Case Series

Metastasis to orbit: A case series from tertiary eye center in Western India

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ABSTRACT

This study aims to understand the pattern of the metastatic tumors to orbit in a tertiary eye center. Metastasis to orbit is extremely rare and challenging to diagnose and often mimics with primary orbital tumor. Due to the tremendous recent advances in cancer therapy, surveillance, ancillary histopathology, and imaging techniques for primary tumor diagnosis, the longevity of patients increases, leading to more chances of detection of orbital metastasis. We retrospectively studied and reviewed a case series of five patients with orbital metastasis from various systemic malignancies from 2018 to 2023. Out of five patients, three patients were from metastasis from breast carcinoma, one from neuroblastoma, and monophasic synovial sarcoma each, found a median age of 49 years (range=3–70 years). The most common symptoms and sign were painful proptosis and restriction of ocular motility, respectively.

Key words: Metastasis to orbit, Breast carcinoma, Neuroblastoma, Monophasic synovial sarcoma.

Orbital metastasis is an uncommon and varied clinical presentation that depends on the underlying tumor. Most of the time, diagnosis is unexpected and delayed affecting subsequent definitive management [1]. The incidence of orbital metastasis ranges from 1% to 13% among reported series [1,2]. The clinical symptoms of orbital metastasis, such as restriction in ocular mobility, proptosis, diplopia, pain, and periorbital swelling, are similar to those of primary orbital tumors, such as idiopathic pseudotumor and IgG4-related orbital disease or any other soft-tissue tumor of orbit.

The purpose of this case series is to review and report metastasis to the orbit, demographic and clinical features, diagnostic challenges, and management of orbital metastasis in relation to the primary tumors at the tertiary eye center of Western India.

CASE SERIES

Five patients diagnosed with orbital metastasis at the M and J Western Regional Institute of Ophthalmology, Civil Hospital, Ahmedabad, Gujarat, tertiary eye center in Western India in a 5-year period (2018–2022) were included in this case series. Approval was taken from the Institutional Ethics Committee. General data included the patient's age, sex, history of primary cancer, clinical presentation, and history of prior treatment of primary tumor, if taken were recorded.

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Tumor data included location in the orbit, laterality, histopathology, immunohistochemistry (IHC) diagnosis, relevant radiological investigation, treatment modality, and outcome, whenever available were evaluated and mentioned in Table 1.

DISCUSSION

It is presumed that 2–5% of patients with systemic malignancies develop orbital metastases [3]. While 85% of patients with orbital involvement carried a known cancer diagnosis, in the remaining 15% metastasis was the initial manifestation of malignancy [1]. Magliozzi *et al.* documented 93 patients over a 38-year period and found a median age of 51 years (range=1–88 years) [3]. We found a median age of 49 years (range=3–70 years) in our case series.

Breast cancer metastasizes to the orbit more frequently, representing 29–53% of cases [4]. The time from diagnosis of breast cancer to the onset of orbital metastases is usually prolonged, with an average of 2–8.5 years [5]. In our case series, a 51-year-old female who had undergone modified radical mastectomy (MRM) post-neoadjuvant chemotherapy developed metastasis after eight years of treatment. In contrast to other primaries, bilateral metastases can be seen in 15–20% of breast carcinoma cases. Overall, orbit remains a rare site even for breast cancer metastasis. Orbital metastasis may present with symptoms such as proptosis, double vision, decreased visual acuity, pain,

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Table 1: Clinicopathological Summary of all cases of metastasis to orbit

