[1]*Aravind Eye Hospital, Tirunelveli, Tamil Nadu, India*

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ABSTRACT

Adenoid cystic carcinoma (ACC) of the lacrimal gland is a rare aggressive malignant epithelial neoplasm. This tumor is rarely seen in children and adolescents. There is a paucity of studies describing the optimal treatment and prognosis of adenoid cystic carcinoma in the paediatric age group. Here, we report a case of lacrimal gland ACC in a 11-year-old girl treated with globe-sparing tumor resection and proton beam radiation therapy (PBRT).

1. Introduction

Adenoid cystic carcinoma (ACC) of the lacrimal gland is the most common primary malignant tumor of the lacrimal gland, which typically affects patients in the fifth decade of life.[1] ACC is rare in children and adolescents.[2] The currently accepted treatment for ACC is radical exenteration with orbitotomy and adjuvant chemotherapy and/or radiation therapy.[3] Despite aggressive treatment such as eye sparing surgery, orbital exenteration, adjuvant radiotherapy, local recurrence and distant metastatic disease are more common.[4] Complex regional orbital anatomy presents a therapeutic challenge, and the aggressive behaviour of the tumor with infiltration through bone, perineural invasion with retrograde intracranial extension, and hematogenous or lymphatic spread contributes to poor prognosis.[5] Here we report a case of paediatric lacrimal gland ACC treated with globe-sparing tumor excision followed by proton beam radiation therapy. Proton beam radiation is a preferable option for the treatment of adenoid cystic carcinoma of the lacrimal gland when the tumor is confined to the orbit.

2. Case Presentation

An 11 years old girl, presented to outpatient department with painless, gradually progressive forward protrusion of left eyeball since 4 months. On examination, Best corrected visual acuity (BCVA) was normal 6/6 in both the eyes. Eccentric proptosis was noted in the left eye with fullness over the left supero temporal region (Figure 1A). Orbital margins were regular and intact on palpation. Not able to insinuate fingers in supero-lateral quadrant with resistance to retropulsion. There was a firm, oval shaped, well defined, non tender swelling over the lacrimal gland region of left eye. No submandibular or preauricular lymph adenopathy. There was 4mm proptosis and 3mm inferior dystopia. Computed Tomography (CT) imaging (Figure 2) showed 28 x 21 x 16 mm sized, well defined isodense mass lesion in upper quadrant of left orbit with extrinsic compression of superior rectus, lateral rectus muscles with mild pressure erosion of superior wall of orbit suggestive of tumor of

* *Corresponding author*.
E-mail address: ks.aparna1991@gmail.com (Aparna K S).

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lacrimal gland**.** After explaining the type of lesion and prognosis**,** we did lateral orbitotomy without removal of the lateral orbital rim. A curvilinear incision is made over the lateral orbital wall. Temporalis fossa is exposed using periosteal elevators. Using a combination of blunt and sharp dissection, the lacrimal gland mass is mobilized (Figure 1B). Eventually the mass can be freed from the surrounding tissue with the capsule intact and removed in-toto.

Histopathology (Figure 3) revealed irregular fragments of poorly circumscribed tumour tissue formed by basaloid and myoepithelial cells arranged in tubules and cribriform pattern, with myxoid substance in lumen. Strangulation of tubules in a hyalinized stroma with interspersed pleomorphism, mitosis and individual cell necrosis seen suggestive of adenoid cystic carcinoma of the lacrimal gland. No high grade transformation or perineural invasion was seen. In Immunohistochemistry tumour cells showed positivity for CK7 in the ductal component, while the myoepithelial cells show positivity for p40 and very focally for S 100.

Patient was referred to oncologist and he advised to undergo proton beam radiation therapy. Lacrimal gland ACC, due to its proximity to many vulnerable structures, seems like an ideal candidate for PBRT.Patient completed 6 cycles of image guided radiation proton beam therapy. Radiation Dose: 52.2 Cobalt Gray Equivalent (CGE) in 29 fractions to lymph – nodal region (pre-post auricular region) with simultaneous use of 58 CGE in 29 fractions to postop bed (left lacrimal gland region) followed by boost of 8 CGE in 8 fractions. Total dose of 66 CGE was given in 33 fractions.

Systemic screening was done with head and neck MRI, CT Chest and USG abdomen by oncology team ruled out systemic metastasis. During the post-operative follow up 1 month, BCVA in both the eyes were 6/6 with no palpable mass. A written informed consent was taken from parents (as the patient is a minor) about the use of clinical data for the purpose of the study. At two years follow-up, she remains disease free without evidence of recurrence. Post-operative MRI scan showed no discrete mass in the left lacrimal fossa. No evidence of intracranial extension or dural involvement.

