Bilateral Kuttner Tumor of Submandibular Glands; A Case Report and Review of the Literature

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Kuttner tumor is a relatively uncommon disease of the salivary gland. It is also known as chronic sclerosing sialadenitis or cirrhosis of the submandibular gland. The examination of the submandibular gland characterizes clinically by a firm swelling of the gland, and histologically by progressive periductal sclerosis, dense lymphocytic infiltration with lymphoid follicle formation, reduction of the secretory gland parenchyma and fibrosis. Clinical, cytologic, histopathologic and immunohistopathologic features with briefly reviewed relevant literature describing 231 cases are discussed. The patients with the mean age of 44 years (range 13-81 years) had submandibular masses known to be present for 1 week to 55 years (mean 23.2 years). There is a slight predilection for occurrence in men. This is the first reported description of bilateral Kuttner tumor of submandibular glands in Thailand. It was initially diagnosed as a primary submandibular gland neoplasm that fine needle aspiration revealed to be chronic sialadenitis.

Keywords: *Kuttner tumor, Chronic sclerosing sialadenitis, Inflammatory pseudotumor, Submandibular gland, Salivary gland*

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Kuttner tumor is a relatively uncommon inflammatory disease of the salivary gland. It has been recognized as a distinct clinicopathologic entity in the new edition of World Health Organization classification of salivary gland tumors[1]. It is also known as chronic sclerosing sialadenitis[1-8] or cirrhosis of the submandibular gland[1]. It is one of the most common diseases exclusively affecting the submandibular gland with highly characteristic clinical manifestations[1-4]. It is occasionally mistaken clinically for malignancy[1,2]. The present report describes a patient with bilateral submandibular masses. Clinical investigations, cytologic, histopathologic and immunopathologic features of both submandibular glands show typically characteristic finding of the Kuttner tumor.

Case Report

A 69-year-old Thai married male patient living in Bangkok, was admitted to Ramathibodi Hospital in May 2003, because of bilateral painless swelling submandibular glands of six months' duration. He had worked regularly as a farmer. There was a 20 pack-year history of cigarette smoking. The underlying disease was thalassemia. The patient had no history of significant illness in the past. There was no history of tuberculosis or malignancy among the members of the families. Physical examinations revealed mild pale. The right and left submandibular glands were firm, and generalized enlargement, which measured 6 x 4 x 2.3 cm and 6 x 4.5 x 3 cm, respectively. No lymphadenopathy or other salivary gland enlargement was present.

Fine needle aspirations of the submandibular mass were performed and revealed chronic sialadenitis in the category of inflammation (Fig. 1). The patient underwent exploratory surgery and resections of bilateral submandibular glands were performed.

The right and left submandibular glands showed firm, tan-brown and generalized enlargement measuring 6 x 4 x 2.3 cm and 6 x 4.5 x 3 cm, respectively (Fig. 2A, 2B). The cut surfaces of both submandibular glands showed ill-defined indurated lesion that merged the surrounding parenchyma. The histopathologic

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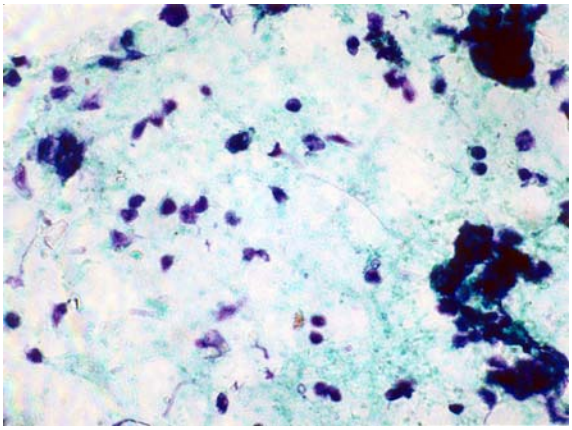

Fig. 1 Fine needle aspirations of the submandibular mass show relatively low cellularity with scattered ductal structures, small isolated fragments of fibrous stroma and moderate numbers of mature lymphoid cells. PAP stain, X400

