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KRAS MUTATION IN A CASE OF ORAL SIALOADENOMA PAPILLIFERUM IN A PATIENT WITH LINEAR NEVUS SEBACEUS SYNDROME.

Giulia Querzoli[1], Francesco Vitali[2], Giulia Simoncini[1], Achille Tarsitano[2], Thais Maloberti[3] Giovanni Badiali[2], Maria Pia Foschini[4]

1 Pathology Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy

2 Oral and Maxillofacial Surgery Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, DIBINEM – University of Bologna

3 Solid Tumor Molecoular Pathology Laboratory, IRCCS Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy

4 Unit of Anatomic Pathology, Bellaria Hospital, Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

BACKGROUND

Linear nevus sebaceous syndrome (LSSN), also known as Schimmelpenning-Feuerstein-Mims syndrome (SFMS) is a rare neurocutaneous syndrome characterized by linear sebaceous nevi that follow the lines of Blaschko, in addition to extracutaneous manifestations involving the central nervous system, eyes, skeleton, and other organs.

Incidence of SFMS is roughly 1 in 1000 live births; it may result from genetic mosaicism involving a lethal autosomal-dominant gene. Several gene mutations have been identified in the affected skin including HRAS, NRAS, and KRAS that are all part of the RAS signaling pathway involved in cell growth regulation. Postzygotic mutations result in mosaic RASopathies that are now identified in a growing spectrum of congenital syndromes including SFMS.

Among oral manifestation of the SFMS include mucosal hyperpigmentation, papillomatosis, eventually causingsoft tissue overgrowth on teeth, and enamel defects, furthermore, hemihypertrophy and fibrous lesions, uvula bifida, retention of teeth and tooth position anomalies, bone cyst of jaw, giant cell granuloma of the jaw or odontoma and further odontogenic neoplasms such as ameloblastoma, ameloblastic fibro-odontoma, and adenomatoid odontogenic tumor (1).

This is the first reported case of a sialoadenoma papilliferum in a Linear Nevus Sebaceus syndrome, that is a typically BRAF (V600E) mutated lesion (2) or in a minority of case HRAS (3).

CASE REPORT

The patient is a 11-year-old female girl. At birth, several extracutaneus manifestations were diagnosed (Left eye inferonasal limbal opacity, left kidney pelvic bifurcation, frontal cortical malformation in the left temporo-insular region with focal epilepsy). Moreover, the patients developed a sebaceus linear nevus on the left side of the face and the neck from the inferior lip to the sternal notch. The patient underwent three laser ablations (one in 2013 and two in 2014) and two surgical resections afterwards. In 2015 the genetic consult hypothesized and then confirmed with a genetic test a linear nevus sebaceous syndrome with mosaic mutation involving KRAS gene (pGly12Asp).

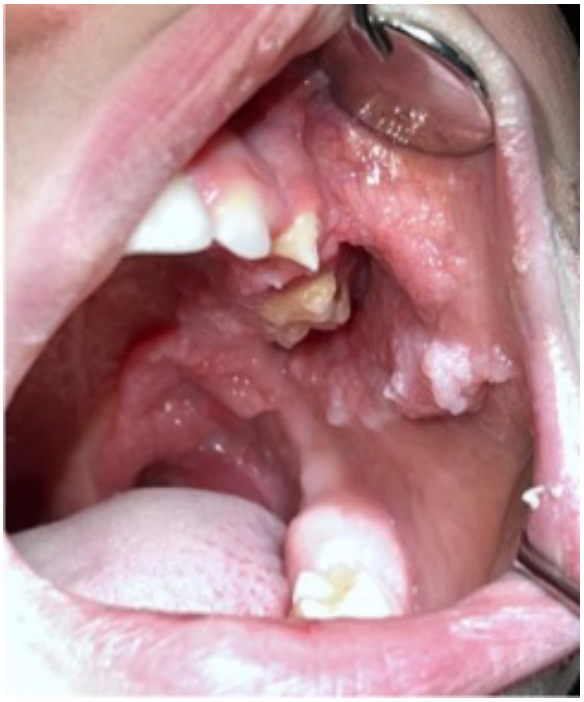
Concurrently, she developed an intraoral lesion affecting the left buccal mucosa, the gingiva of the left upper maxilla with associated dental eruption disorder, the left hard palate and the left soft palate with involvement of the uvula (Fig 2). In 2023 she underwent to surgical resection of the intraoral neoplasm. Histologically, the tumor was characterized by biphasic differentiation, consisting of exophytic papillary structures covered by stratified squamous epithelium locally contiguous with a proliferation of papillomatous ductal epithelium located under neath the mucosal surface.