S. No.	Primary tumour/ histological subtypes/laterality	Age/ sex	clinical symptoms/ signs	Laterality and location in orbit	Investigations	Other findings and relevant Investigations	Treatment
Case-1	Breast cancer/ Invasive lobular carcinoma of the left breast	47/F	Left eye proptosis, decreased visual acuity and left orbital pain - Absence perception of light in left eye, and reduced visual acuity in the right eye	Bilateral left side > right side orbit	MRI of the orbits revealed multiple lobulated soft tissue nodular altered signal intensity lesion intraconal& extraconal aspect of retro-orbital in both orbits with diffuse enlargement and involvement of extraocular muscles	Few skin nodules on the chest wall, ER, PR strongly positive and Her2neu negative	- Orbital lesions were irradiated with the use of external beam radiotherapy, - Vision in the right eye could be salvaged after 3 months. - Continue treatment with Letrozole and bisphosphonate
Case-2	Breast cancer/ Infiltrating duct carcinoma of the left breast	51/F	Left eye, infraorbital rim	Left inferior aspect of the orbit	MRI-Moderate to intense enhancing mass lesion extraconal mass lesion inferior aspect left orbit, bone destruction, extension to the roof of maxillary bone (Fig. 2b)	ER, PR - Positive and Her2neu- negative	Premenopausal, post-neoadjuvant chemotherapy MRM done 2015- residual tumor present, adjuvant CT and RT. cT4bN1
Case-3	Breast cancer/ Infiltrating duct carcinoma of left breast	70/F	Left eye, swelling superiomedial orbit, ptosis	Right orbit, superiomedial aspect	MRI-Altered signal intensity lesion involving the right extraconal orbital region.	ER, PR - Positive and Her2neu- negative	Hormonal therapy, tamoxifen and letrozole
Case-4	Neuroblastoma	3/M	Left eye proptosis and swelling	Left orbit-superiorolateral aspect	MRI- ill-defined iso-hypodense soft tissue lesion noted extraconal involving sup. lateraland sup. rectus causing bony erosion of roof and lateral wall orbit (Fig. 2a)	On CT scan, mass in left adrenal- image guided biopsy revealed diagnosis of neuroblastoma. Further confirmed by IHC. Synaptophysi, chromogranin, CD56, neuron specific enolase, negative for desmin	4–6 cycles of multi-agent chemotherapy, carboplatin, cyclophosphamide, doxorubicin, and etoposide.
Case-5	Monophasic synovial sarcoma	64/F	Right eye proptosis and pain	Right orbit, superiolateral aspect	5×4.5 cm mass on superiolateral aspect of right orbit	Patient had history of excixion of mass with negative margins around right knee, diagnosed as monophasic synovial sarcoma, later confirmed by IHC- Vimentin, CK, bcl-2, calponin positive and S100, desmin, CD34 negative	Surgery (Wide excision with negative margins)+chemotherapy (combination treatment with doxorubicin and ifosfamide)

MRI: Magnetic resource imaging, IHC: Immunohistochemistry, CT: Computed tomography, M: Male, F: Female

chemosis, ptosis, or orbital bony involvement [6]. Three out of five cases in our case series were breast cancer patients having a median age was 51 years and painful swelling along with proptosis was their common presentation. Out of three cases of metastatic breast cancer to orbit, one case was bilateral orbital involvement associated with many metastatic skin nodules corresponding to invasive lobular carcinoma of the breast, which has the propensity of hematogeneous metastasis to the body [7].

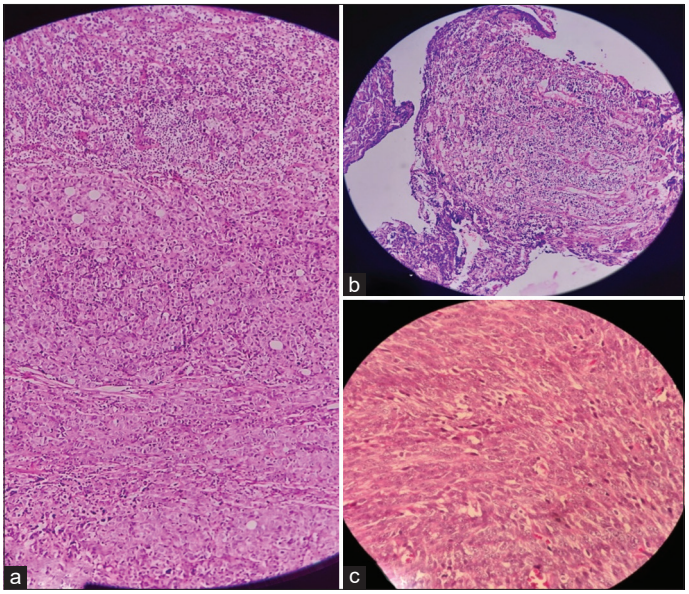

Figure 1: (a) H and E stain (×20) shows sheets of pleomorphic ductal epithelial cells of breast having vesicular nuclei admixed with inflammation; (b) H and E stain (×10) shows infiltration of small round cells of neuroblastoma in fibrocollagenous tissue and congested vessels; (c) H and E stain (×20) shows fascicles of monomorphic spindle cells having vesicular nuclei of monophasic synovial sarcoma and congested vessels