We followed up our patient monthly for every 3 months, then every 3 months for 2 years without any recurrence. Evaluation was done by Radiation oncologist as follows: MRI head and neck was done one month following PBRT, then clinical evaluation every 3 months and MRI head and neck every 6 months for 2 years, after that planning clinical follow up every 3 months and imaging annually or if there is any clinical indication. The study adhered to the ethical principles outlined in the Declaration of Helsinki. A written informed consent was taken from the from parents (as the patient is minor) about the use of clinical data and clinical photographs for the purpose of study.

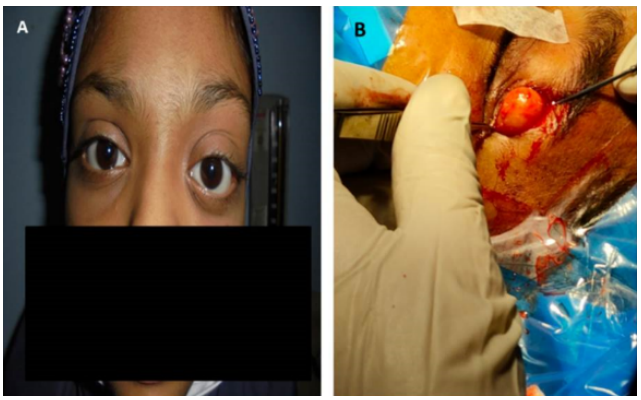

Fig. 1: A: Clinical photograph showing fullness in thesupero-temporal area with inferior dystopia. **B**: Gross image showing well encapsulated mass, during lateral orbitotomy

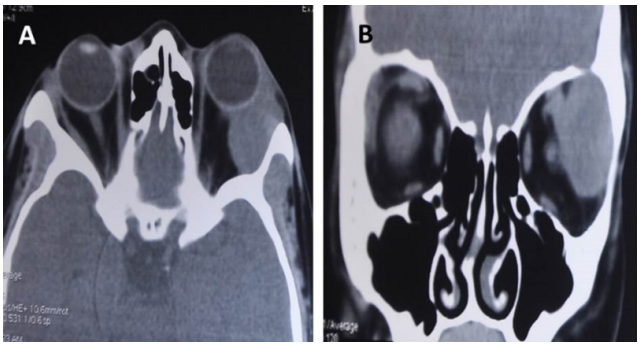

Fig. 2: A: Axial CT, **B:** Coronal CT showing well defined iso-dense mass lesion in upper quadrant of left orbit with extrinsic compression of superior rectus, lateral rectus muscles with mild pressure erosion of superior wall of orbit**.**

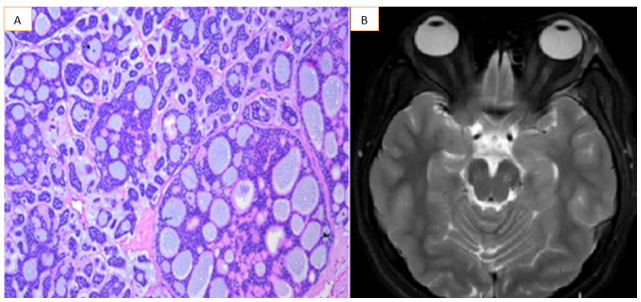

Fig. 3: A: Histopathology picture showing irregular fragments of poorly circumscribed tumour tissue formed by basaloid and myoepithelial cells arranged in tubules and cribriform pattern, with myxoid substance in lumen. **B:** Post-operative MRI T2 weighted image showing no discrete mass in the left lacrimal fossa.

