Clinical Case Report

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Neck xanthogranuloma mimicking malignancy in a patient with diabetes mellitus

A case report and literature review

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Abstract

Rationale: Xanthogranulomatous inflammation (XGI) is a rare inflammatory process, which mostly affects the kidney and gallbladder. It usually simulates an aggressive neoplastic process. Occurrences in the neck are extremely rare and would usually be associated with a preexisting cyst or glandular tissues.

Patient concerns: A 49-year-old diabetic patient presented with a right painful neck mass for a week. The pretreatment computed tomography (CT) imaging with contrast demonstrated a huge ill-defined heterogeneous-enhanced lesion abutting surrounding musculatures and great vessels. Both fine needle aspiration (FNA) and ultrasound-guided core biopsy of the neck mass showed inflammatory cells only.

Diagnoses: Histologic evaluation found granulation tissue with histiocytes and occasional Touton giant cells confirming the diagnosis of xanthogranuloma.

Interventions: Open excisional biopsy demonstrated a yellowish mass-like lesion with abscess inside.

Outcomes: The patient recovered from the disease without posttreatment comorbidities.

Lessons: This case highlights the need for physicians to maintain awareness of this clinical entity and delayed- or overtreatment should be avoided in these patients due to preoperative ambiguous diagnosis.

Abbreviations: CT = computed tomography, DM = diabetes mellitus, FNA = fine needle aspiration, H&E = hematoxylin–eosin, IgG4-RD = IgG4-related disorders, XGI = xanthogranulomatous inflammation.

Keywords: computed tomography, neck, Touton giant cells, xanthogranuloma, xanthogranulomatous inflammation

1. Introduction

Xanthogranulomatous inflammation (XGI) is an uncommon inflammatory condition initially described by Oberling as a benign lesion in retroperitoneal organs.[1,2] Pathogenesis of XGI remains largely unknown, with current proposed hypotheses including defective lipid metabolism, disruption of immune response, mechanic lymphatic obstruction, and inherited lysosomal disorders.[3] Definite diagnosis relies on ultimate pathologic analysis because clinical and imaging information are usually nonspecific. XGI typically presents in the kidney and gallbladder whereas occurrences at the neck are extremely rare.[1,2] Coexistence of abscess is not uncommon, with *Escherichia coli* as the most common pathogens.[2] Following definite diagnosis, extended surgical resection remains the established optimal management, with vigilant follow-up being mandatory from the time of initial treatment. To the best of our knowledge, the present case represented the first incidence of neck xanthogranuloma in the absence of congenital cysts or glandular tissues. Despite the aggressive course the present case follows, it is considered to portend fair clinical outcomes for the patient.

2. Case presentation

A man in his 40s presented to our clinic with a right painful neck mass for a week. His medical history included untreated diabetes mellitus (DM) but he denied any history of recurrent neck infection or swelling. Laboratory studies showed a white-cell count of 12,300/μL and the C-reactive protein level was elevated to 253 mg/L. Flexible laryngoscope revealed swelling at the right pyriform sinus involving surrounding posterior pharyngeal wall and aryepiglottic fold. Subsequent computed tomography (CT) imaging demonstrated a huge heterogeneous-enhanced lesion abutting surrounding musculatures and great vessels (Fig. 1). The retrieved specimen of fine needle aspiration (FNA) and repeated ultrasound-guided core biopsy of the neck mass showed necrotizing inflammation only.

