



CASE REPORT

Ectopic palatine tonsil meningioma in type 2 neurofibromatosis: a few times documented phenomenon

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Abstract

Type 2 neurofibromatosis is a hereditary neurocutaneous entity, characterized by associations with cranial and spinal meningiomas; extra neural cases are infrequent. There are oral meningiomas reports, however their presence at the palatine tonsils have not been described. This is a patient, with type 2 neurofibromatosis inherited from her father. The guest, presented progressive odyno-dysphagia whose etiology was WHO I meningioma in palatine tonsils, while the cranial image showed same lineage meningiomas that were surgically treated. This rare phenomenon in the context of an uncommon disease and the events that would explain the arrival of meningiomatous tissue to the palate are discussed.

Keywords: meningioma; neurofibromatosis 2; palatine tonsil.

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Introduction

The Neurofibromatosis type 2 (NF-2) (ORPHA: 637) is less frequent than neurofibromatosis type 1 (NF-1), it has a prevalence of 1-9 / 100,000 inhabitants¹; the meningiomas presence constitutes part of the NF-2 minor diagnostic criteria, they are the second most common extra-axial tumors after schwannomas²; the natural history characteristics of meningiomas in NF2 are: slow growth, recurrence and appearance of same nature new tumors, including in the resected tumor bed. Unlike NF-1, in NF-2 lesions have a low rate of malignancy³; the growth pattern and tumor grade are affected by radiotherapy, which may have little benefit⁴. Between 26 and 36 genetic mutations have been described in NF2 meningiomas, the main ones: mutation of the NF-2 gene at the 22q locus and in the cell membrane tumor suppressor protein, MERLIN⁵; extraneural and multiple meningiomas are little mentioned, aggressive and affect hereditary phenotypes and truncated mutations; their preferred treatment is extirpation, like those located in neural tissues⁶. In this case, the patient presented major and minor criteria for NF-2, the meningioma on the palate was compatible with the same histopathological lineage as on the intracranial meningiomas. Our purpose is to discuss about extra neural,

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non-metastatic and not associated with invasion from cranial meningiomas and our objective is to explain the events that would allow meningiomatous tissue to reach the palate.

Case report

The patient currently in her third decade of life, was diagnosed during her childhood with hereditary NF-2, had history of cutaneous neurofibromas surgically treated, there was no exposure to radiotherapy; reported that for 3 years, with no apparent cause, has had a sensation of pharyngeal foreign body, is accompanied by progressive dysphagia for solids without difficulty for liquids (HP: 0200136), in addition headache with evening predominance (HP: 0002315) and walk difficulty (HP: 0002355). Hearing loss and tinnitus (HP: 0000360), nocturnal snoring, and increased dysphagia are the major complaints.

The physical examination highlights were: the presence of café-au-lait macules on the legs, hips and back (HP: 0000957), medialized left tonsillar pillar, uvula displaced, the tonsil with an exophytic, violaceous upper pole lesion with a diameter of two centimeters; neurological examination revealed bilateral sensory hearing loss predominantly on the right ear, peripheral vertiginous syndrome predominantly on the right (HP: 0002321), non-ophthalmoparesis, spastic tetraparesis predominantly in the lower limbs. (HP: 0001285). Karnofsky performance scale (KPS) was 90%. Imaging studies reported intracranial and oropharyngeal lesions (Figure 1a-f, Figure 2a), contrasted body scan tomography did not show other lesions.

The upper pole lesion of the palatal tonsil was excised by the otorhinolaryngology team, in other surgical time than the intracranial procedure, it was observed to be pale, pedunculated 1.5 x 1.5 cm, with a histopathological result of WHO I fibrous meningioma (Figure 2c-i)

In the neurosurgical procedure, parasagittal meningiomas were excised (Figure 1g-m), the result of which was WHO I fibrous type. Eight months later, the patient presented altered consciousness and tetraplegia (HP: 0030182). A total excision of brainstem glioma was performed. it was a WHO II astrocytoma, improving its condition, currently with KPS 80% and in observation of: acoustic schwannomas, remaining tentorium, convexity and falx meningiomas that do not present symptoms; she abstains from radiation therapy because of the risk of detrimentally influencing the natural history of the lesions.

