SHORT COMMUNICATION

A Case of Apocrine Carcinoma Arising in a Sebaceous Naevus: Detection of *HRAS* G13R Mutation

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RAS mutations are known pathogenic genomic alterations in a sebaceous naevus (SN) (1). Secondary tumours of SN are mostly follicular tumours and adnexal gland tumours (2), and some carry *RAS* mutations (1). We describe here a case of apocrine carcinoma (AC) with an *HRAS* mutation that developed as a secondary tumour of a latent SN.

CASE REPORT

A 68-year-old man was referred to our hospital because of a nodule on the occipital scalp where he had a hairless patch after childhood trauma. The tumour was a pink pedunculated nodule measuring 28×25 mm (**Fig. 1**A). Yellow-orange hairless patches were not observed in the surrounding area. Excision was performed. Histopathology revealed a polymorphous ductal structure consisting of tumour cells with nuclear atypia in the dermis (Fig. 1B, C). In addition, decapitation was observed on the luminal surface of the ductal nests. Immunohistochemical study revealed oestrogen receptor (–), progesterone receptor (–), androgen receptor (+), GCDFP15 (+), cytokeratin 7 (+), HER-2 (2+) and S-100 (–). In addition, the tumour cells were negative for p63 expression (Fig. 1D). Whole-body computed tomography did not reveal any tumour that could metastasize to the skin. Based on these findings, the tumour was diagnosed as AC. Moreover, hyperplastic apocrine glands were observed on the lateral margin of the specimen independently from AC, and p63 was positive in the peripheral layer of the glands (Fig. 1E, F), suggesting collision or association with an SN. Subsequently, wide resection revealed BCC and additional malformed apocrine glands in the surrounding area. To clarify whether the AC developed from an SN, genotyping of *RAS* was performed. DNA was extracted from paraffin-embedded tissue sections of AC, hyperplastic apocrine glands and BCC, followed by DNA sequencing of exon 2 of *HRAS* and *KRAS*. A heterozygous mutation in *HRAS*, p.Gly13Arg (G13R), was identified in the AC and hyperplastic apocrine glands, but not in BCC (**Fig. 2**). The KRAS Gly12 residue was wild type (data not shown). Immunohistochemical study using anti-RAS G13R antibody also confirmed RAS G13R in the AC and hyperplastic apocrine glands (Fig. 2). Consequently, the AC in this patient was thought to have developed from an SN. For additional materials and methods, see Appendix S1.

DISCUSSION

AC is a rare adnexal carcinoma that develops mainly on the scalp, face, trunk and genitalia, and arises sporadically or originates from specific conditions, such as apocrine adenomas, accessory breast tissues, or SN. AC on the scalp should be differentiated from metastatic breast cancer. Moreover, it is necessary to determine whether AC on the scalp developed from an SN, because wide resection including the SN is desir-
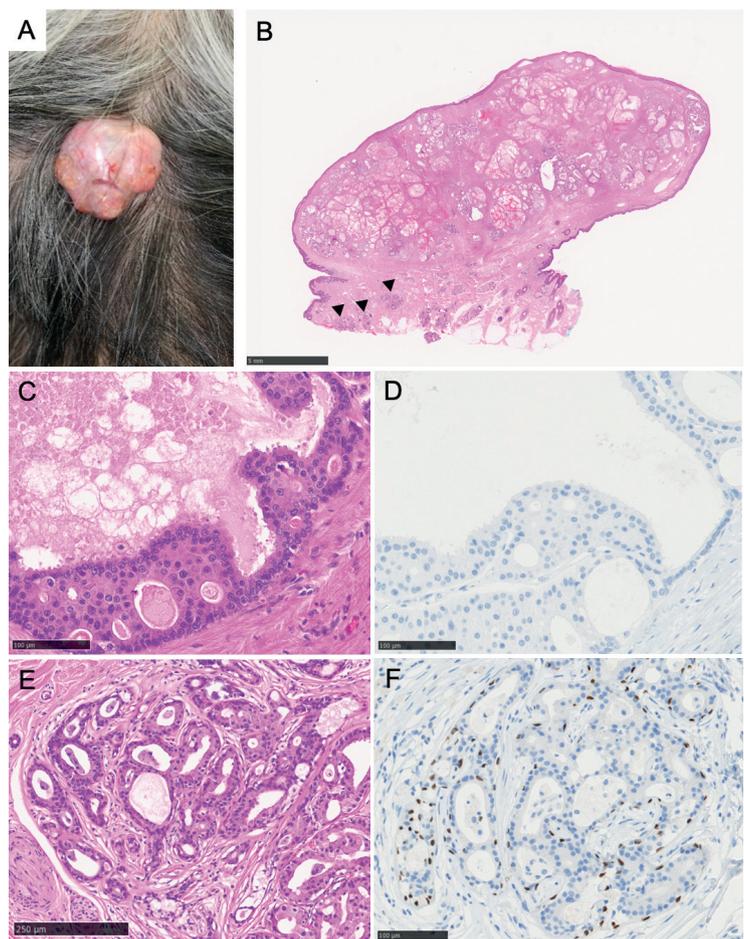