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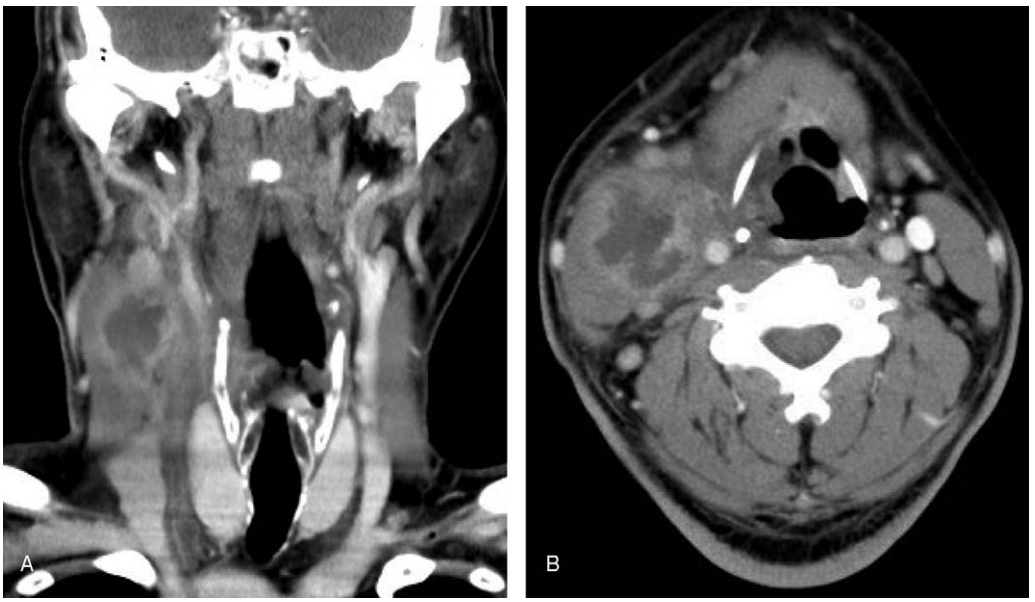

Figure 1. Pretreatment computed tomography with contrast shows a 4.7 × 3.7 × 3.5-cm heterogeneous-enhanced lesion abutting surrounding musculatures and great vessels. (A) Axial view. (B) Coronal view.

As the patient did not have significant improvement in terms of lesion size after empirical ampicillin-sulbactam, decision was made to perform open biopsy under general anesthesia. The intraoperative findings found a yellowish mass-like lesion that involved the surrounding tissues and bled easily upon manipulation. The lesion and its internal abscess was meticulously dissected in an en bloc manner. Further histologic evaluation found tissues to have a dense infiltrate of histiocytes surrounded by fibrous stroma and occasional Touton giant cells (Fig. 2A and B). Cystic lining and lymph node components were not identified. Following immunohistochemical staining showed positive for CD68 and negative for S100 (Fig. 2C). Culture of the abscess sample grew *Klebsiella pneumonia* and he underwent another course of antibiotics treatment. Postoperative follow-up of the patient in the subsequent 6 months found him to be disease-free.

3. Discussion

The term XGI describes an uncommon type of chronic destructive process of the normal tissue in the affected organ. XGI mostly affects the kidney and gallbladder as xanthogranulomatous pyelonephritis and xanthogranulomatous cholecystitis, and accounts for approximately 19.2% of all pyelonephritis and 1.8% of all cholecystitis, respectively. XGI can occur in patients of any age, but is mostly found in patients aged 40 to 60, with a slight female predilection.[1,2] The disease may present as either localized or multifocal lesions accompanied by abscess formation, with *E coli*, *Proteus mirabilis*, and *Klebsiella* spp. as the most common pathogens.[2] When faced with young patients with multisystem involvement, the possibility of inherited lysosomal disorders should be considered.[3] XGI typically follows an aggressive course, and despite high propensity for relapse noted in specific tissues such as ocular tissues, subsequent malignant transformations were extremely rare.[4,5] As for occurrence in other organs such as the kidney or gallbladder, XGI displays relatively low recurrence rate in cases of complete resection of the original lesions.[3–5] With optimal treatment, XGI is generally considered to yield good clinical outcomes. However, due to limited reports of cases occurring at the head neck region and insufficient information regarding long-term follow-up (Table 1), further evaluation is warranted to better determine the prognosis of head neck XGI.