Discussion

The extra neural meningiomas in NF-2 are mostly given by invasion of intracranial primaries meningiomas from: orbit, pterygopalatine-subtemporal fossa, nasal-oral cavity and neck, being considered as aggressive forms of the disease, primary lesions without relation to another intracranial one are the 2% of meningiomas⁷; Hoyer classified in type 3 extraneural meningiomas those with no relation to neurophoromans or metastases, he called these ectopic meningiomas⁸. The case presented has these characteristics, so is considered as an oropharynx ectopic meningioma.

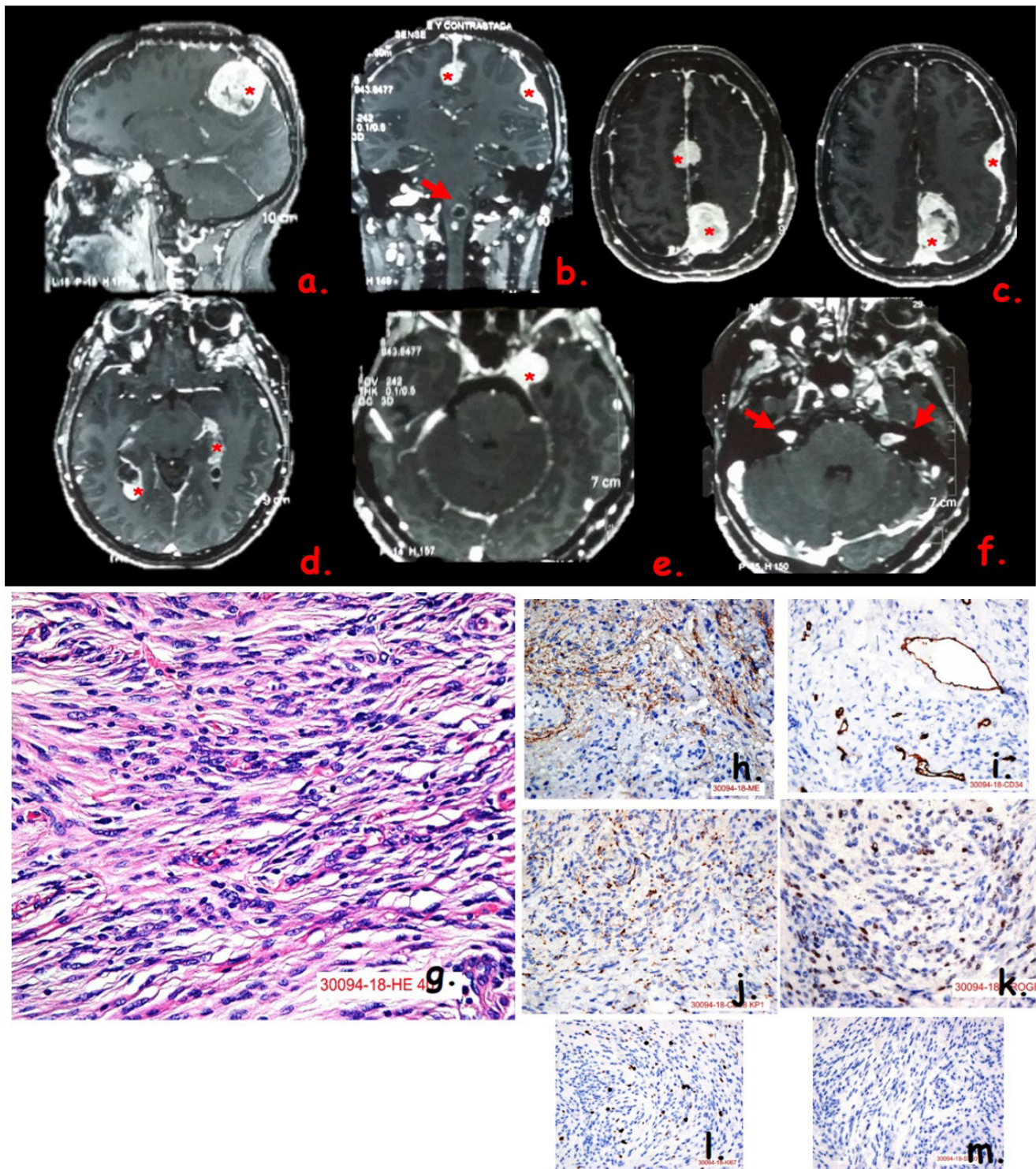


Figure 1. (a) Cerebral Falx meningioma in MRI sagittal section; (b) Cerebral falx, and convexity meningiomas and brainstem glioma (red arrow) in MRI coronal section; (c) Cerebral falx and convexity meningiomas in MRI axial slices; (d) Tentorium meningiomas in MRI axial section; (e) Sphenoidal minor wing meningioma in MRI axial section; (f) Bilateral vestibular schwannomas in MRI axial section; (g) Hematoxylin-eosin X40 stain: swirling cap cells, no mitosis; (h) Epithelial membrane antigen IQ; (i) CD34 IQ; (j) CD68 IQ; (k) Progesterone IQ; (l) Ki-67 IQ; (m) S100 IQ. (Source: imaging and pathology center of the Carlos Andrade Marín Hospital, Quito-Ecuador). Meningiomas with contrast enhancement (Red*). Magnetic Resonance image (MRI). Immunohistochemistry (IQ).