3. Discussion

Due to the small number of patients with lacrimal gland ACC, there is a paucity of literature regarding treatment outcomes and prognosis in younger population. Proptosis in paediatric population is mostly benign. In a retrospective study by Tao et al,[6] the most common benign lacrimal gland tumor was pleomorphic adenoma, in which proptosis is the main symptom. The most common malignant tumor in the lacrimal gland was ACC and the most common reason to seek medical advice was pain in and around the eye. But our patient presented with painless proptosis. So our first clinical differential was benign neoplasm of the lacrimal gland. So we decided to proceed with excision biopsy of the mass.ACC are highly invasive tumors with a tendency to invade along nerves and blood vessels; they can even infiltrate and extend through bone.[7] Most tumors arise de novo, but the few that arise from benign mixed tumors have a better prognosis.[8] With conventional therapy, 10-year survival rates are 20% to 30% only. This poor prognosis is because of high rates of intracranial extension and distant metastases, especially to lung and bone.[9] Histopathology reveals it as malignancy of modified myoepithelial and ductal differentiated cells. Three histological growth patterns: the cribriform (Swiss cheese), solid and tubular forms, seen in varying combinations and dominance. The cribriform pattern is the most common, while the solid pattern is least frequent.[10] Our patient had 80% cribriform pattern and 20% solid pattern. Management of lacrimal gland adenoid cystic carcinoma includes multimodal treatment including combinations of surgical removal, intra-arterial chemotherapy and radiotherapy. Options of surgical management include globe sparing surgery or exenteration. Esmaeli et al studied a series of 11 patients (median age 55 years) undergoing globe-sparing surgery followed by radiotherapy for lacrimal gland carcinoma (7 of the patients had LGACC). All 11 patients were disease free at median follow-up after surgery of 33 months, suggesting that a globe-sparing approach followed by adjuvant radiotherapy or chemo-radiotherapy is associated with reasonable loco-regional control and ocular toxicity profile.[11] Tellado MV et al reported that young patients with adenoid cystic carcinomas have a better prognosis than do adults, probably due to their tumors having less aggressive histologic features.

We have separated the mass from adjacent structures and well encapsulated mass was removed in toto and sent for biopsy. Considering the age of the patient, and poor psycho-social development due to loss of visual function and facial disfigurement, and the lack of clear survival benefit with orbital exenteration, we decided not to proceed with further destructive procedures. We have clearly explained the potential risk of higher local recurrence to the parents. Photon beam radiation does offer better patients survival over conventional modalities and more acceptable cosmetic results, and, at least in the short term, useful visual functioning.[9,11]

A proton beam is composed of charged particles (protons) with a well-defined range of penetration into tissue. As the proton beam penetrates, its particles slow down and deposit a large portion of their energy near the end of their range. A high dose of protons is delivered to a structure, followed by a rapid drop-off, limiting off-target radiation of surrounding normal tissues as compared to other radiation modalities. Because of its precision, PBRT has gained acceptance in the treatment of anatomic areas containing many closely arranged, radiosensitive structures such as choroidal melanomas, as well as head and neck, orbital, and intracranial tumors. The property of proton beams known as the Bragg peak—a high dose of protons is delivered to a structure, and followed by a rapid drop-off, limiting off-target radiation of surrounding normal tissues as compared to other radiation modalities, makes it a precise modality for these tumors.[12] But it is not tried much because of high cost and lack of availability.

The current intra arterial cytoreductive chemotherapy (IACC) treatment protocol is as follows: intra-arterial cis-platinum and intravenous doxorubicin followed by orbital exenteration, removal of involved orbital bone, radiotherapy, and repeat intravenous doxorubicin and cis-platinum.[5,13] To date, there is limited literature on IACC for treating ACC, but it has been promising. The long-term systemic side effects of chemotherapy or secondary malignancy in a child are unknown.

Manjandavida et al[14] compared 3 treatment protocols-surgery + external beam radiotherapy (EBRT) (group 1), surgery + EBRT + adjuvant chemotherapy (group 2), and neoadjuvant chemotherapy + surgery + EBRT + adjuvant chemotherapy (multimodal treatment) (group 3) in 40 patients with lacrimal gland ACC, without systemic metastasis. They concluded that multimodal treatment with sequential neoadjuvant chemotherapy, followed by surgery, extended-field stereotactic EBRT, and adjuvant chemotherapy seems relatively more effective in providing local tumor control and eye salvage and in minimizing the risk of systemic metastasis in ACC of the lacrimal gland.

As lacrimal gland ACC is less prevalent in paediatric population, as well as high cost and low availability of PBRT, there is a paucity of literature regarding treatment outcomes of this modality in paediatric population. In our best knowledge, this is the first reported case of ACC in paediatric age, treated with glob sparing surgery followed by proton beam radiation. The patient was followed for 2 years, with no recurrence and no known complications.

Although most lacrimal gland lesions are benign, for any circumscribed supero-temporal orbital mass lesions, possible malignant neoplasm of the lacrimal gland should be kept in mind as a differential diagnosis, regardless of the age of the patient. Globe lobe-preserving surgery along

with proton radiation is a preferable choice for the treatment of adenoid cystic carcinoma of the lacrimal gland when the tumor is confined to the orbit.

4. Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

5. Conflict of Interest

None.

6. Source of Funding

None.

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Author biography

Maneksha Velu, HOD

Aparna K S, Fellow

Kavya Shetty, Medical Consultant

Jeyapriya T, Post Graduate

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