Based on available case studies to date, XGI rarely affects head neck regions, but if it does, it usually develops at the orbit, ocular

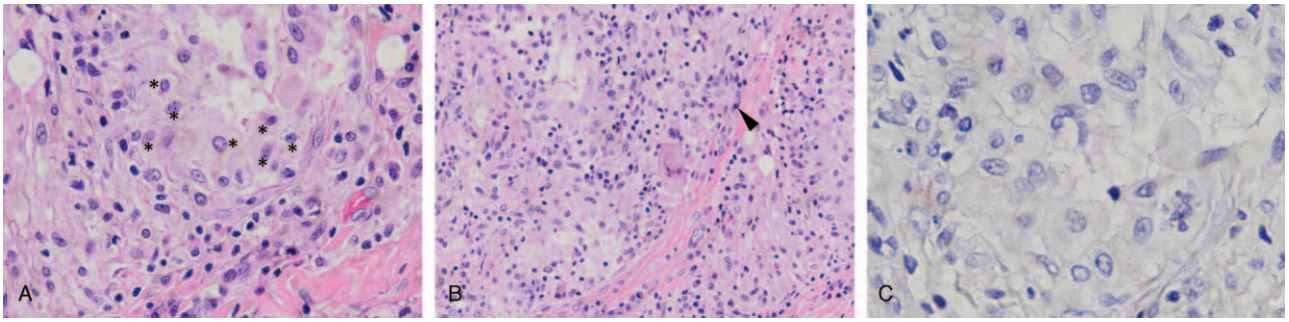

Figure 2. Histopathological photographs of the retrieved specimen. (A) Xanthoma cells (asterisk) (hematoxylin–eosin [H&E], original magnification ×400). (B) Touton giant cell (arrow) (HE ×200). (C) Immunohistochemistry analysis for S100-staining demonstrated negative results (original magnification ×400).

Table 1

Demographic features of reported neck XGI.

	Refs.	Age	Gender	Coexisted structures	History of antecedent FNA biopsy	Underlying disease	Treatment	Outcome
Case 1	Dale et al 1988[6]	65	M	Parotid gland	No	HTN, DM, mitral valve replacement	Surgery	N/A
Case 2	Choyce et al 1993[7]	60	F	Parotid gland	Yes	Thyrotoxicosis, AF, pleomorphic adenoma*	Surgery	N/A
Case 3	Patfield et al 1993[8]	60	F	Parotid gland	No	Pleomorphic adenoma†	Surgery	N/A
Case 4	Chow et al 1996[9]	65	M	TGDC	Yes	Right shoulder subcutaneous lipoma	Surgery	N/A
Case 5	Esson et al 1998[10]	72	F	Parotid gland	Yes	None	None	Die of lymphoma 22 months after initial diagnosis
Case 6	Stephen et al 1999[11]	56	M	Parotid gland	Yes	None	Surgery	N/A
Case 7	Cocco et al 2005[12]	61	M	Parotid gland	Yes	Hodgkin's lymphoma	Surgery	In remission in 24 months followed-up
Case 8	Jang et al 2010[13]	66	M	Parotid gland	Yes	N/A	Surgery	N/A
Case 9	Turkmen et al 2012[14]	52	M	Parotid gland	Yes	Parotitis‡	Surgery	N/A
Case 10	Sarioglu et al 2012[15]	39	F	2nd BCC	Yes	Epidermal cyst	Surgery	N/A
Case 11	Taskin et al 2015[16]	40	M	TGDC	Yes	None	Surgery	Reported no complications in follow-up periods
Case 12	Present case	49	M	None	Yes	DM	Surgery	In remission in 12 months followed-up

AF = atrial fibrillation, BCC = branchial cleft cyst, DM = diabetes mellitus, F = female, FNA = fine needle aspiration, HTN = hypertension, M = male, N/A = not available, TGDC = thyroglossal duct cyst, XGI = xanthogranulomatous inflammation.

* Pleomorphic adenoma of an accessory lobe of the ipsilateral parotid gland status postparotidectomy 26 years ago.

† Pleomorphic adenoma of an accessory lobe of the ipsilateral parotid gland status postparotidectomy 15 years ago.