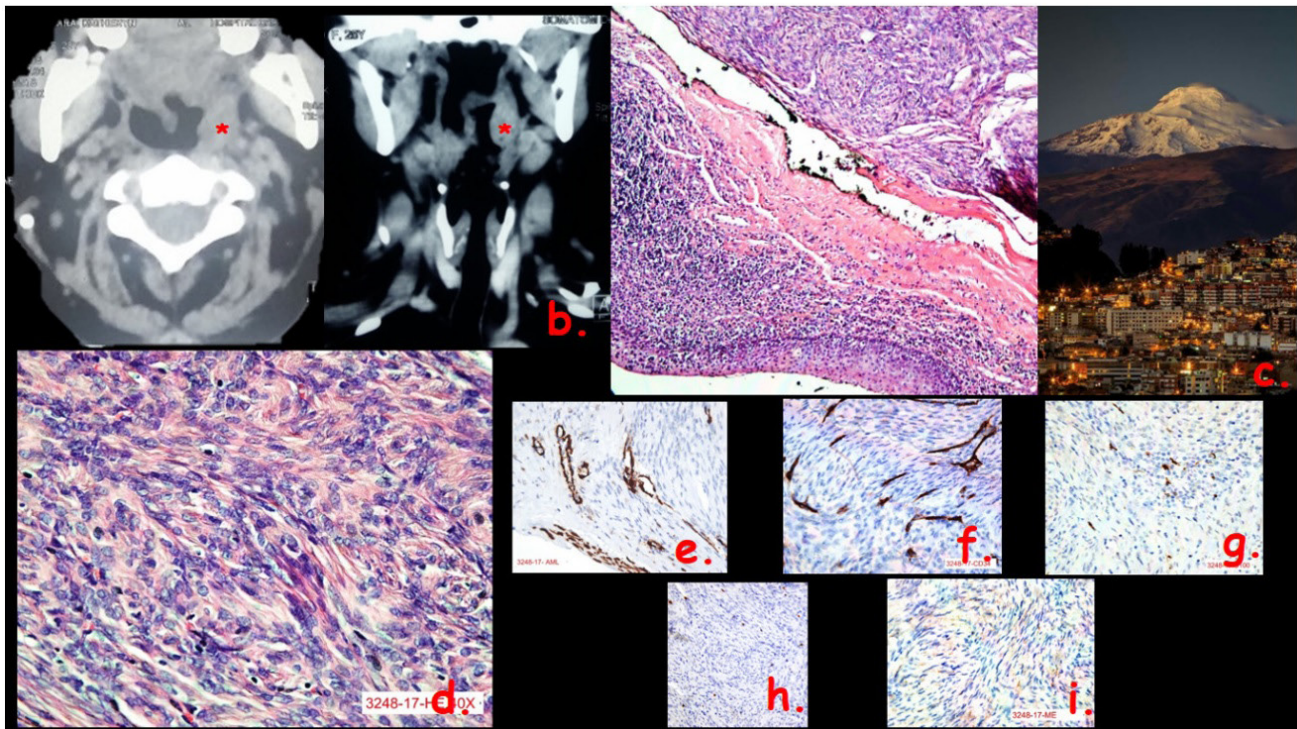
