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Co-existence of metastatic uterine sarcoma and orbital sarcoidosis: A case report and literature review

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Abstract. A 77-year old lady with previously treated endometrial sarcoma presented with progressive left upper lid mechanical ptosis secondary to superior orbital mass. An orbital biopsy confirmed the diagnosis of orbital sarcoidosis. Further systemic work up revealed suspicious pulmonary nodules which were found to be endometrial sarcoma metastases rather than systemic sarcoidosis on image guided biopsy. She was treated with 20 months of chemotherapy for metastatic sarcoma. The ptosis completely resolved, however, pulmonary metastases progressed despite chemotherapy. The co- existence of malignancy with sarcoidosis should be considered in all cases of new onset sarcoidosis. Biopsy of suspicious lesions, close observation and multidisciplinary team management is advocated for these patients.

Key words: Sarcoidosis, sarcoma, metastasis

Introduction

Sarcoidosis is a multisystem chronic condition of unknown aetiology, characterised by persistent granulomatous inflammation (1). It promotes malignancy by inducing tumour promoting and immune regulating substances (2). In 1972, Brincker first demonstrated a relationship of sarcoidosis and lymphoproliferative disorder (3). Subsequently, there have been numerous reports of the coexistence of sarcoidosis and metastasis either preceding or following carcinoma (4,5). The association between sarcoidosis and sarcoma is less commonly reported in literature (6). Here, we present a rare case of orbital sarcoidosis in a patient with metastatic uterine/endometrial sarcoma where the investigation of orbital sarcoidosis led to the diagnosis of coexistent asymptomatic metastatic disease.

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Case report

A 77 years old Caucasian lady presented to the outpatient clinic with progressive left upper lid ptosis without significant past ocular history (Figure 1). She had a background history of uterine/endometrial sarcoma (undifferentiated FIGO 1B stage) which was treated surgically (total abdominal hysterectomy and bilateral salpingo-oopherectomy) 5 years earlier with no recurrence noted on regular six-monthly radiological surveillance up to 2 years post-surgery.

Clinical examination revealed 3 mm of left relative ptosis with a palpable firm non tender mass in the supero-anterior orbit. Visual acuity was 6/9 in each eye. Exophthalmometry measurements were 16mm in right eye and 17mm in left eye, giving 1mm of left

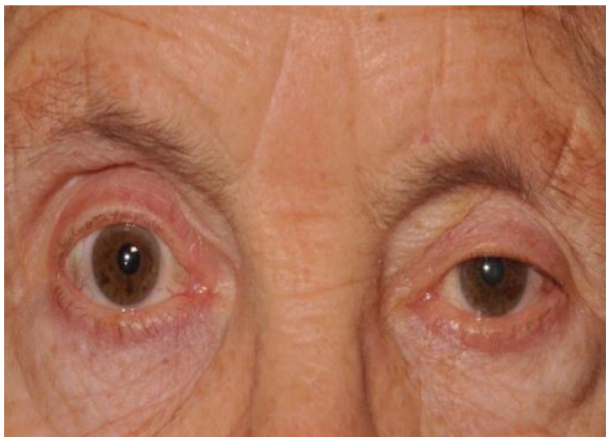

Figure 1. Clinical photograph showing left upper lid ptosis at initial presentation.

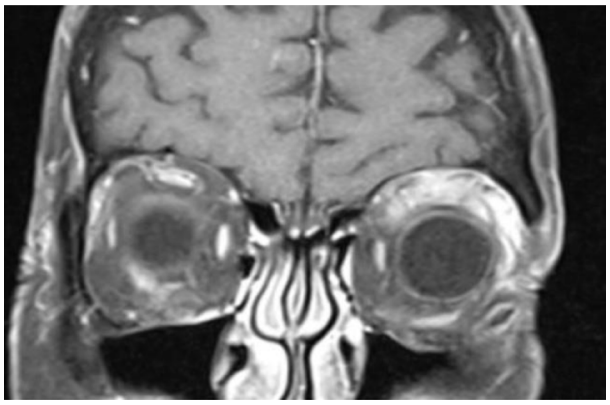

Figure 2. MRI of the orbit showing heterogenous enhancing soft tissue mass in left antero-superior orbit.