Fig. 1. Clinical presentation and histopathology of the tumour. (A) Clinical image showing a pink pedunculated nodule on the occipital scalp. (B) Loupe statue showing an exophytic tumour with tubular structures in the dermis. Hyperplastic tubular structures (*arrowheads*) are present in the lateral margin of the tumour (haematoxylin and eosin (HE) staining; *scale bar*=5 mm). (C) Tumour nests show tubular formation with a monolayer of cuboidal cells. Decapitation is observed (HE staining, *scale bar*=100 μm). (D) p63 immunohistochemical staining in the tumour nests. p63 is negative in the nuclei of the tumour cells (*scale bars*=100 μm). (E) Hyperplasia of tubular structures with wide lumens in the lateral margin of the tumour (HE staining, *scale bar*=250 μm). (F) p63 immunohistochemical staining in the hyperplastic tubular structures. p63 is positive in the peripheral layer of the glands (*scale bars*=100 μm).
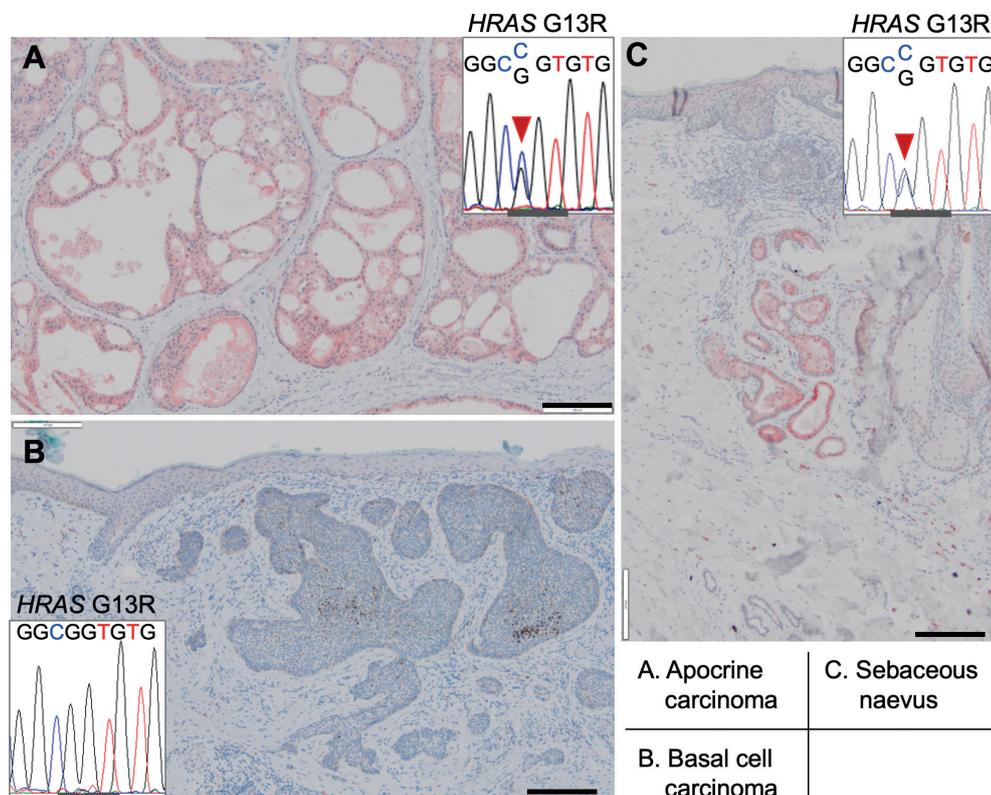
Fig. 2. Immunohistochemical staining of Ras G13R and DNA sequencing of *HRAS* exon 2. Immunohistochemical staining of G13R and DNA sequencing of *HRAS* exon 2 in: (A) the apocrine carcinoma, (B) sebaceous naevus, and (C) basal cell carcinoma. *Scale bars=200 µm.*

able. To distinguish between apocrine glands in SN and secondary AC by immunohistochemistry, p63 staining is useful, since loss of p63 expression in the tumours reflects the loss of myoepithelial cells associated with the carcinogenesis of apocrine lesions (3). In SN, genetic alterations occur in *HRAS*, *KRAS*, *TP53* and *NOTCH2* (1, 3, 4). Among these, *HRAS* G13R is the most common somatic mutation and it activates MAPK/PI3K pathways. DNA sequencing and immunohistochemical staining are available to detect this mutation. Many secondary tumours also have the same mutations as the original lesions (1, 4, 5). However, in the 3 cases of sporadic AC that we examined (Table SI), no mutations in exon 2 of *HRAS* (Fig. S1) or *KRAS* were found. Although this study has some limitations, it suggests that it is useful to perform genetic analysis in order to clarify whether SN exists as a precursor lesion when adnexal tumours secondary to SN are suspected.

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