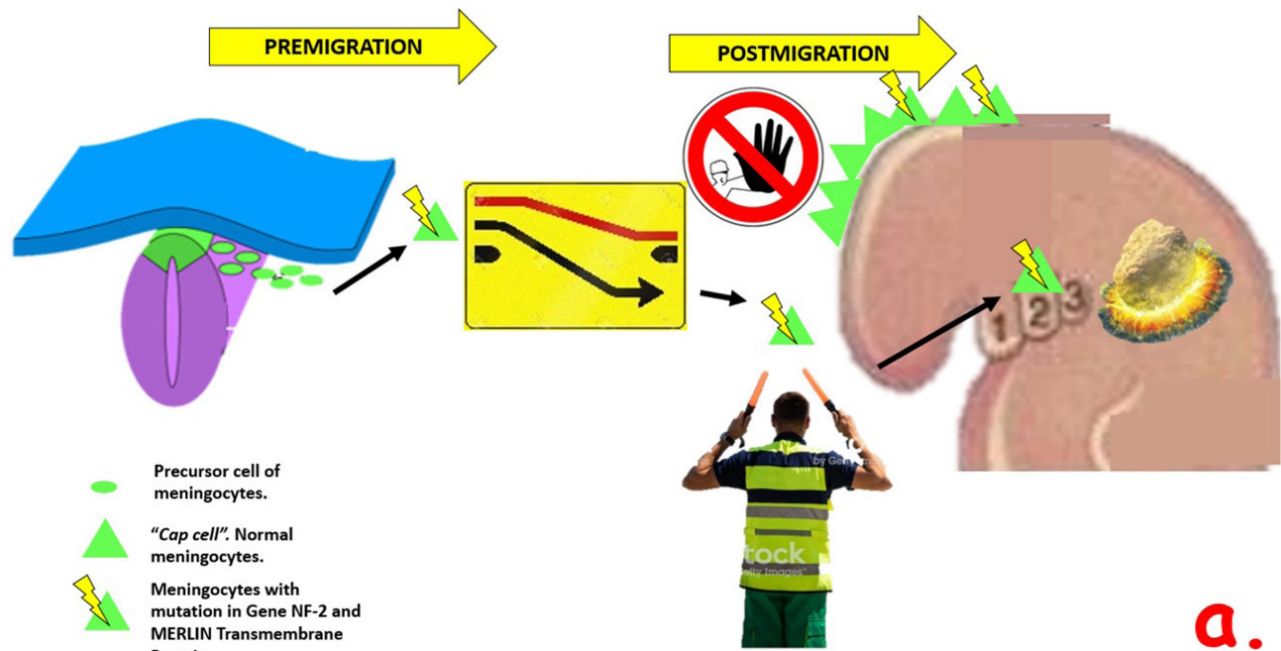


