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CASE REPORT

Kimura disease of submandibular gland

Submandibular Kimura disease

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Kimura disease (KD) is a rare benign chronic inflammatory disorder of unknown aetiology prevalence in young adult Asian males. Head and neck region especially salivary gland and cervical lymph node are the most commonly affected. In contrast to parotid gland, submandibular gland involvement is rarely reported. Diagnosis is always challenging due to variable presentations that may mimic other inflammatory or neoplastic conditions, and non-specific imaging, cytology, and histopathology findings. Generally, there was several treatments modality reported but showed variable response with high recurrence rate. The treatment for submandibular gland KD specifically is not well describe due to its rarity. We present a case of KD with submandibular gland and cervical lymph node involvement in elderly man that mimic malignancy and highlight the challenging in management.

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Kimura disease (KD) is a rare chronic inflammatory disorder of unknown aetiology and was first described in Chinese language literature in China 84 years ago.[1] It is become well known as KD in 1948 after Kimura et al. published the definitive histologic description.[2] Head and neck regions, specifically the salivary gland and regional lymph node are frequently involved.[3] Young adult Asian males in their second to fourth decade of life are predominantly affected, with male to female ratio ranging from 3.5:1 to 6.7:1.[3,4] Sporadic cases have been reported in Europe and America and showed a lower incidence of salivary gland involvement in non-Asian.[4]

The parotid gland is the most common salivary gland affected, while the submandibular gland is rarely reported and the reason for this predilection is still unknown.[3,4] It is paramount important to examine the patient systematically as KD can be systemic and may involve multiple organs, especially the kidney.[3] The marked variable and non-specific presentation of KD that may mimic other inflammatory and neoplastic conditions contribute to the challenges in the diagnosis. In addition, the diagnosis of KD is based on clinicopathological features, but unfortunately, there is no pathognomonic feature histologically.[3]

CASE REPORT

A 68-year-old male, with no underlying medical illness, presented with a history of painless right neck swelling for 10 years which rapidly increased in size over the past 3 months. There were no upper aerodigestive tract obstructive symptoms and no constitutional symptoms.

Upon examination, there was a 6 cm x 5 cm swelling at the right submandibular region. It was smooth surface with no overlying skin changes, firm in consistency, non-tender, immobile and not fixed to overlying skin (Figure 1). The lesion was ballotable on bimanual palpation, but the floor of mouth was not raised. There was no palpable swelling at the other level or contralateral side of the neck. Other ears, nose and throat examinations were unremarkable. He was subjected for fine-needle aspiration cytology (FNAC) twice but unfortunately, the samples were unsatisfactory. Subsequently a tru-cut biopsy was performed but again the result was inconclusive. A computed tomography (CT) scan of the neck was done which revealed an enlarged and heterogeneous enhancement of the right submandibular gland, measuring 3.3 cm x 4.5 cm x 5.4 cm (Figure 2). In addition, there was presence of multiple lymph node enlargements at the right level I to level IV.

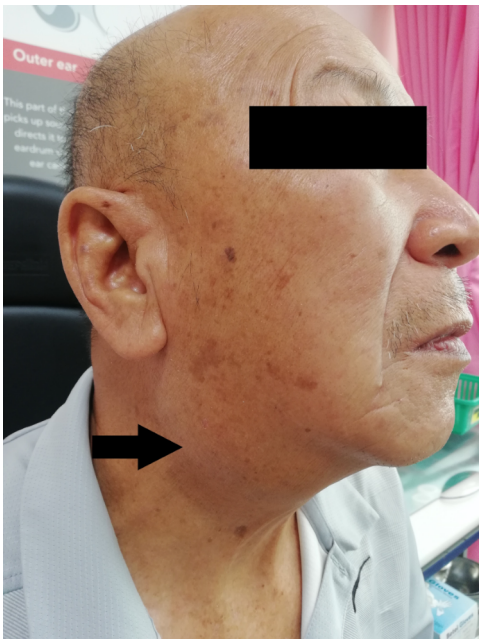

Figure 1 *A 6 cm x 5 cm swelling at the right submandibular region, smooth surface with no overlying skin changes*

