Sjögren syndrome (SS) is the second most common autoimmune disease, affecting mainly middle-aged women. The disease might occur alone (primary SS) or in association with other autoimmune diseases such as rheumatoid arthritis (secondary SS). The important symptoms of SS, dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca), result from lymphocytic infiltration and destruction of the exocrine glands, particularly the salivary and lacrimal glands.1 Patients with SS have an elevated risk of developing malignant neoplasms, particularly hematologic malignancies, with most being non-Hodgkin B-cell lymphoma.2 Other cancers, such as oral cancer, breast cancer, and thymoma, might also occur in patients with SS. However, the coexistence of SS with nasopharyngeal carcinoma (NPC) has rarely been reported, with only one case involving secondary SS described in the literature to date.3 Here we describe a case of NPC in a patient with primary SS.

Case

A 58-year-old woman with a 2-year history of symptomatic dry eye and mouth was diagnosed with primary SS. Initial general physical examination revealed conjunctival congestion and mucosal atrophy of the tongue with atrophic glossitis. Laboratory serologic analysis showed positive titres for antinuclear antibodies (1:1280, speckled) and anti–Sjögren syndrome antigens A and B (> 240 U/mL and 172 U/mL, respectively). Screening for SS showed decreased salivary gland function and globular sialectasis on parotid sialography. Results of a Schirmer test during the ophthalmologic examination were positive for dry eyes, and a labial salivary gland biopsy (Figure 1) revealed focal chronic sialadenitis characterized by intense lymphocytic inflammatory infiltrate (focus score >2; >100 lymphocytes/4 mm² of glandular tissue). These findings were consistent with the diagnosis of primary SS. The patient was treated with hydroxychloroquine and pilocarpine, and her condition was well controlled.

During a routine outpatient follow-up visit in the rheumatology department at the Tri-Service General Hospital in Taipei City, Taiwan, a mass was palpated in her left neck, and she was referred to our otolaryngology department for further evaluation and management. Physical examination revealed a firm, mobile lymph node of about 2 × 2 cm in the left level III neck. Nasopharyngoscopy showed an exophytic bulging mass at the left lateral wall of the nasopharynx. Otoscopy showed a dull left tympanic membrane, and an audiogram revealed mild conductive hearing loss as shown by a flat tympanogram for the left ear. Based on these findings, a nasopharyngeal biopsy (Figure 1) revealed focal chronic sialadenitis characterized by intense lymphocytic inflammatory infiltrate (focus score >2; >100 lymphocytes/4 mm² of glandular tissue). These findings were consistent with the diagnosis of primary SS. The patient was treated with hydroxychloroquine and pilocarpine, and her condition was well controlled.

Magnetic resonance imaging of the head and neck revealed an enhancing tumour in the posterior and lateral walls of the nasopharynx and enlarged bilateral cervical lymph nodes above the supraclavicular region (Figure 2). In accordance with the American Joint Committee on Cancer tumour-node-metastasis staging system,4 she was diagnosed with NPC at stage III (1 primary tumour, 2 regional lymph nodes, no distant metastases).

Subsequently, the patient underwent an 8-week course of concurrent chemoradiotherapy (CCRT) with

**EDITOR’S KEY POINTS**

- In patients with primary Sjögren syndrome (SS), it is important to be aware of the possibility of developing lymphadenopathy in the neck, which might contribute to primary head and neck cancers other than lymphoma.
- When a patient with nasopharyngeal carcinoma and SS presents for radiotherapy, a reduced radiation dose should be considered to lessen the risk of developing cranial nerve palsy.
- The development of primary SS and nasopharyngeal carcinoma might be caused by previous Epstein-Barr virus infection.