Figure 2. (a) Diagram of the pathophysiology of the migration in ectopic meningiomas to the second branchial bag. (Created by: Author JMAI); (b) Palatine tonsillar meningioma in axial and coronal neck tomography; (c) Hematoxylin-eosin X10 stain image: palatine tonsil lined by squamous and respiratory epithelium (pseudostratified) in the stroma showing mesenchymal neoplasia constituted by swirling of spindle cells with large nuclei and small nucleoli of arachnoid tissue, two different tissues (clearly delimited respiratory and nervous) next to it, an image that exemplifies the contrast of these two tissues; the landscapes contrast between the Nevado Cayambe and the City of Quito. (Source: Carlos Andrade Marín hospital pathology laboratory and photo of the Ecuadorian Ministry of Tourism); (d) hematoxylin-eosin X40; (e) Smooth muscle antigen IQ; (f) CD-34 IQ; (g) S-100 IQ; (h) Ki-67 IQ; (i) Epithelial membrane antigen IQ. (Source: imaging and pathology center of the Carlos Andrade Marín Hospital, Quito-Ecuador). Ectopic palatine tonsil Meningioma (Red*). Immunohistochemistry (IQ).

The pathophysiology is not clarified, several theories have been proposed in the embryological development of the neural crest arachnoid precursors cells, their remnants are evidence of the failure in cranial migration, the mechanisms that originate ectopic meningiomas are: (1) failure in cell signaling to their destinations in arachnoid tissues, "staying in the middle of the road" (2) erroneous cell signaling implanting itself in tissues other than neural, (3) interruption of its migration paths by the presence of other abnormal cells that will form intracranial lesions, the latter two allow meningocytes to collide with mesenchymal and endodermal tissues and (4) the dedifferentiation of normal peripheral neural tissues to meningocytes, the latter less approved^{9,10}; the crash of neuroectodermal cells to the epithelium (endodermal origin) of the second pharyngeal bag which is the primordium of the palatine tonsils could occur between the third and fifth month of intrauterine period, a time when infiltration of lymphatic tissue in this structure also occurs¹¹; as a hypothesis applied in our case (Figure 2a).

In the NF-2 embryology, the following play a leading role: the mutation of the NF-2 gene and the tumor suppressor MERLIN, overexpressed in experimental models, in extra neural structures such as: the branchial arches, the dorsal aorta and para-aortic splenopleura, in addition, a high expression in cells that migrated from the dorsal neural crest, in contrast to almost zero expression in those same cells in the premigration stage, this corroborates the role of the mutation of the NF-2 and MERLIN gene in migration, adhesion cell, motility and proliferation during development⁹, which supports the explanation of migration failure and ectopic tumor settlement in our patient.

The associations of neurofibromatosis and anomalies of the second branchial arch is an unclear phenomenon, there are reports of persistence of clefts, cysts and hamartomas in suprahyoid and pharyngeal structures in NF¹², however, ectopic meningiomas are not considered as part of these anomalies.

Symptoms in NF-2 due to intracranial lesions present between the age of 20 and 30 years (minor diagnostic criteria, especially in vestibular schwannomas)³, this same evolution was found in reports of primary extracranial neck meningiomas where parapharyngeal locations are mentioned; the main symptomatology was the mass sensation with dysphagia, which concludes that presentation is common in people under 30 years old⁸, including sporadic extra neural meningiomas, NF-1 and NF-2 parapharyngeal ectopic primary meningiomas^{13,14}, although it is not exclusive to NF, for instance, a sporadic pharyngeal ectopic case is mentioned without an association of any intracranial lesion or any syndrome¹⁵; the palatine tonsils are one of the affected second pharyngeal bag structures, other damaged parts with the same origin mentioned in NF-2 are: the carotid-thyroid space, the laryngopharynx and the sub and retrolingual space, all of them with evidence of intracranial lesions¹⁶, it is important to study the neck in NF-2 patients with dysphagia under fourth decade of life, as in our case, because the possibility of development meningiomatous lesions in the second branchial arch.

