RESEARCH ARTICLE

Spectrum of metastatic tumours to orbit over the last twenty years in a tertiary care eye hospital-A retrospective study

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Abstract

Objective: To assess the type and presentation patterns of tumours metastasising to orbit.

Method: The retrospective study was conducted at the Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan, and comprised data of all patients with orbital metastatic lesions over a 20-year period, from January 1, 2004, to December 31, 2023. Data was analysed using SPSS 22.

Results: Of the 30 patients, 17(56.7%) were males and 13(43.3%) were females. The highest incidence of orbital metastatic disease was among those aged <10 years 9(30%) and >60 years 11(36.7%). Roof was the commonest site of involvement within the orbit 13(43.3%). Proptosis was the main feature at presentation. Diagnosis was made clinically in 14(46.7%) patients and histologically in 16(53.3%). All the 30(100%) cases were referred to the oncology service for further management. Of them, 2(6.7%) patients were lost to follow-up, 20(66.7%) died within one year of diagnosis, and 8 (26.6%) patients were still under treatment.

Conclusion: The diagnosis of orbital metastasis should always be considered for orbital lesions in all age groups, especially in patients with a known cancer elsewhere. Orbital metastasis usually becomes evident at an advanced stage of underlying malignancy, leading to a high mortality rate.

Key Words: Orbital metastasis, Orbital tumours, Orbital malignancies.

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Introduction

Orbital metastasis often heralds an advanced stage of malignancy and poses a great challenge clinically. Although relatively infrequent, this insidious involvement of the orbit by the cancer cells can deeply influence the prognosis and patient morbidity.[1] An earliest possible identification of metastatic lesion in orbit followed by thorough investigation to pinpoint the primary lesion is vital for a better prognosis.

Orbital metastatic deposits are far less common than uveal metastases, and around 2-4% of orbital biopsies lead to a diagnosis of a metastatic disease.[1,2] The discovery of the metastatic orbital lesion before the primary neoplasm is mostly seen, with the primary sites commonly being lungs, breast, gastrointestinal tract (GIT), prostrate, thyroid, melanomas, kidneys and adrenal glands.[2-4] On the contrary, majority of the tumours metastasising from the breast have had the primary treatment before the orbital presentation.[5] In some cases, the primary site may not be determined at all.[4]

Clinically, orbital metastasis may present as proptosis, globe displacement, diplopia and restricted ocular movement, orbital and ocular pain, ptosis or even a palpable mass.[6-8] Every patient, with a known history of active or past cancer, presenting with any of these symptoms must be evaluated for orbital metastasis. It is estimated that about half of the patients with orbital metastasis are unaware of a primary malignancy when they see their ophthalmologist.[8] This fact highlights the crucial role of the ophthalmologist in diagnosing the pathology at the earliest in order to initiate a proper management plan to maximise the chances of an optimistic outcome.

Imaging, including computed tomography (CT) scan and magnetic resonance imaging (MRI), plays a crucial role in detecting and identifying an orbital lesion and differentiating between benign and malignant diseases.[9] However, the radiological features of orbital metastases are still not diagnostic unless against a known background of an active metastatic disorder.[10] Thus, the definitive diagnosis, in cases where an element of uncertainty is present, relies on histological and immunohistochemical (IHC) analysis of a tissue biopsy through either excisional or incisional approach.

The current study was planned to assess the type and presentation patterns of tumours metastasising to orbit.

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Materials and Methods

The retrospective study was conducted at the Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan, and comprised data of all patients with orbital metastatic lesions over a 20-year period, from January 1, 2004, to December 31, 2023. Only data of patients with conclusive clinical or histological evidence of metastasis to the orbit were included, while cases in which there was an element of contiguous spread to the orbits from adjacent organs as well as leukaemia and lymphoma involving the orbit were excluded.

After approval from the institutional ethics review board, the data was retrieved from the archives using consecutive sampling technique. All the pictures of patients and their radiological records had been taken with written informed consent of the patients, including the permission to share publicly for academic purposes.

All the cases had been evaluated and managed by the Orbit and Oculoplastic Department as well as by oncology services at the same hospital and at other sites. The diagnosis of orbital metastasis had been made clinically on the basis of history, examination and imaging where sufficient evidence was available to indicate metastatic disease. In cases where biopsy was indicated, either excisional or incisional, it was performed by a senior professional and submitted to the coordinating Pathology Department, where histological analysis was performed on all specimens and IHC study had been done as and when required.

The current study used a computerised flowsheet to document and tabulate general data, tumour data, clinical findings, diagnostic techniques, treatment and prognosis. General data included the patient's age, gender and history or knowledge of a pre-existing primary tumour. Tumour data included the location and type of the primary tumour, laterality (right orbit, left orbit, both orbits), location within the orbit and other secondary sites in addition to the orbit, as evaluated by CT, MRI, clinical, surgical or pathologic observations. The involvement of other ocular sites for metastasis was recorded as well. Patient outcomes were also tabulated where the record was available.

