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Marginal zone lymphoma of mucosa associated lymphoid tissue-lymphoma of the lacrimal gland in a young patient with Klinefelter syndrome: a case report

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Abstract

Background Klinefelter syndrome is considered one of the most common sex chromosome disorders affecting males. The presence of an extra X chromosome can alter the tendency to develop various cancers, including lymphomas. Lacrimal gland lymphoma is a disease of the elderly, with a median age of presentation of 70 years.

Case presentation In this article, we report a case of a 35-year-old Arabian Saudi male with a known case of Klinefelter syndrome who presented to oculoplastic clinic complaining of progressively growing superior-temporal mass in the left eye. After evaluation and imaging, an incisional biopsy from the lacrimal gland mass was obtained and histopathological evaluation showed atypical lymphoproliferative infiltrate consistent with extranodal marginal zone lymphoma of mucosa associated lymphoid tissue. The mainstay treatment was external beam radiotherapy, which showed significant improvement in the case.

Conclusion This is considered the first reported case of lacrimal gland lymphoma in young patient with Klinefelter syndrome, which increases the association between Klinefelter syndrome and lymphomas.

Keywords Lacrimal gland, Lymphoma, Klinefelter syndrome

Background

Klinefelter syndrome is considered one of the most common sex chromosome disorders affecting males [1]. It is characterized by at least one additional extra X chromosome; with the most frequently noticed phenotype being 47, XXY [2]. The clinical features of Klinefelter are; hypogonadism, gynecomastia, infertility, reduced muscle and bone density, sparse body hair, and having arm span longer than the height of the lower body. The clinical features of Klinefelter syndrome are highly variable, which can lead to delayed or missed diagnosis [3–6]. The higher the number of X chromosome, the greater the clinical manifestations of Klinefelter syndrome [7]. Patients with Klinefelter syndrome are more predisposed to different kinds of malignancies, such as lymphoma, leukemia, male breast cancer, extragonadal germ-cell tumor, and lung cancer [3].

The most common type of malignancy associated with Klinefelter syndrome is male breast cancer, especially associated with 47 XXY mosaic [8, 9].

The correlation between Klinefelter syndrome and lymphoma is scarce, and rare cases have been reported because of the low diagnosis rate [3, 10].

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Ocular adnexal lymphoma accounts for 2% of all extranodal lymphoma, however, lacrimal gland lymphoma constitutes 7–26% of all ocular adnexal lymphoma [11–14].

Regarding lymphoma of the lacrimal gland, the majority of cases are non-Hodgkin B cell lymphoma (99%), among these extranodal marginal zone B cell lymphoma accounts for 68%, followed by follicular lymphoma, diffuse large B cell lymphoma, and mantle cell lymphoma with incidence of 10%, 10%, and 7%, respectively [15].

Lacrimal gland lymphoma rarely presents in young patients, and it is considered a disease of the elderly with a median age of presentation of 70 years [16].

In this article we present a rare case of young patient with Klinefelter syndrome with lacrimal gland extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT-lymphoma), this is considered this first reported case of a patient with Klinefelter syndrome having lacrimal gland lymphoma and, in this case, we will elaborate more about the association of Klinefelter syndrome and lacrimal gland lymphoma.

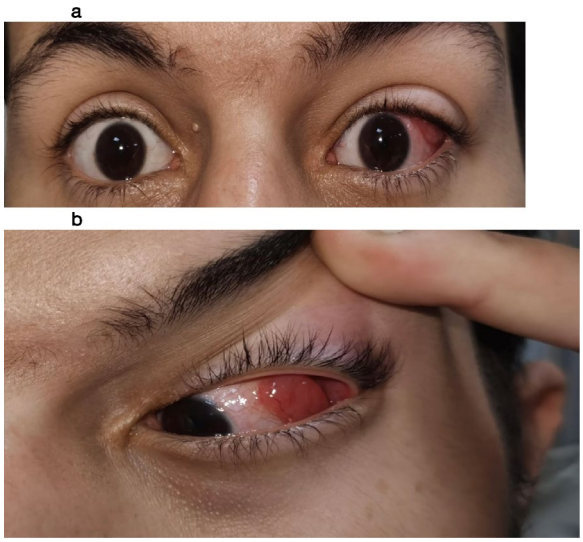

Fig. 1 **a** External photo showing left upper eyelid swelling with superio-temporal mass. **b** Everted left eyelid showed a large fleshy red superior-temporal mass with a smooth surface, giving an initial diagnosis of lacrimal gland tumor