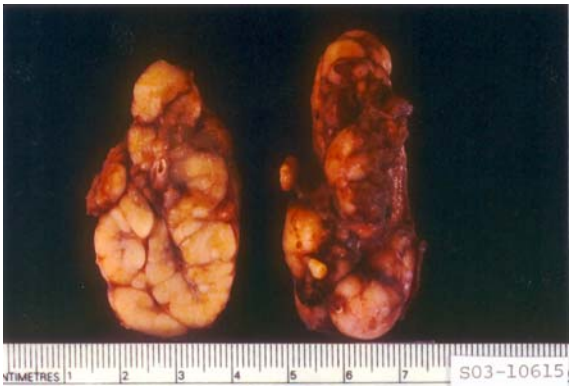

Fig. 2A The sagittal section of the right submandibular gland shows film, tan-brown and generalized enlargement measuring 6 x 4 x 2.3 cm

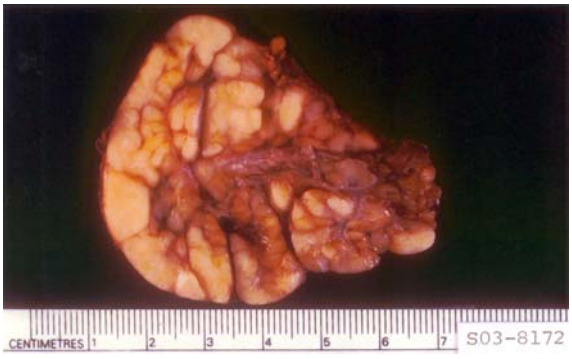

Fig. 2B The coronal section of the left submandibular gland shows film, tan-brown and generalized enlargement measuring 6 x 4.5 x 3 cm

feature revealed marked interstitial fibrosis with lymphocytic and plasmacytic inflammatory cells infiltration (Fig. 3A, 3B). There was nearly complete loss of acinar cells in some areas. The intercalated and intralobular ducts were dilated. The lymphoid infiltration was present both within and between the lobules. The lymphoid infiltration was very dense with formation of germinal center. Neither epimyoepithelial islands nor lymphoepithelial lesions were seen. Special immunohistopathologic investigations on the sections of both submandibular glands revealed the lymphocytes in the general infiltrate to be predominately (CD20, CD45RB) B cells. B lymphocytes in the

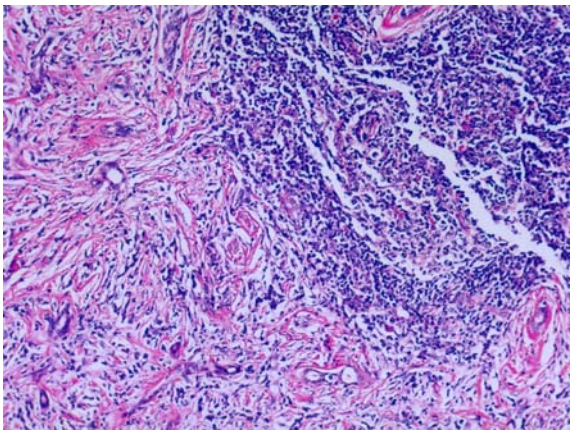

Fig. 3A The histopathologic features of bilateral submandibular glands reveal lymphoid infiltration within and between the lobules. The lymphoid infiltrations are very dense with formation of germinal center. H&E, X100

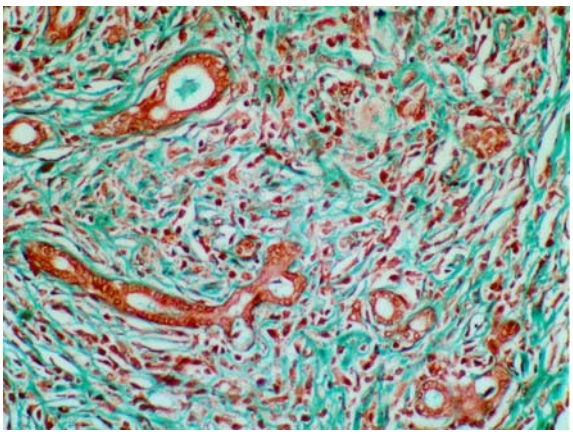

Fig. 3B The histopathologic features of bilateral submandibular glands reveal marked interstitial fibrosis with lymphocytic and plasmacytic inflammatory cells infiltration. Masson trichrome, X200