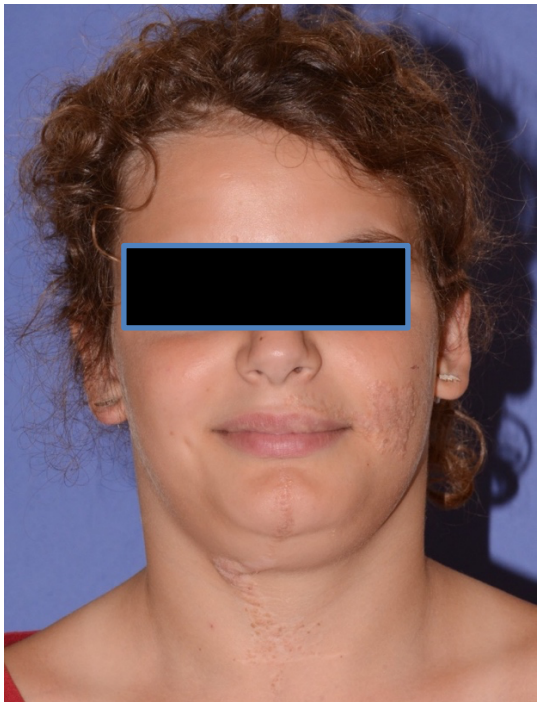
The ductal epithelium was double-layered or multilayered structures, lined by luminal cuboidal to columnar cells and cuboidal to flattened basal cells (Fig.3A). The luminal cells had round to oval, bland nuclei and inconspicuous nucleoli without atypia. Accidental areas of mucinous metaplasia can be seen in the ductal.

Immunohistochemical studies of our case have shown that CK7(Fig.3B) was strongly expressed in the ductal luminal cells while p63(Fig.3C) was strongly expressed in the basal cell layer. Ki67 less than 10% cells in both components. BRAFV600E in both the glandular and squamous tumor components showed negative staining.

The lesion was p16 negative. The patient's DNA was extracted from the tissue sample, amplified using PCR. The determined sequences were compared against the reference sequence. A somatic mutation in KRAS gene (p.Gly12Asp) was detected.

GRAPHS & TABLES





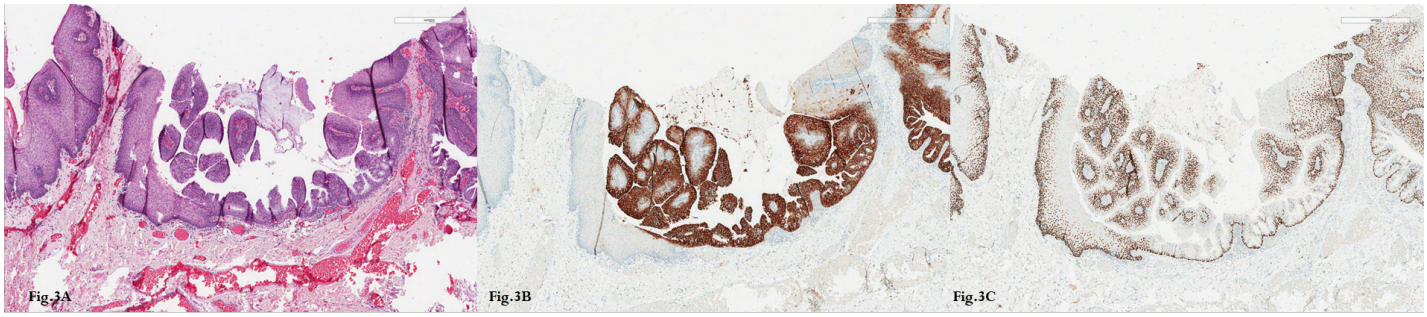


Fig.3A Fig.3B Fig.3C

REFERENCES

1. Friedrich RE, Gosau M, Luebke AM, Hagel C, Kohlrusch FK, Hahn M, VON Kroge S, Hahn J, Wieland I, Zenker M. Oral HRAS Mutation in Orofacial Nevus Sebaceous Syndrome (Schimmelpenning-Feuerstein-Mims-Syndrome): A Case Report With a Literature Survey. In Vivo. 2022 Jan-Feb;36(1):274-293. doi: 10.21873/invivo.12701. PMID: 34972725; PMCID: PMC8765160.
2. Chen S, Peng J, Yuan C, Sun L, Zhang R, Sun Y. Sialadenoma papilliferum: clinicopathologic, Immunohistochemical, molecular analyses of new five cases and review of the literature. Diagn Pathol. 2021 Mar 12;16(1):22. doi: 10.1186/s13000-021-01084-5. PMID: 33712056; PMCID: PMC7953575.
3. Ide F, Ito Y, Kikuchi K, Satomura K, Ogawa I, Yamamoto H. Activating HRAS mutation in a case of inverted ductal papilloma of the salivary gland. Pathol Int. 2021 Dec;71(12):844-848. doi: 10.1111/pin.13166. Epub 2021 Sep 21. PMID: 34547823.

CONCLUSION

This is the first case of a sialoadenoma papiliferum described in the context of a linear sebaceus nivus syndrome. Moreover, the molecular pattern of this lesion showed absence of the typical BRAF mutation and the presence of a KRAS mutation, which is pathognomic of the linear sebaceus nivus syndrome.