Data were analysed using SPSS 22. Descriptive statistics were applied to summarize demographic and clinical characteristics. Chi-square tests were used to assess associations between categorical variables, while independent-samples t-tests (or Mann-Whitney U tests for non-normal distributions) compared continuous variables across groups. Statistical significance was set at $p<0.05$.

Results

Of the 30 patients, 17 (56.7%) were male and 13 (43.3%) were female. There was no significant difference between males and females for having an orbital metastasis ($p>0.05$) even though the common primary tumour sites were not the same. Among the male patients, 8 (47.1%) were under the age of 20, and 9 (52.9%) were 20 years or older. In contrast, among the female patients, only 2 (15.4%) were under 20 years of age, while 11 (84.6%) were older. While analysing age and gender together, there were two spikes noted in the incidence of orbital metastatic disease; one at <10 years and then during 7th

Table: Orbital location of metastatic lesions with relation to their primary sites of origin.

Site within the orbit	No. of Patients	Site of Origin	Site within the orbit	No. of Patients
Periorbital soft tissue	4 (13.3%)	Thyroid, Neuroblastoma	Periorbital soft tissue	4 (13.3%)
Roof	13 (43.3%)	Neuroblastoma, HCC, Thyroid, Lung, Breast, CUP, Meningioma	Roof	13 (43.3%)
Lateral extraconal space (including lacrimal glad)	8 (26.7%)	RCC, Neuroblastoma, Thyroid, Breast, Ewing, Lung, Plasma cell	Lateral extraconal space (including lacrimal glad)	8 (26.7%)
Medial extraconal space	3 (10.0%)	Neuroblastoma, Breast, CUP,	Medial extraconal space	3 (10.0%)
Intraconal space	2 (6.7%)	Gut, Breast	Intraconal space	2 (6.7%)
Muscles	2 (6.7%)	Breast	Muscles	2 (6.7%)
Diffuse orbital involvement	4 (13.3%)	Fibrosarcoma knee, Ear, CUP, Neuroblastoma,	Diffuse orbital involvement	4 (13.3%)

HCC: Hepatocellular carcinoma, CUP: Carcinoma of unknown primary, RCC: Renal cell carcinoma..

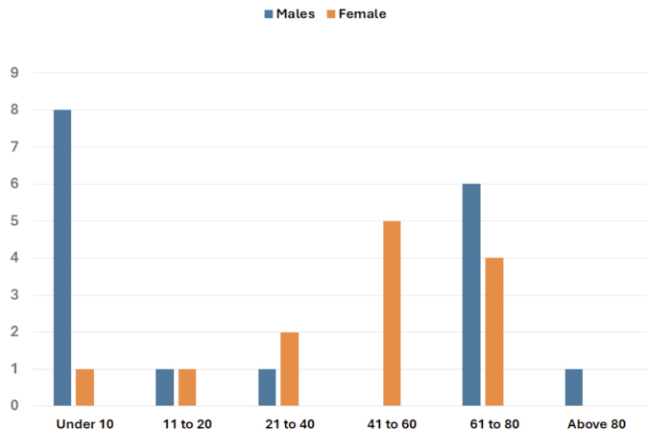

Figure-1: The incidence of metastatic orbital diseases in different age and gender groups.

to 8th decade of life. There was a male preponderance at those spikes (Figure 1).

Half of the patients 15(50%) had a known primary tumour at the time of their orbital metastasis presentation, while the rest did not have any prior documented malignancy.

The primary tumour site was successfully identified in 27(90%) patients. Among these, breast, lung and thyroid cancers were the most common primary sites in adults, each accounting for 4(13.3%) patients. Notably, neuroblastoma, originating from the adrenal glands, was the primary tumour in 7(23.3%) patients, all of whom were children aged <10 years. The remaining cases included primary tumours arising from bone 2(6.7%),

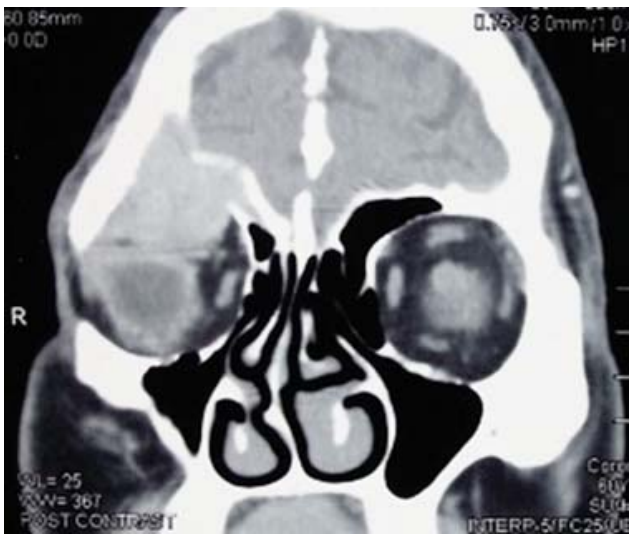

Figure-2: Computed tomography (CT) scan showing the coronal view of a metastatic lung cancer mainly involving the roof of the right orbit and extending onto lateral and medial walls. Erosion of orbital roof is also present.