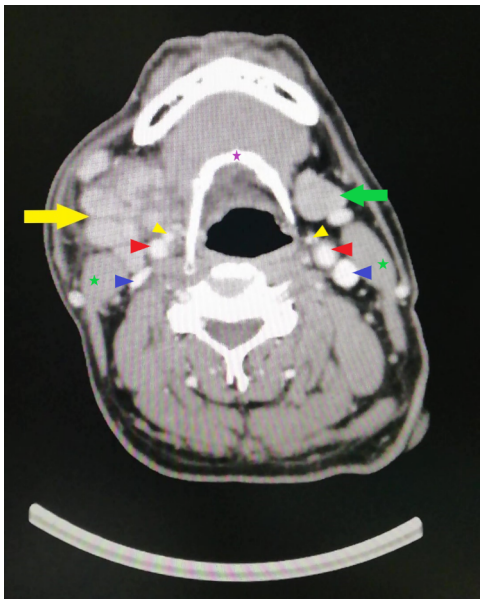

Figure 2 *CT neck shows right submandibular gland enlargement, measuring 3.3 cm x 4.5 cm x 5.4 cm, with heterogeneous enhancement (yellow arrow). Left submandibular gland - green arrow; external carotid artery – yellow arrowhead; internal carotid artery – red arrowhead; internal jugular vein – blue arrowhead; sternocleidomastoid muscle – green star; hyoid bone – purple star.*

In view of suspected malignancy with inconclusive pre-operative cytology and histopathology results, he was counselled for right submandibulectomy with intra-operative frozen section. A modified radical neck dissection will be performed if frozen shows features of malignancy. Intra-operatively the well-

encapsulated tumour measuring 10 cm x 8 cm was confined to the right submandibular gland (Figure 3). Part of the tumour was sent for a frozen section and the immediate result showed the features of chronic sialadenitis; salivary gland tissue infiltrated by lymphocytes and dense eosinophils, without malignant cells seen (Figure 4). Thus neck dissection was deferred. Histopathology examination (HPE) of the specimen showed features favouring KD; salivary gland tissue was infiltrated with lymphocytes, plasma cells and mast cells with dense eosinophilic infiltrates forming an eosinophilic abscess (Figure 5). Subsequently the patient was referred to rheumatologist for medical therapy and was started on oral corticosteroid. He was started on oral prednisolone tapering dose every 2 weeks for 2 months' duration (started with 30 mg, then 25 mg, 20 mg and 15 mg, once-daily dose) and maintenance with 10 mg once daily. The wound was completely healed and no neck swelling after 3 months of follow-up.

DISCUSSION

KD is a benign inflammatory disorder with no evidence or reported case of malignant transformation to date.[5] Although it is benign, the main problem of KD is that its characteristic commonly resembles other inflammatory or haematological malignancies in which the pre-operative cytology examination usually provides an unsatisfactory or inconclusive result. Angiolymphoid hyperplasia with eosinophilia, Hodgkin lymphoma, angioimmunoblastic T cell lymphoma, allergic granuloma, Langerhans cell histiocytosis, Castleman disease, and immunoglobulin G4-related disease are among diseases that have features mimic KD.[3]

Although the major salivary gland is among the common site for KD, however submandibular gland involvement is relatively very rare (5.5% to 6.5%), compared to the parotid gland (33.3% to 37%).[1,3] The diagnosis of submandibular gland KD may be more challenging due to its rarity and more difficult to differentiate from the cervical lymph node.

Our patient underwent FNAC twice but both samples were unsatisfactory for examination. The accuracy of FNAC is variable for salivary gland lesions, depending on the experience of FNAC operator and cytopathologist, use of rapid on-site evaluation, sample preparation, reporting terminology and characteristics of the salivary gland tumours.[6] Therefore the clinical usefulness of preoperative FNAC should be evaluated carefully, based case by case and depending on the local diagnostic performance.

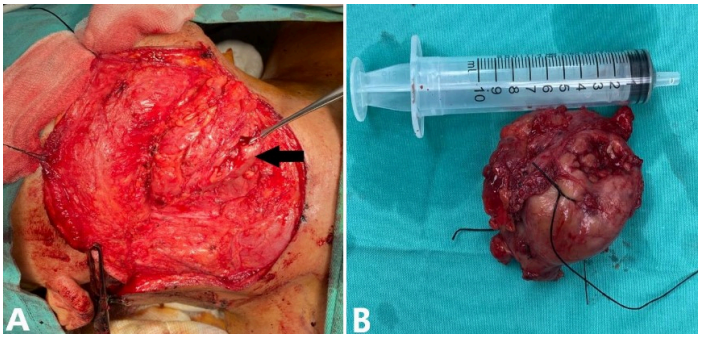

Figure 3 *Intra-operative view shows well-encapsulated tumour confined to right submandibular gland (A). Removed tumour measuring 10 cm x 8 cm, tag with string and sent for histopathological examination (B)*