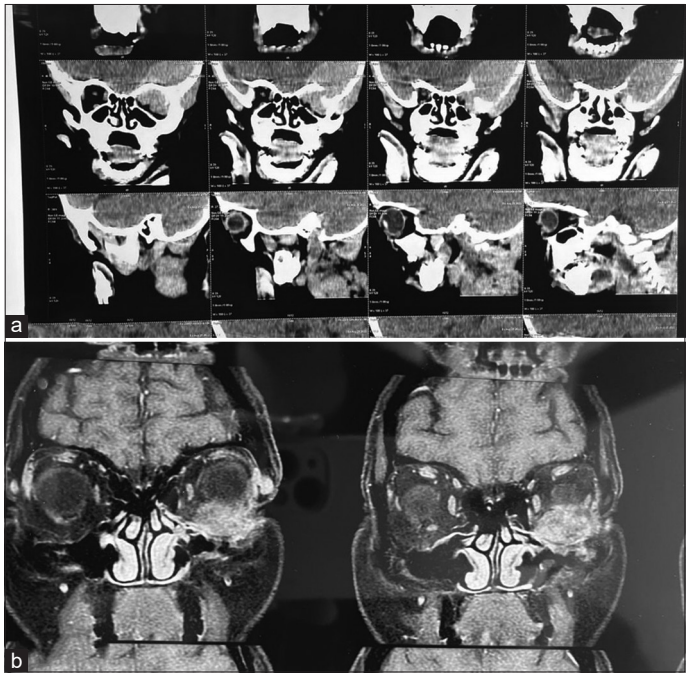

Figure 2: (a) Magnetic resource imaging (MRI) of head/neck and orbit neuroblastoma ill-defined iso-hypodense soft-tissue lesion noted extraconal involving superior lateral and superior rectus muscle causing bony erosion of roof and lateral wall orbit; (b) MRI of orbit mass of left infraorbital rim in carcinoma of breast metastasis. Moderate to intense enhancing mass lesion extraconal mass lesion inferior aspect left orbit, bone destruction, and extension to roof of maxillary bone

The other two cases were of invasive duct carcinoma of the breast (Fig. 1a). The treatment can be adjusted depending on the clinical presentation, the extent of the metastatic disease, and the immunohistochemical status of the primary tumor. The prognosis of breast cancer with an orbital involvement has been reported to be very poor with survival ranges from 1 to 116 months with a mean of 31 months [7]. All three cases were lost to follow-up in our series.

Neuroblastomas are the most frequently identified extracranial tumors that affect children under the age of 4 years old, with an incidence of approximately 1–3 in 100,000 cases [8]. Orbital neuroblastoma metastasis is relatively rare and is associated with poor prognosis. Ahmed *et al*., studied a series of neuroblastoma cases, of which, the most common presentation was proptosis, restricted eye movement, and 12.5% were having an orbital metastasis, giving a male-to-female ratio of 2:1. The average age of presentation was 29.8 months (15–69 months) [9]. Orbital involvement falls in the high-risk category and therefore aggressive multi-agent chemotherapy consisting of very high doses is employed [9]. Neuroblastoma cases with initial symptoms of orbital involvement are rare, accounting for approximately 8% of all neuroblastomas. Our case of a 3-year-old male child presented with proptosis and subsequently detected adrenal neuroblastoma (Fig. 1b). The role of IHC and systemic workup is necessary to diagnose and rule out other small round cell tumors in the pediatric age group in this region. On the last follow-up, the child had taken the first dose of chemotherapy.

Synovial sarcoma (SS) is a rare malignant soft-tissue neoplasm that accounts for approximately 5%–10% of all soft-tissue tumors, often presents in children and young adults, and primarily occurs in the para-articular regions of the extremities [10]. The orbit is an extremely rare location for metastatic SS. Our study has a case of monophasic SS with metastasis to orbit, presenting as proptosis (Fig. 1c). To the best of our knowledge, we have not found any metastatic monophasic SS to orbit in the English literature. IHC is required for diagnosis and to rule out other primary spindle cell neoplasms arising from the orbit. The patient did not come for a follow-up after the orbital biopsy.

Although our study has a limited period and a small number of cases due to the rarity of orbital metastasis, a larger study from India is required for a better understanding of the epidemiology, the interval between primary to metastasis, the mode of spread of tumor, and response to treatment to the primary tumor. In literature, the majority of orbital metastases are carcinomas; the frequency of different sites of primary disease varies between different reports mainly due to study period, number of cases, and geographical variation in certain tumors. The most common is breast carcinoma (28–58.5%), followed by lung, melanoma, and liver cancer [4].

CONCLUSION

In concordance with the literature, our study also shows breast cancer commonly metastasizes to the orbit. While neuroblastoma should be considered as differentials in a small round cell tumor of a child presenting as orbital mass, a necessary systemic workup should be done to detect primary. Appropriate IHC and molecular study will be necessary to detect this extremely rare orbital metastasis of monophasic SS.

The prognosis of orbital metastasis remains poor due to the higher stage of disease and systemic metastasis. Metastasis to orbit is rare, so, ophthalmologists must remain vigilant. A higher level of suspicion, systemic workup, and IHC for precise diagnosis and appropriate timely management are important to salvage vision and life.

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