Case presentation

A 35-year-old Saudi Arabian male with a known case of Klinefelter syndrome (karyotype 47, XXY) presented to oculoplastic clinic complaining of progressively growing superior-temporal mass in the left eye and puffiness over the left upper eyelid over the past 4 months. The patient denied any history of night sweats, weight loss, or fatigue. The only symptom the patient was experiencing was infertility, which led him to visit a male infertility specialist for a work-up. Consequently, genetic testing was performed, and the patient was diagnosed with primary infertility owing to Klinefelter syndrome. There was no family history of a similar condition. Upon examination, visual acuity (VA) was 20/20 in both eyes, pupil was round, regular, and reactive with no relative afferent pupillary defect, and the color vision and confrontation visual field testing were unremarkable for both eyes. Externally there was left upper eyelid swelling, with no tenderness or redness, upon eversion of the left eyelid there was a large fleshy red superior-temporal mass with a smooth surface, giving an initial diagnosis of lacrimal gland tumor in the left eye, while the lacrimal gland of the right eye was normal (Fig. 1a, b). The extraocular movement was full in both eyes and there was no diplopia reported by the patient. The anterior and posterior segments examination was normal. Magnetic resonance imaging (MRI) scan (Orbit Protocol) of the orbit showed a left lacrimal enhancing lesion most likely lymphoma or hemangioma (Fig. 2a, b). To confirm the diagnosis, the patient underwent incisional biopsy of the left lacrimal gland and the sample was sent for histopathology evaluation.

The histopathology result (Fig. 3a, b), revealed atypical lymphoproliferative infiltrate consistent with extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma). The patient was referred to oncology within 1 month after the proven diagnosis had been made, where a metastatic workup was done. MRI of the orbit, and CT (computed tomography) of the chest, abdomen, and pelvis confirmed disease is limited to the left lacrimal gland. After that, the patient received external beam radiotherapy as a mainstay of treatment. The patient received 24 Gray of radiotherapy over 12 days (12 sessions). Upon follow-ups, the mass was shrinking in size, with no ocular complications. Further follow-ups have been given to the patient for reassessment.

Discussion and conclusion

Klinefelter syndrome is considered one of the most common sex chromosome disorders affecting males [1]. It is characterized by at least one additional extra X chromosome; with the most frequently noticed phenotype being 47, XXY [2]. In total, 1 in 650 male newborns are affected with Klinefelter syndrome, and 75% of patients with Klinefelter syndrome are left undiagnosed [17]. The reason behind this is many patients with Klinefelter syndrome will not manifest the typical features of the disease for other reasons, making early detection and diagnosis difficult [18].

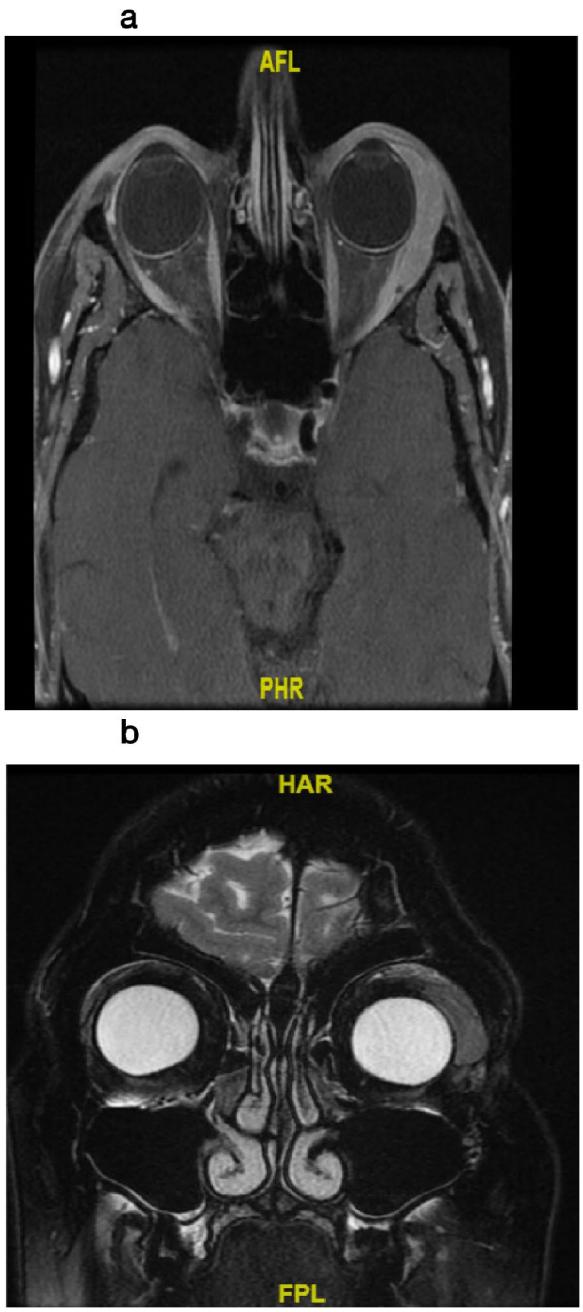

Fig. 2 **a** and **b** Magnetic resonance image of axial and coronal sections, respectively, showing a well-circumscribed left orbital extraconal mass lesion occupying the lacrima fossa, measuring 3.3 × 1 × 2.90 cm at maximum dimensions, compressing the left left lateral rectus inferiomedially, the superior rectus medially and the globe anteriorly

The presence of an extra X chromosome can alter the tendency to develop various cancers, but assessing the likelihood of developing different kinds of malignancies is difficult owing to the under-diagnosis of the condition [3, 10].