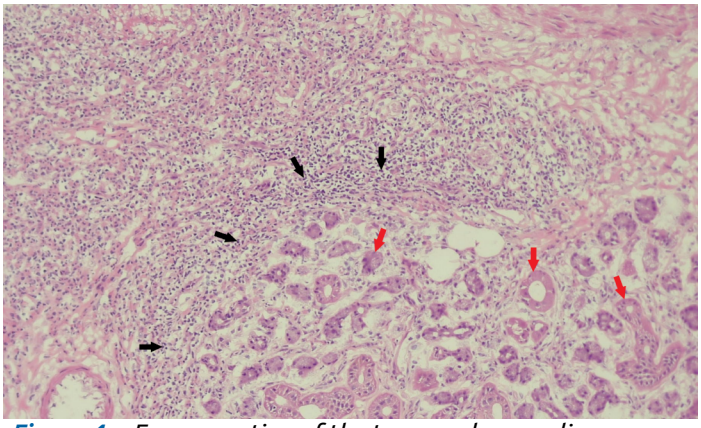

Figure 4 *Frozen section of the tumour shows salivary gland tissue densely infiltrated by lymphocytes (black arrow) x100. Salivary gland acini and ducts – red arrow.*

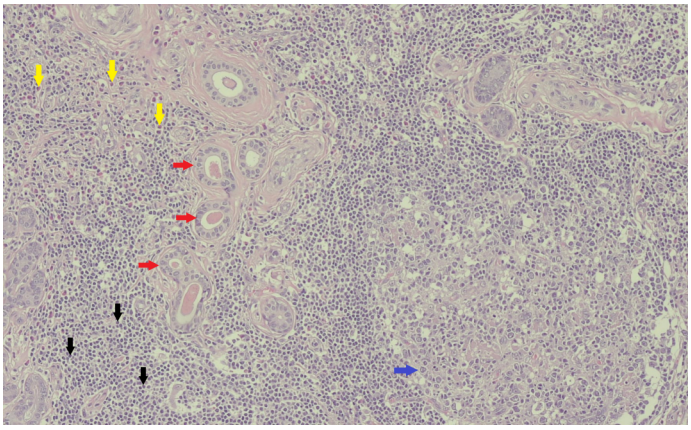

Figure 5 *The tumour shows salivary gland tissue infiltrated with lymphocytes (black arrow) and plasma cells with dense eosinophilic (yellow arrow) infiltrates forming eosinophilic abscess, H&E x100. Salivary gland acini and ducts – red arrow; hyperplastic follicle with germinal centre (blue arrow).*

Specifically the role of FNAC in KD is usually disappointed and the majority of cases required an open biopsy.[7] As increasing number of KD cases reported recently, few studies had highlighted certain cytologic characteristic features favouring the disease, which include presence significant

amount of eosinophils, polymorphous lymphoid population, fragments of collagenous tissue and Warthin-Finkeldey polykaryocytes. Due to the non-diagnostic FNAC result, we performed a tru-cut biopsy as it showed higher accuracy with a lower inadequacy rate.[8] The risk of tumour seeding in FNAC and tru-cut biopsy are very low, 0.00012% and 0.0011% respectively.[9] Unfortunately the tru-cut biopsy also failed to provide a definitive preoperative diagnosis.

The next investigation in line is incision biopsy but we decided against it because it may provide a route for tumour seedling to skin and automatically upstage the tumour as well as cause a bad painful experience to the patient. Furthermore taking into consideration of another pre-operative biopsy may produce a similar indefinite result, we counselled the patient for submandibulectomy for diagnostic and therapeutic in the same setting. Intra-operative frozen section was very helpful procedure in our case as it determines the extent of surgery and reduces the morbidity related to more extensive surgery without conferring an extra benefit or disease control. A meta-analysis study showed frozen section accuracy is clinically acceptable in salivary gland tumours.[10]

Imaging studies either ultrasound, CT scan or magnetic resonance imaging (MRI) also showed non-specific findings for KD.[5] KD should be suspected if present of multiple ill-defined enhancing masses within and around the parotid gland with associated regional lymphadenopathy seen in CT scan or MRI.[11] CT scan of our patient showed heterogeneous submandibular gland enlargement with presence of multiple cervical lymph nodes, thus more common diagnosis like salivary gland malignancy or lymphoma were initially suspected.