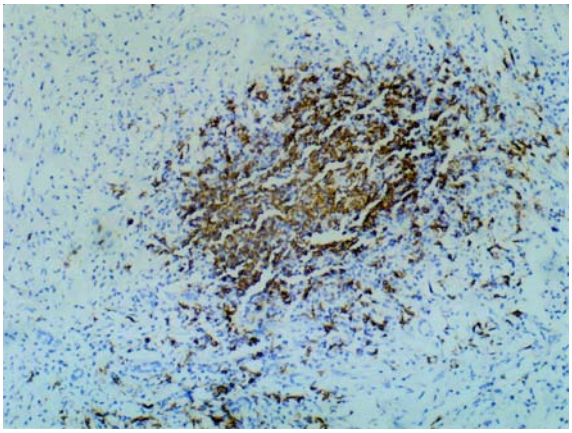

Fig. 4 The immunohistopathologic features of bilateral submandibular glands reveal general infiltration of CD 20 positive B lymphocytes with focally infiltrate in the center of the lymphoid follicles of Kuttner tumor. CD20, X100

center of the lymphoid follicles of Kuttner tumor were present (Fig. 4).

Discussion

Kuttner tumor is a chronic inflammatory process of the salivary gland producing a firm, swollen appearance occurring almost exclusively in the submandibular gland that often cannot be distinguished from a true neoplasm[1-8]. Kuttner H. published the first report of Kuttner tumor in 1896[6,8,9]. It is a benign disease of uncertain cause, postulated mechanisms include infection-related inflammation, sialolithiasis (demonstrated in 0-84.3% of the affected salivary glands), disorder of secretory function leading to ductal inspissation and autoimmune reaction[1,3-5,9-11].

The submandibular gland has a propensity for enlargement secondary to non-neoplastic disease [8,12]. The most frequent pathology of the submandibular gland is inflammation[8,12]. Kuttner tumor is a common fibrosing chronic inflammatory lesion of the submandibular gland. It is one of the most common diseases exclusively affecting the submandibular gland with highly characteristic clinical manifestations[1,2,4]. However, chronic sclerosing sialadenitis of the parotid gland has been published[5].

Patients presenting with Kuttner tumor are usually adults[3-8]. The reported ages of patients range from 13 to 81 years with a mean age at surgery of 44 years[3-8]. There is usually a slight male predominance[3-8]. The male to female ratio is 1.1:1[3-8]. Most patients experience recurrent pain, discharge and swelling that is often associated with eating, but others only have asymptomatic hard swelling of the submandibular gland[3-8]. The lesion is always firm and patients can feel a discrete growth of the salivary gland[3-8]. The glandular involvement is usually unilateral[3-6,8], but can be bilateral[7]. The published durations at surgery range from 1 week to 55 years with a mean duration of 23.2 months[3-8]. Lith has been present in the gland or duct in 72.6% (Table 1)[3,4].

Cytology

The fine needle aspiration (FNA) cytology of Kuttner tumor is characterized by the relatively low cellularity, probably attributable to the fibrosis, making it difficult to aspirate the cellular elements[7]. Scattered ductal components with paucity or absence of acini is noted[7]. The ducts intimately surrounded by collagen sheaths or lymphoid cells[7]. Small isolated fragments of fibrous stroma are presented[7]. Moderate to large numbers of lymphoid cells are presented but lack definite atypia[7]. The presence of a heavy lymphoid infiltration can raise the differential diagnosis of other lymphoproliferative processes such as intraglandular reactive lymph node, benign lympho-

Table 1. Summary of 231 reported cases of Kuttner tumor of the submandibular glands