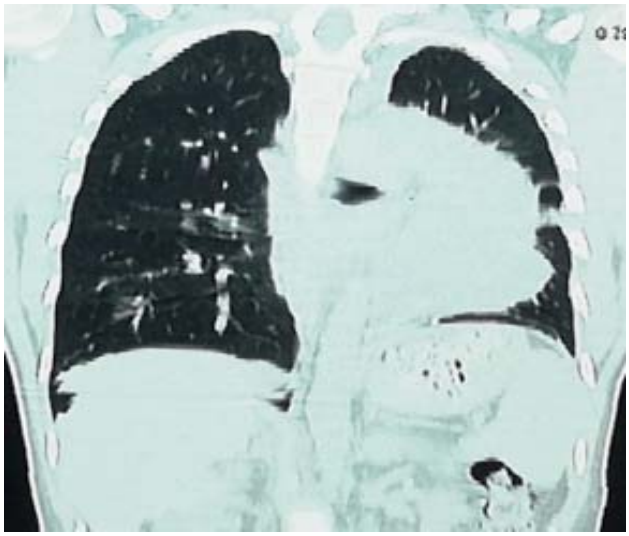

Figure-3: Computed tomography (CT) scan of a patient of left lung cancer showing the lesion involving the left lung and the mediastinum. The patient also had metastatic lesions in the skull and orbit.

liver, kidney, brain, gut, middle ear, and plasma cells of bone marrow 1(3.3%) each. In 3(10%) cases, the primary tumour site remained unidentified, and these were classified as carcinoma of unknown primary (CUP) (Table).

The left orbit was most frequently involved 14(46.7%) patients, followed by the right orbit 11(36.7%). Bilateral orbital involvement was observed in 5(16.7%) patients. Within the orbit, the orbital roof had the highest affinity for metastatic disease 13(43.3%) (Figure 2). Other common sites included the lateral extraconal space, including the lacrimal gland, 8(26.7%) patients, periorbital soft tissues 4 (13.3%), and the medial extraconal space 3(10%). Less frequent involvement was noted in the intraconal space and the muscles 2(6.7%) patients each.

The most common presenting complaint was proptosis, or forward displacement of the eye, observed in 25(83.3%) patients. Other presenting features included periorbital swelling 6(20%), dystopia, or abnormal eye position, with or without proptosis 4(13.3%), and, less commonly, orbital pain, ptosis, or drooping eyelid, and enophthalmos, or backward displacement of the eye.

The diagnosis of orbital metastasis was established clinically in 14(46.7%) patients based on a combination of detailed history, clinical examination, and imaging findings that strongly suggested metastatic disease in the context of a known primary malignancy and/or concurrent extraorbital involvement. In the remaining 16(53.3%) cases, a biopsy was necessary to confirm the diagnosis. Of these, 12(75%) underwent excisional biopsy, meaning complete removal of the lesion, and 4(25%) had

incisional biopsy, meaning removal of a portion of the lesion.

All the 30(100%) cases were referred to the oncology service for further management. Of them, 2(6.7%) patients were lost to follow-up, 20(66.7%) died within one year of diagnosis, and 8 (26.6%) either survived beyond one year or remained under treatment.

Discussion

Metastasis to orbit is uncommon. Various studies have reported the orbital metastatic disease to be 2-4% of all orbital tumours.[1-3] Many authors have shared their experiences dealing with orbital metastatic disease, highlighting different aspects of the issue.[8,11-13]

Recently a systematic review was done on the available literature on orbital metastasis regarding the clinical characteristics, management strategies and treatment outcomes.[14] The review included 262 studies for analysis and concluded that metastasis to orbit is rare, but causes significant morbidity in cancer patients.[14]

Differences exist between the frequencies of the common primary tumour sites across the globe, possibly due to underlying geographical variation and genetics, but majority of the studies have shown breast cancer being the commonest primary tumour to disseminate to orbit.[15-17] Other common documented primary sites are lungs, liver, kidneys, skin and prostrate.[17] Neuroblastoma is the commonest childhood malignancy to metastasise to orbit.[17]

Lung cancer is known to be one of the globally prevalent primary sites for orbital tumours, but histological documentation of orbital metastatic lesions usually does not reflect the same prevalence. This might be because lung cancer, especially small cell lung cancer, being one of the most aggressive cancers, has a high metastatic potential earlier in the course of the disease, and may quickly spread and involve multiple major organs besides orbit.[18] (Figure 3)

In the current sample, there was no significant difference between males and females for having an orbital metastasis even though the common primary tumour sites were not the same. While analysing age and gender together, it was interesting to note that there were two spikes in the incidence of orbital metastatic disease; one <10 years and then during the 7th to 8th decade of life. Another interesting observation was that there was a male preponderance at those spikes (Figure 1).