The definitive diagnosis of KD is based on the HPE of the excised lesion, but again there is no specific features.[5] Many studies described the common findings were reactive follicular hyperplasia, large number of eosinophils, lymphocytes and mast cells infiltrate, eosinophilic microabscess formation, presence of polykaryocytes and varying degree of fibrosis and vascular proliferation.[4,5,7] These characteristics are consistent with our HPE findings.

Several treatment modalities have been proposed however the definitive treatment is still unclear, with variable response and high recurrence rate up to 80%.[5] Generally the treatments that have been reported are surgical excision, systemic corticosteroids, radiotherapy, cytotoxic agents, cyclosporin, pentoxifylline, leflunomide, mycophenolate mofetil and imatinib.[11] A combination of at least two therapies produces a better result in term recurrence rate.[11] The treatment of submandibular gland KD specifically was not well described in the literature due to the rarity of the involved organ. We believed the treatment principle is similar to other benign submandibular gland tumours with submandibulectomy usually the treatment of choice. Submandibulectomy is generally a safe procedure due to its relatively superficial location of the submandibular gland and less complexity of the surrounding structures. Our patient underwent submandibulectomy and was subsequently followed by oral corticosteroid as adjunct medical therapy. There was no residual tumour at the operated site and no new lesion after 3 months of follow-up. We think this regime is a good combination as surgery help to reduce the tumour bulk and subsequently reduces the dosage and duration of corticosteroid required. Long-term use of corticosteroids especially in the elderly may result in multiple systemic complications.

CONCLUSION

KD is a rare benign chronic inflammatory disorder of unknown aetiology that substantially causes challenges to the managing team from diagnosis to treatment and effort to reduce the recurrence. It has variable presentations, but the involvement of the submandibular gland is very rarely reported. Its characteristic resembles other inflammatory or malignancy conditions and the rarity of the involved region contributes to the difficulties in managing the present case. Due to this non-specific presentation, the investigation of choice should be case-to-case basis, and every effort should be taken to get a preoperative diagnosis without delaying the treatment.

REFERENCES

1. Li TJ, Chen XM, Wang SZ, Fan MW, Semba I, Kitano M. Kimura's disease: a clinicopathologic study of 54 Chinese patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;82:(5)549–55.
2. Kimura T, Yoshimura S, Ishikawa E. On the unusual granulation combined with hyperplastic changes of lymphatic tis- sues. Trans Soc Pathol Jpn. 1948; 37:179-180.
3. Zhang X, Jiao Y. The clinicopathological characteristics of Kimura disease in Chinese patients. Clin Rheumatol. 2019;38:(12)3661-7.
4. Chen H, Thompson LD, Aguilera NS, Abbondanzo SL. Kimura disease: a clinicopathologic study of 21 cases. Am J Surg Pathol. 2004;28:(4)505–13.
5. Sun QF, Xu DZ, Pan SH, Ding JG, Xue ZQ, Miao CS, et al. Kimura disease: Review of the literature. Intern Med J. 2008; 38:668–72.
6. Pusztaszeri M, Rossi ED, Baloch ZW, Faquin WC. Salivary gland fine needle aspiration and introduction of the milan reporting system. Adv Anat Pathol. 2019;26:(2)84-92.
7. Sherpa M, Lamichaney R, Roy AD. Kimura's disease: A diagnostic challenge experienced with cytology of postauricular swelling with histopathological relevance. J Cytol. 2016;33:(4)232-5.
8. Schmidt RL, Hall BJ, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of ultrasound-guided core needle biopsy for salivary gland lesions. Am J Clin Pathol. 2011;136:(4)516-26.
9. Shah KS, Ethunandan M. Tumour seeding after fine-needle aspiration and core biopsy of the head and neck--a systematic review. Br J Oral Maxillofac Surg. 2016;54:(3)260-5.
10. Schmidt RL, Hunt JP, Hall BJ, Wilson AR, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of frozen section for parotid gland lesions. Am J Clin Pathol. 2011;136: (5)729-38.
11. Park SW, Kim HJ, Sung KJ, Lee JH, Park IS. Kimura disease: CT and MR imaging findings. AJNR Am J Neuroradiol. 2012;33:(4)784-8.