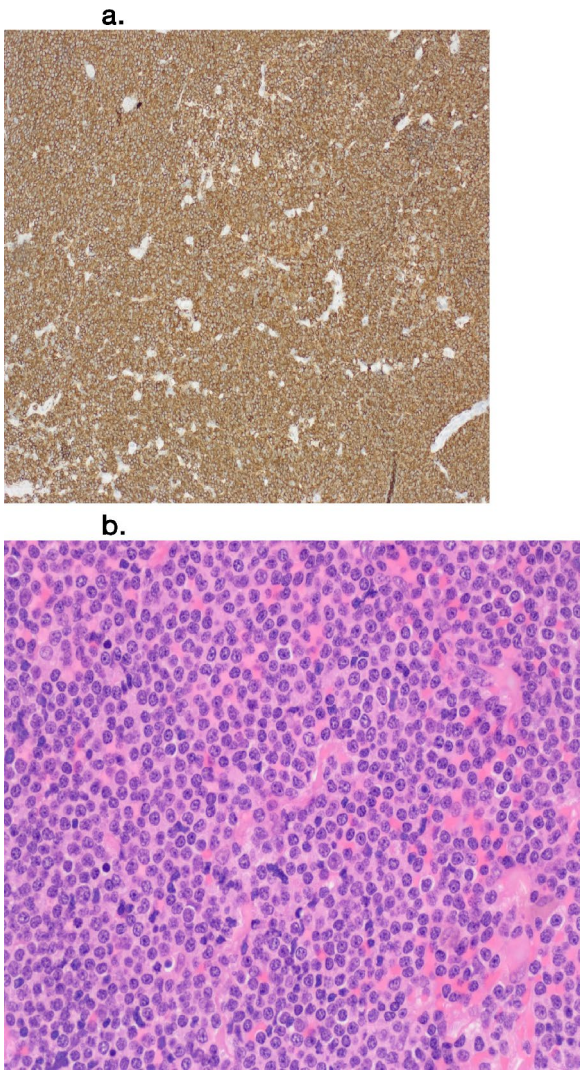

Fig. 3 **a** and **b** CD 20 immunoreactive lymphoid infiltrate—MALT cell lymphoma. Hematoxylin and eosin stain showing monotonous lymphoid infiltrate

Klinefelter syndrome is associated with several types of malignancies, most commonly, mammary, genital, and hematological malignancies [3, 10]. The correlation between Klinefelter syndrome and lymphoma is scarce, and rare cases have been reported because of the low diagnosis rate; however, the mortality rate from non-Hodgkin lymphoma was all statistically significantly higher in patients with Klinefelter syndrome compared with the general population [3, 10].

One of the documented cases of non-Hodgkin lymphoma is a 66-year-old Japanese male who was complaining of right cervical lymph node swelling. A biopsy of the lesion was obtained and revealed non-Hodgkin's lymphoma of diffuse pleomorphic type. Despite

receiving various types of chemotherapies, the patient died [5]. In another case, a patient with Klinefelter syndrome complaining of testicular mass was diagnosed with non-Hodgkin lymphoma. Unfortunately, the patient died from complications of his lymphoma [18]. Unlike our case, where the directed therapy has led to a positive outcome in the conclusion. One of the youngest case reports that has been published is a 9-year-old child with Klinefelter syndrome with gastric MALT-lymphoma who received *Helicobacter pylori* eradication therapy with six cycles of chemotherapy. The patient had a positive outcome, with 2 years of follow-ups not showing signs of recurrence [19]. In accordance with our case, this can reflect the presence of good outcomes in young patients with Klinefelter syndrome with MALT lymphoma, who received directed therapy.

Regarding lymphoma involving the adnexa, MALT-lymphoma is considered the most common subtype of non-Hodgkin lymphoma involving the lacrimal gland but is an extremely rare disease in children and young adults with a median age of presentation of 70 years [16, 20–23]. Cassell *et al*. reported that most incidences of MALT lymphoma occurred between the ages of 50 and 60 years [24]. Furthermore, Claviez *et al*. have reported that extranodal marginal zone B cell lymphoma of MALT is infrequent in children [25]. In literature, there were no reported cases of lacrimal gland lymphoma in patients with Klinefelter syndrome.

In this article, we reported a rare case of a young patient with Klinefelter syndrome and MALT-lymphoma of the lacrimal gland after the incisional biopsy, which showed atypical lymphoproliferative infiltrate consistent with the diagnosis. As mentioned earlier, lymphoma of the lacrimal gland is a very rare disease in young patients, the association between lacrimal gland lymphoma and Klinefelter syndrome cannot be ruled out in this case, as the presence of the extra X chromosome increases the likelihood of developing different kind of malignancies. Keeping in mind, the possibility of incidental findings in this rare case.

Ophthalmologists should have a high suspicion for masses involving the ocular adnexa, especially in syndromic patients, such as those with Klinefelter syndrome.

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Author contributions
AK, RA, BA, and SA all equally contributed to the article by writing and reviewing the study, the authors read and approved the article.

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Availability of data and materials
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Declarations

Ethics approval and consent to participate
Informed consent was obtained from the patient to voluntarily participate in this article.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

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