Authors & Year	Total cases	M:F	Mean age at surgery & range (years)	Mean duration (months) & range	R:L:B	Presented lith in gland (%)
Isacsson G et al, 1981[3]	108	1.3:1	44.1	12 (1 week to 55 years)	-	84.3
Chan KC et al, 1998[4]	112	1:1.2	42 (13 to 81)	35 (2 weeks to 28 years)	-	68.4
Williams HK et al, 2000[5]	1	1:0	83	5	0:0:1	0
Ochoa ER et al, 2001[6]	1	1:0	65	18	1:0:0	0
Cheuk W et al, 2002[7]	7	6:1	62 (47 to 72)	15 (2 months to 6 years)	2:2:3	0
Huang C et al, 2002[8]	1	1:0	45	1.5	1:0:0	0
Larbcharoensub N et al	1	1:0	69	6	0:0:1	0
Total	231	1.1:1	44 (13 to 81)	23.2 (1 week to 55 years)	-	72.6

M:F = Male:Female, R:L:B = Right:Left:Bilateral

epithelial lesion and low-grade lymphoma[3,13]. The diagnosis of Kuttner tumor must be made in combination with the stereotypic clinical manifestations. Several large series on FNA have reported a high sensitivity and specificity of this procedure in the diagnosis of salivary gland masses[3,14]. FNA cytology is a simple, cost-effective and safe technique that has been used increasingly in the workup of the salivary gland lesions[3,14].

Histopathology

In general, a heterogeneously distributed inflammatory infiltrate comprise lymphocytes and plasma cells with periductal fibrosis and proliferation of lamellar collagen fibers[2,15]. The degree of inflammation and fibrosis varies from case to case and also from lobule to lobule within the same gland[2]. The histopathologic features of Kuttner tumor may evolve through four different histologic stages[2-5,8].

The early first histological stage shows mild, focal chronic lymphocytic and plasmacytic inflammatory cell infiltration, usually periductal with periductal fibrosis and duct ectasia containing inspissated secretion[3-5,8]. The lobular architecture of the gland is usually preserved.

In evolving, second histological features have more severe periductal sclerosis and dense lymphocytes infiltration, ductular epithelial hyperplasia and focal metaplasia with occasional epimyoepithelial islands and destruction of the lobular architecture[3,4]. Periductal lymphoid follicles with reactive germinal centers are sometimes present within the gland. There is fibrosis in the centers of the lobules and atrophy of acini[8].

The progressive third histological stage reveals more prominent lymphocytic and plasmacytic infiltration with secondary lymphoid follicle formation[3-5,8]. The features include extensive fibrosis with acinar atrophy, periductal hyalinization and ductal dilatation with reduction of the secretory gland parenchyma[4,8]. The duct lining the epithelium adjacent to sialoliths commonly shows squamous metaplasia, thickening and ulceration that are associated with marked periductal inflammation[3,4,8]. Dilated excretory portion sometimes demonstrates squamous metaplasia and an increased number of goblets-like mucous and ciliated cells[4]. Focal granulomas are probably a reaction to extravasation of mucus and have been observed in some cases[2,17].

The final fourth histological stage discloses destruction of the lobular architecture and sclerosis-cirrhosis with parenchymal loss[3,4,8]. Replacement by fatty and/or connective tissue with or without inflammatory reaction is noted[3].

The histopathology of bilateral submandibular glands of the presented case correlates with the late stage of Kuttner tumor. The hyperplastic and dilated ducts containing secretions suggest an obstructive element to the cause of the chronic sclerosing sialadenitis.

Immunohistopathology

Immunohistochemical studies of the lymphoid population in Kuttner tumor show the presence of activated B cells in the lymphoid follicles, while the T cells in the interfollicular zone exhibit great predominance of helper/inducer T cells over suppressor/cytotoxic T cells (CD3), in a topographic distribution similar to the antigenically stimulated lymph node[4,8].