‡ Recent parotitis 10 days ago.

adnexa, and locations of intracranial structural/cystic anomaly (e.g., choroid plexus, Rathke's cleft cyst/craniopharyngioma in the pituitary gland, colloid cyst of 3rd ventricle).[5] Only 11 patients have been reported to have solitary neck XGI; 8 cases of parotid gland, 2 thyroglossal duct cyst and one 2nd branchial cleft cyst (Table 1). We found XGI development in glandular tissue to occur exclusively at the parotid glands (Table 1). Two of the reported 8 parotid XGI cases had associated history of previously operated accessory lobe pleomorphic adenoma years ago, whilst another was of ongoing inflammation (Table 1). Notably, a 72-year-old patient[16] who was initially diagnosed as xanthogranulomatous parotitis was later found to actually be B-cell lymphoma; both her parotid and small intestinal tumor lesion that developed 6 months later showed pathologic similarities that were highly indicative of XGI development, however, atypical presentation indicated need for further bone marrow biopsy, and finally confirmed the diagnosis of lymphoma. Therefore, though rare, it reminds us physicians of the need to discriminate between XGI and hematologic malignancies.

As opposed to previous patients, our case is the first incidence of neck xanthogranuloma in the absence of congenital masses or glandular tissues. Plausible mechanism for his xanthogranuloma was uncontrolled diabetes mellitus (DM), as diabetic patients are commonly considered to be immunocompromised due to impairment at all steps of leukocyte activity, including adherence, chemotaxis, phagocytosis, and bactericidal activity malfunction.[17] This, in turn, may induce leukocyte dysfunction and lysosomal defects in macrophages,[12,18] and aberrant immune responses and severe inflammation may occur, with subsequent phagocytosis of the lipids released from the necrotic tissues via recruited macrophages,[6,19] all of which are considered possible mechanisms for xanthogranulomatous inflammation (XGI) development. Another hypothesis is post-FNA trauma related XGI, similar to those proposed in salivary glands.[7] However, the association of trauma contributing to our patient's XGI may be weak, because XGI is considered a chronic granulomatous process, yet time elapse from the date of biopsy to surgical excision in our case did not exceed 30 days.

Due to limited ability to distinguish neck xanthogranuloma from other disease entities using only images, tissue biopsy for pathologic analysis remains the gold standard of diagnosis.[3] The hallmark pathologic characteristics of XGI include the coexistence of foamy (lipid-laden) macrophages, Touton giant cells, and lymphocyte aggregation with or without necrobiosis.[11] Differentiation entities include other benign histiocytic pathologies, such as dendritic cell disorders (further divided into Langerhans cell histiocytosis and non-Langerhans cell histiocytosis) and macrophage cell disorder (e.g., hemophagocytic lymphohistiocytosis, Rosai–Dorfman disease).[3,20] It is worth noting that previous studies have found association between IgG4-related disorders (IgG4-RD) and XGI because IgG4-positive plasma cells may present as a nonpredominant cell population in XGI. In Hong's study that looked at 57 resected xanthogranulomatous cholecystitis, they found that XGI occasionally coincides in patients with already known IgG4-RD.[8]

Consensus regarding the best strategy in treating isolated neck XGI has not been reached due to the rarity of the disease.[5,7,9–11,13–16,20–22] After comprehensively reviewing previous publications, we found that neck XGI management mostly relied on curative surgical excision.[7,9–11,13–16,20–22] A wide open surgical field might be needed in cases where inflammation extends to adjacent tissues.[7,9–11,13–16,20–22] Efficacies of other widely employed alternatives in orbit XGI, such as steroid, immunesuppressants, or chemotherapies remained unclear.[5] Future studies are needed to test their therapeutic effectiveness and to identify populations at risk of recurrent or severe XGI.

4. Conclusion

In conclusion, this report of a diabetic patient with isolated abscess-formative neck XGI treated with surgical resection reminds us clinical physicians to bear in mind this benign diagnosis when treating neck swellings that are suspicious for malignancy. Vigilant follow-up should be mandatory to detect new lesions, early recurrence, or occurrence of additional systemic disorders from the time of initial treatment.

Author contributions

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Writing – review & editing: Tzu-Pai Chen, Yu-Hsuan Lin.

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