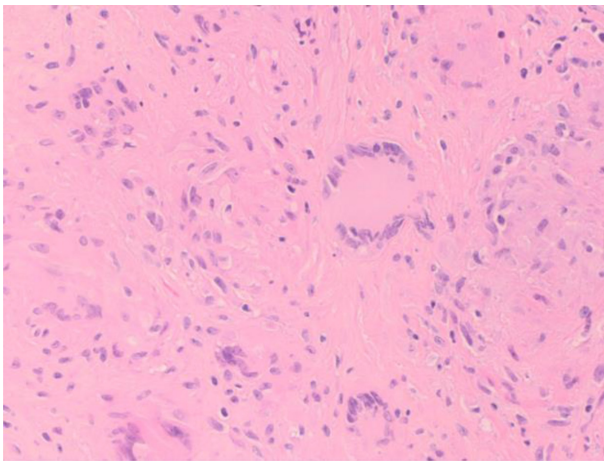

Figure 3. Pictomicrograph depicting non-caseating granuloma in orbital biopsy specimen characteristic of sarcoidosis.

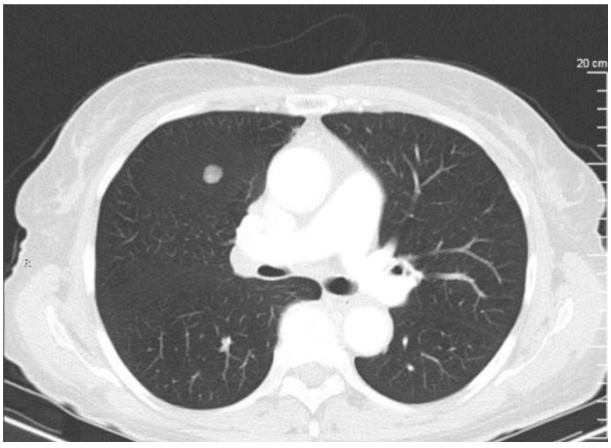

Figure 4. CT thorax during systemic work up showing multiple pulmonary nodule.

relative proptosis. She had no anisocoria, full ocular motility and normal anterior and posterior segments. Blood inflammatory markers including serum angiotensin-converting enzyme (ACE) level were normal. An enhancing soft tissue lesion measuring 20 x6 mm in left anterior-superior orbit, not involving muscle or lacrimal gland, was seen on magnetic resonance imaging (MRI) (Figure 2). An incisional orbital biopsy demonstrated non-caseating granulomatous inflammation consistent with sarcoidosis (Figure 3). No other clinical features of systemic sarcoidosis were identified.

The computed tomography (CT) scan of the thorax, performed as a part of systemic work up for sarcoidosis, revealed multiple large (8-12mm) pulmonary nodules and few scattered tiny nodules along with enlarged hilar and mediastinal lymph nodes (Figure 4). Image-guided biopsy of the nodules demonstrated, on histological analysis, undifferentiated pleomorphic cells with inconspicuous mitosis and focal necrosis and high Ki-67 proliferation, suggestive of recurrent metastatic pulmonary sarcoma secondary to uterine/endometrial sarcoma.

Treatment was initiated by oncology department at our hospital with first line chemotherapy (doxorubicin, olaratumab and prednisolone), to which the orbital lesions responded very well with complete resolution of ptosis on clinical examination (figure 5). However, the pulmonary lesions were found to be

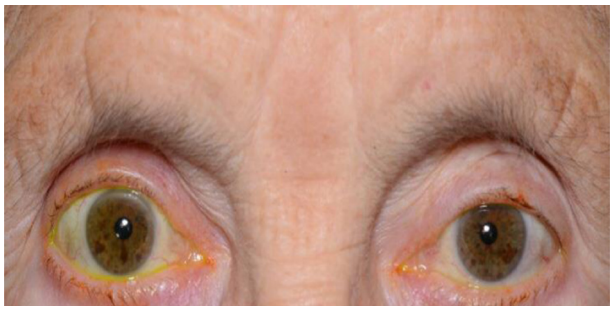

Figure 5. Clinical photograph showing complete resolution of left upper lid ptosis following chemotherapy.

progressive, for which the second line chemotherapy (trabectedin) was commenced. Due to symptomatic drop in left ventricular ejection fraction as an adverse reaction to trabectedin, third line chemotherapy (Docetaxel and Gemcitabine) was started. After receiving 20 months of chemotherapy, it was finally stopped due to side effects and persistently progressive pulmonary lesions. She is currently undergoing palliative care under oncology team.

