Intraneural perineurioma is an uncommon tumor of the peripheral nerve that is composed of spindle cells in an onion bulb-like pattern and centrally located axons and Schwann cells.

Most cases occur predominantly in the major nerve trunks of the hand and upper extremities. Intraneural perineurioma was first described as localized hypertrophic neuropathy in 1964. It was once believed to be a localized form of generalized hypertrophic neuropathy, which also had onion bulb-like structures. However, hypertrophic neuropathies mainly consist of proliferating Schwann cells resulting from repeated demyelination and remyelination. In 1980, Mitsumoto suggested that localized hypertrophic neuropathy was perineurioma based on the evident electron microscopic findings. Electron microscopy revealed that the tumor cells have slender cytoplasmic processes with frequent interdigitation, basal lamina and many pinocytotic vesicles that were characteristic features of perineurial cells, not of Schwann cells.

In 1995, Emory et al. reported that intraneural perineurioma is a clonal neoplasm associated with an abnormality of chromosome 22. Huguet et al. identified a deletion of chromosome 22q11 in intraneural perineurioma using a FISH method.

To our knowledge, this is the first reported case of an intraneural perineurioma involving the small nerves in the tongue along with the result of FISH targeting chromosome 22q11.2 in Korea.

**CASE REPORT**

A 16-year-old male presented with a submucosal mass in his tongue that was not accompanied by sensory or motor signs or symptoms. He had recognized it six years before but the size of the mass had not increased since then. He recently complained of the mass without any associated symptoms. There was no prior medical history. A physical examination revealed a protruding mass at the right lateral side of the tongue (Fig. 1) measuring 1.0 cm in the greatest dimension. The overlying mucosa was light brown without inflammatory signs. The mass was excised,
and found to contain an ill-defined border that was firmly attached to the surrounding tissue. The patient was well 6 months after the excision.

The resected specimen was a fragment of the tongue tissue, measuring $1 \times 0.8 \times 0.4$ cm. The mucosa was intact, and an ill-defined firm mass measuring $1.0 \times 0.8 \times 0.6$ cm was present in the submucosa. The cut surface of the mass was pinkish gray and fibrotic.

Histological examination of the hematoxylin eosin stained sections and immunohistochemical analysis against CD34 (1:2,500; Immunotech, Beckman-Coulter, Fullerton, Calif), S-100 protein (1:500, Zymed, San Francisco, CA, USA), synaptophysin (1:100, Dinona, Seoul, Korea), epithelial membrane antigen (EMA) (1:10, DAKO, Glostrup, Denmark) and Glut-1 (1:100, Neomarker Fremont, USA) were performed. The mass consisted of tortuous and thickened peripheral nerve bundles (Fig. 2A, B) with proliferating spindle cells, showing an onion bulb like structure. The spindle cells had slightly large nuclei with vesicular chromatin and indistinct nucleoli and myxoid cytoplasm (Fig. 2C). The spindle cells at the periphery of the onion bulb like structures showed a positive reaction to the Glut-1 antibody (Fig. 2D) and a negative reaction to the S-100 protein (Fig. 2E) or EMA antibodies. S-100 protein positive Schwann cells were present at the center of the onion bulb-like structures (Fig. 2E). Axons were identified by synaptophysin immunohistochemical staining. The thickened nerve bundles also contained abundant capillaries, which were highlighted by the immunohistochemical staining for CD34.

Fluorescence in situ hybridization analysis (FISH) was performed using DiGeorge/VCFS region probe (Vysis) to target chromo-
Intraneural perineurioma is an unusual peripheral nerve tumor. No case has been reported in Korea. Intraneural perineurioma predominantly involves major nerves in the upper extremities and most commonly in the median nerve. However, some cases involve unusual sites including spinal roots C8 and T1, digit, facial nerve, oral mucosa, and a small unnamed nerve of the tongue. Intraneural perineuriomas involving the small nerves in the oral mucosa or tongue appear as nodular lesions composed of haphazardly arranged enlarged nerve bundles. The tumor cells showed one or two green and/or red signals. The ratio of the orange to green signals was 1.08, which indicated our case did not have a chromosomal deletion at 22q11.2 or 22q13.

**DISCUSSION**

Intraneural perineurioma is an unusual peripheral nerve tumor. Some 22q11.2, which was the previously reported to be a locus of a chromosomal deletion in intraneural perineurioma. The DiGeorge/VCFM region probe originally targeted the TUPLE1 locus at 22q11.2 (orange signal) and the ARSA locus at 22q13 (green signal). The tumor cells showed one or two green and/or red signals. The ratio of the orange to green signals was 1.08, which indicated our case did not have a chromosomal deletion at 22q11.2 or 22q13.

The current case showed immunoreactivity to Glut-1 but not to EMA despite the high primary antibody titer (1:10) and various antigen retrieval methods used. EMA reactivity may be difficult to demonstrate in perineuriomas without the use of antigen retrieval techniques, a higher concentration of antisera, or longer incubation times. For those reasons, other perineural markers including Glut-1 and claudin-1 were recently reported. These immunohistochemical stainings make it easier to demonstrate the perineural differentiation of the perineuriomas. In the case with negative EMA immunoreactivity, the electron microscopic findings are most useful for diagnosing the perineurioma. However immunohistochemical stainings for Glut-1 and claudin-1 can also demonstrate the perineural differentiation in lesions containing onion bulb-like structures.

The genetic aberrations in chromosome 22 associated with the NF2 gene were previously noted in soft tissue perineuriomas, meningiomas and schwannomas. Subsequent molecular analyses of the NF2 gene at chromosome 22 in perineuriomas including intraneural perineurioma indicated a role of NF2 gene abnormalities in perineurioma tumorigenesis. Emory et al. reported an abnormal chromosome 22 with additional material translocated onto the long arm at band q11.2 based on karyotype analysis and a loss of the centromere either of chromosome 14 or 22 according to a FISH study. Huguet et al. identified a deletion of chromosome 22q11 using a FISH study. However, the current case did not show any chromosomal aberration at 22q11.2 and 22q13. Brock et al. reported an addition in chromosome 2 and 3 not in chromosome 22 based on karyotyping.

There is some controversy regarding the treatment of an intraneural perineurioma involving the major nerves: resection with anastomosis or a conservative approach. However, a resection is initially performed for both diagnosis and treatment in most cases of intraneural perineurioma involving the peripheral small nerves. Because the biological behavior of intraneural perineurioma is benign, a complete excision is sufficient for cases of intraneural perineurioma involving the peripheral small nerve. A recurrence after a complete excision has not been noted. However, intraneural perineurioma can progress without treatment.

**REFERENCES**