It must be emphasised that half of our patients were unaware of a primary malignancy and presented only due to orbital symptoms. This fact highlights the need to consider and investigate the diagnosis of orbital metastatic disease actively. All cases of lung cancers were pre-diagnosed due to widespread involvement before presenting to the health facility. The cases of multiple myeloma, middle ear rhabdomyosarcoma, gut, knee and ankle joint tumours were also diagnosed before orbital presentation. On the other hand, most cases of visceral malignancies were established only after the appearance of orbital metastases.

Lung cancer predominantly involved males (75%) probably due to higher prevalence of smoking in males in the study population, while thyroid cancer patients were mostly females (75%). Neuroblastoma showed a clear tendency to involve males, and accounted for 6 out of 7 of such patients. No specific pattern could be inferred from the remaining cases due to fewer number of patients of those malignancies. It is interesting to state the fact that none of the current male patients was found to have a prostatic cancer metastasising to orbit, or at least none could be established with such a diagnosis despite the fact that prostate has been frequently shown to metastasise to orbit in various studies.[16,17]

All cases of lung cancers and 75% of breast cancers in the current study showed metastasis to the left orbit irrespective of the laterality of the primary organ. Furthermore, about 70% of neuroblastomas showed an affinity for the right orbit, while only 1 case involved the left orbit alone, and 1 invaded both the orbits. Overall, the involvement of the left orbit was found to be most common, with 14 cases having metastatic disease in the left orbit alone, 11 in the right orbit alone, and 5 having bilateral involvement.

Within the orbit, the orbital roof had the highest affinity for metastatic disease (43.3%). Lateral extraconal space also harbours a high incidence of metastasis, and in the current study about a quarter of patients exhibited the involvement of this area. Other common sites were periorbital soft tissues and medial extraconal space. Less frequent involvement was seen for intraconal space and the muscles. It may be noteworthy that the lung cancer was only found in the roof, while breast cancer could metastasise to any part of the orbit. Extraocular muscle involvement was only seen in breast cancer cases, while the integrity of the intraconal compartment could only be breached by breast and gut tumours. Neuroblastoma was another malignancy that was found at multiple sites within the orbit.

Orbital metastases tend to manifest abruptly in contrast to the benign orbital tumours, and the symptoms

progress rapidly.[19] Proptosis is one of the commonest presenting features of orbital metastasis[20], and it accounted for 83% of the current patients. Other common presenting features were dystopia, periorbital swelling, orbital pain and ptosis. Infrequently, patients may present with enophthalmos of the involved side due to neoplastic infiltration, causing fibrosis of extraocular muscles and retro-bulbar stromal tissues.[21]

The orbital metastasis generally carries a poor prognosis and the survival rate depends on the type of primary tumour, stage of the disease, and the extent of spread at diagnosis. Brain metastasis shows a relatively better survival rate of 46% at one year.[22] The one-year survival rate in the current orbital metastasis patients was found to be 26.6%. This implies that the orbital metastasis usually comes to attention at an advanced stage of underlying malignancy and the diagnosis is hence delayed. This further highlights the need for improvement in screening and therapeutic approaches in order to detect and manage such cases at an earlier stage.

The current study has limitations, including the retrospective design and the relative infrequency of orbital metastases cases which affected the sample size. However, the cohort provided valuable insights into the characteristics and outcomes of the condition within the studied population.

Conclusion

Diagnosis of cases involving orbital metastasis should be considered for orbital lesions in all the age groups, especially in patients with a known primary carcinoma elsewhere. At times, the metastatic lesion may be diagnosed even before the primary lesion is even suspected. The orbital metastasis usually becomes evident at an advanced stage of underlying malignancy, and the diagnosis is hence delayed, leading to a high mortality rate.

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FT: Concept, design, data collection, writing and critical revision.
TA: Concept, data interpretation and drafting.
SA: Literature review, data validation and statistical analysis.
AM: Data management, organization and assistance in data analysis.
FT: Editing, formatting and preparation for submission.
SAK: Figures and tables preparation and proofreading.
MS: Review, quality control and final approval.