Discussion

We believe that this is the first case to our knowledge of isolated orbital sarcoidosis co-existing with asymptomatic pulmonary metastasis from previously treated endometrial/uterine sarcoma. The orbital sarcoidosis responded well to steroids given as part of her oncology treatment, as may be expected.

Although, lung is most common organ involved in sarcoidosis, ocular disease may be the initial presentation in sarcoidosis in approximately 25% cases (7). Uveitis is most common presentation in ocular sarcoidosis; however, it may involve any part of the eye including various structures in the orbit and lacrimal apparatus such as lacrimal gland, soft tissue, extraocular muscles and optic nerve sheath (8,9). It frequently involves antero-inferior orbit (10) in contrast to our case where it involved antero-superior orbit.

Orbital sarcoidosis is an uncommon manifestation of sarcoidosis and is usually seen in females over 50 years of age (11). In a large case series of 202 patients with ocular sarcoidosis, Obenauf et al found orbital lesions in only 2 (0.9%) patients (12). It presents as a rapidly progressive non tender pseudo-tumour, occasionally with proptosis which is commonly misdiagnosed for a malignant orbital tumour. It is usually found in association with systemic involvement (10,13). There are only few reports in literature with patients with isolated orbital sarcoidosis without systematic involvement (13,14).

Several studies have suggested that the patients with sarcoidosis are at two-fold greater risk of developing cancers such as haematological malignancies, lung cancer as well as in other organs affected in sarcoidosis (4,6,15,16). On the other hand, sarcoidosis has also been reported to occur in patients with malignancies (5). So far, to our knowledge, the occurrence of orbital sarcoidosis with endometrial/uterine sarcoma is not reported in the literature.

The diagnosis of sarcoidosis is based on the presence of non- caseating granuloma on tissue biopsy along with associated systemic features (17). The development of sarcoidosis in patients with a history of cancer has been reported to be associated with primary tumour recurrence or a new secondary malignancy (15). Occasionally, in patients with malignant disease, non-caseating epitheloid cell granuloma are found in lymph node draining a region containing malignant tumour or in vicinity of the tumour itself, without any clinical evidence of systemic sarcoidosis. These tumours associated granulomas in the lymph nodes have been termed as 'sarcoid-like reaction' (18). We believe that the orbital lesion in the present case, based on its location, is a case of sarcoidosis rather than sarcoid-like reaction. Contrary to the usual association of elevated serum ACE in sarcoidosis, it was normal in the present case. This correlates with the finding of Birnbaum et al, who suggested that normal ACE level does not exclude sarcoidosis especially in case of isolated ocular disease (19).

Several mechanisms have been proposed to explain this relationship between sarcoidosis and cancers; chronic inflammation, immune dysfunction, shared etiological agents and genetic susceptibility to both cancer and autoimmune diseases (20). We believe that immune response to the tumour may as well increase the activity of sarcoidosis, whereas the cancer chemotherapy may suppress the activity of the sarcoidosis, as seen in the present case. Moreover, the occurrence of

sarcoidosis in cancer patients is regarded as poor prognostic sign especially in patients under 65 years of age (21). In our patient too, the metastatic lesions were resistant to all lines of chemotherapy.

To conclude, a high degree of suspicion is needed by ophthalmologists to consider the possibility of malignancy or metastasis in patients with sarcoidosis, particularly with previous history of cancers, and the biopsy of suspicious lesions should be undertaken to characterise the lesion. Close monitoring and aggressive treatment are needed as this subgroup of patients are considered to have a worse prognosis.

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