**POINTS DE REPÈRE DU RÉDACTEUR**

- Dans le cas de patients atteints du syndrome de Sjögren (SS) primitif, il importe d’être au fait de la possibilité qu’une lymphadenopathie se développe au cou, qui pourrait contribuer à des cancers primitifs de la tête et du cou autres qu’un lymphome.
- Lorsqu’un patient atteint d’un carcinome nasopharyngien et du SS se présente en radiothérapie, il faudrait envisager une dose réduite de rayonnement pour réduire le risque de développement d’une paralysie des nerfs crâniens.
- Le développement du SS primitif et d’un carcinome nasopharyngien pourrait être attribuable à une infection antérieure par le virus d’Epstein-Barr.
a total dose of 7000 cGy to the primary tumour, plus
6000 cGy to the involved lymph nodes and 8 cycles of
40 mg/m² of cisplatin every 7 days. During the course
of treatment, the patient experienced severe dry mouth,
oral mucositis, recurrent swelling of bilateral parotid
glands, and radiation-related dermatitis. One month
later, prophylactic chemotherapy was given by adjuvant
5-fluorouracil infusion after the completion of CCRT,
and she exhibited left facial palsy. There was no evi-
dence of tumour recurrence at the 15-month follow-up.

Discussion
Primary SS is associated with an elevated risk of
developing lymphoproliferative neoplasms. The most
common associated cancer is non-Hodgkin B-cell lym-
phoma, which affects about 5% of patients with primary
SS. A retrospective analysis demonstrated that the over-
all incidence of all cancers in patients with primary SS is
2.6 times that of the general population. Parotidomegaly,
lymphadenopathy, inflammatory neuropathy, and vascu-
litis are important risk factors for the development of
lymphoma. Thus, in a patient with primary SS and a
history of rapidly developing neck lymphadenopathy,
potential malignancies should be considered.

In our patient, the development of non-Hodgkin lym-
phoma was the first possibility considered because of her
clinical presentation and the known incidence of cancer
with primary SS. However, when lymphadenopathy occurs
in the neck, it is important to rule out primary head and
neck cancers. In addition, involvement of the nasophar-
ynx should be considered because lymphoid hyperplasia of
exocrine glands has been regarded as a typical histologic
feature of the disease. One report described primary SS in
a patient with nasopharyngeal lymphoid hyperplasia mas-
quering as NPC. Biopsy of the nasopharynx is necessary
to make a definitive diagnosis. Our patient was eventually
diagnosed with NPC with neck metastasis.

It has been reported that NPC is one of the well docu-
mented EBV-associated carcinomas. The link of EBV
infection to NPC was established by the detection of
elevated anti-EBV antibody titres in patients with NPC.
Epstein-Barr virus infection also might play a role in the
pathophysiology of various autoimmune diseases, such
as systemic lupus erythematosus, rheumatoid arthritis,
Figure 2. Fat-suppressed T1-weighted magnetic resonance imaging:
A) Nasopharyngeal tumour (arrows) over the bilateral nasopharyngeal space. B) Multiple enlarged necrotic nodes (arrowheads) about 2.7 cm in maximum dimension in the bilateral neck above the supraclavicular region.
and primary SS. Although the pathogenesis of primary SS is still poorly understood, some reports have indicated a correlation between primary SS and EBV. Thus, the development of primary SS and NPC in our case might have been caused by previous EBV infection. Further studies and review of more cases are required to investigate the possible role of primary SS in the course of NPC.

Concurrent chemoradiotherapy is the main treatment of NPC. However, a rare complication in NPC patients is radiation-related cranial nerve palsy, most frequently involving the hypoglossal nerve. Our patient developed the complication of facial nerve palsy, which is extremely rare in NPC patients who have received radiotherapy. We suspected that the underlying SS and the effects of radiation might have contributed to this complication. Some studies have shown that patients with autoimmune collagen vascular diseases had an elevated risk of complications associated with radiotherapy. These authors pointed out that reducing the total dose of radiation by more than 10% could lessen the severity and frequency of acute and late effects in patients with autoimmune diseases receiving radiotherapy. Therefore, when a patient with NPC and SS presents for radiotherapy, a reduced radiation dose should be considered to lessen the risk of developing cranial nerve palsy.

Conclusion
To the best of our knowledge, the present case is the first one to report NPC in a patient with primary SS. We have emphasized the importance of being aware of the possibility of the development of lymphadenopathy in the neck, which might contribute to primary head and neck cancers other than lymphoma. The administration of CCRT to patients with NPC and SS should be performed with caution. The association between primary SS and NPC requires further investigation.

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Competing interests
None declared.

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