The most frequent histotype of meningiomas associated with NF-2 is meningothelial, while the mutation of the NF-2 gene is the most present in these, even in sporadic forms¹⁷; In the most extensive series of cases of primary ectopic neck meningiomas, they report the transitional type as

the most present, they do not mention whether these coincided with the intracranial or intraspinal lesions lineage in the NF-2 participants⁸, our case was fibrous type (the second most frequent type of WHO I meningiomas), cranial and palatal types were the same nature, with specific differences in immunohistochemistry (Table 1).

Table 1. Immunohistochemistry comparison between of the NF-2 patient meningiomas.

	Intracranial meningioma.	Palatal tonsil meningioma.
Vimentin and Epithelial membrane antigen (EMA).	+++ diffuse.	++ diffuse.
Progesterone.	++ diffuse.	+ diffuse.
Smooth muscle antigen (SML).	+/-.	+ Focal in accompanying vessels.
CD-34.	+ Focal in accompanying vessels.	+ Focal in accompanying vessels.
S-100.	+ focal.	+ Weakly focal.
CD-68.	+	+/-.
Ki-67.	Negative.	Negative.

The number of cranial and extracranial lesions reported in similar cases was not variable in the analysis, but in molecular studies they conclude that several lesions, including multiple types, MISME Syndrome (Meningiomas, schwannomas, ependymomas and gliomas) is proportional to the degree of aggressiveness and recurrence¹⁸, but not to malignancy, also more present in direct hereditary forms¹⁹, while series of case studies of extracranial meningiomas report coincidences of bilateral lesions on the face and neck in NF-2⁸, our patient inherited her pathology from her father, for therefore, this trait could be demonstrated with its phenotype of having several lesions: acoustic schwannomas, supratentorial meningiomas and in the palatal tonsil and brainstem glioma.

The impact of the presence of ectopic meningiomas on the NF-2 overall survival and prognosis has not been shown to be related, however there are molecular bases of mutated aggressive forms that could be associated with this phenomenon, even neural lesions play a more important role in the evolution of astrocytomas and ependymomas of the brainstem and spinal cord⁶, in this case the greatest impact on the patient morbidity was the brainstem glioma.

The cornerstone of treatment is the radical excision of the lesions; adjuvant radiotherapy and chemotherapy are controversial, in general the annual growth rate and possibility of recurrence is slower than sporadic lesions², small lesions are preferably followed with observation since radiotherapy has the risk of modifying the benign nature and natural history, increasing its growth rate, even reporting malignancy²⁰⁻²²; In our case, we proceeded to total excision of the lesion in the palatine tonsils, performing total tonsillectomy and excision of parasagittal meningioma at the cranial location,

as we mentioned before, the patient was complicated with growth of a brainstem glioma which was performed total exeresis, currently the patient is in control of other injuries; In view of the increased growth of existing lesions, surgical intervention will be proposed over other medical procedures such as radiotherapy.

Conclusions

- Our patient belongs to The NF-2 with strong inheritance features has a great possibility of expression of meningiomas in ectopic locations;
- The palatine tonsil is part of the neck and the oral cavities meningiomas that are more frequent after the nervous system;
- Multiple intracranial meningiomas like our case report can be associated with ectopic locations;
- The physicians who follow NF-2 patients should think about extra neural locations in presence of atypical symptoms and in ages under 30 years;
- Our case, just like the most NF-2 patients, the most important etiology are the embryological theories to explain the palate tonsil meningiomas, because are congenital tumors originating from development and can be under-diagnosed;
- The total excision is the preferred treatment and the small lesions are better to observe than to use radiotherapy, this strategy that was used in our case;
- The recurrence is expected and malignancy is rare, important to maintain long-term follow-up in our case.

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To our patient, the main motivation for our research.

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