Pathogenesis

The etiologic factor of Kuttner tumor is not attributable to a single etiologic agent. It represents a common pathologic endpoint with a nonspecific clinical presentation. The pathologic etiology is postulated to be a disorder of secretions termed "obstructive electrolyte sialadenitis"[6]. Sialolithiasis is the most common etiologic factor, which was found varying in 0-84.3% of cases[2-5,8-11,17,18]. Obstruction of the duct system by sialoliths leads to lymphocytic infiltration, fibrosis, parenchymal atrophy and immune reactions of the duct system[1-5,8]. This mineralization may develop about a nidus of exfoliated cellular debris, a mucus plug, a bacterial colony, or a foreign body, and primarily composed of calcium salts in the form of hydroxyapatite. Most salivary calcium is associated with secretory granules and they speculated that this is the likely source of the calcium involved in salivary calcification. Ultrastructural analysis shows crystals containing calcium and phosphorus[19]. The associated cilopathies of the main excretory ducts by transmission and scanning electron microscopic study in obstructive sialadenitis has been reported[20]. The presence of reactive follicles in most cases indicates an immunologic component to the process[6]. Thus, it is possible that the setting of chronic immune stimulation resulting from mechanical duct obstruction and release of antigens from parenchymal cells provides a substrate for the development of mucosa-associated lymphoid tissue (MALT) lymphoma[6].

Kuttner tumor is entirely a benign lesion of uncertain cause. There has been no report of malig-

nancy[8]. Kuttner tumor is not associated with Sjogren's syndrome, other systemic autoimmune diseases or progression to lymphoma. However, a case report of extranodal marginal zone B cell lymphoma of MALT type of the salivary gland arising in sclerosing sialadenitis (Kuttner tumor) has been published[6].

The present report describes the final stage of the Kuttner tumor of bilateral submandibular glands in a 69 year-old man of a clinically, macroscopically, cytologically, histopathologically and immunohistopathologically identical tumor. The authors believe that, this is the first reported description in the literature of Thailand.

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รายงานผู้ป่วยเนื้องอกต่อมน้ำลายอักเสบร่วมกับเกิดพังผืดเรื้อรังคูทเนอร์

นพดล ลาภเจริญทรัพย์, อัจฉราพร พงษ์ทิพพันธ์

เนื้องอกต่อมน้ำลายอักเสบร่วมกับเกิดพังผืดเรื้อรังคูทเนอร์ เป็นเนื้องอกที่พบของต่อมน้ำลายใต้ขากรรไกรล่าง ลักษณะที่ตรวจพบ คือ มีต่อมน้ำลายแข็ง บวม ลักษณะทางพยาธิวิทยาพบเป็นพังผืดรอบ ๆ ท่อน้ำลาย มีเซลล์อักเสบเรื้อรังและกลุ่มเซลล์เม็ดเลือดขาวเกิดขึ้น มีการลดลงของส่วนสร้างน้ำลาย ในผู้ป่วยชายไทยอายุ 69 ปี รายงานลักษณะทางคลินิก เซลล์วิทยา พยาธิเนื้อเยื่อวิทยา และอิมมูนโนพยาธิเนื้อเยื่อวิทยา ร่วมกับทบทวนจดหมายเหตุทางแพทย์บรรยายลักษณะโรค 231 ราย ผู้ป่วยมีอายุเฉลี่ย 44 ปี (อายุระหว่าง 13 ถึง 81 ปี) โดยพบก้อนเนื้องอกที่ต่อมน้ำลายเป็นระยะเวลา 1 สัปดาห์ถึง 55 ปี (ระยะเวลาเฉลี่ย 23.2 ปี) โดยพบในเพศชายมากกว่าในเพศหญิงเล็กน้อย รายงานโรคเนื้องอกต่อมน้ำลายอักเสบร่วมกับเกิดพังผืดเรื้อรังคูทเนอร์ ได้รับการวินิจฉัยเบื้องต้นโดยการเจาะดูดและสรุปการวินิจฉัยโดยผลพยาธิวิทยาจากการผ่าตัดต่อมน้ำลายใต้กระดูกขากรรไกรล่างทั้งสองข้าง ซึ่งพบเป็นกรณีศึกษาแรกของประเทศไทย