Onychomatricoma: Genome-wide analyses of a rare nail matrix tumor

Javier Cañueto, MD,[a] Ángel Santos-Briz, MD, PhD,[b] Juan Luis García, MD, PhD,[c] Cristina Robledo, PhD,[c] and Pablo Unamuno, MD[a]
Salamanca, Spain

Background: Onychomatricoma (OM) is a rare benign tumor of the nail matrix in which genome-wide analyses have never been performed. It is clinically characterized by an increased transversal curvature of the nail plate, a longitudinal yellowish discoloration, and splinter hemorrhages. Once the nail plate has been removed, fingerlike fibrokeratogenous projections appear through the proximal nailfold. Histologically, it is a fibroepithelial tumor with well-established features. In this article, a comprehensive review of this tumor is made.

Objective: We performed a genome-wide analysis of an OM, in an attempt to shed light on the mechanisms underlying its development.

Methods: We report a 36-year-old man who was given a diagnosis of OM involving his fourth right toenail. To investigate molecular genetic alterations, we carried out two approaches, fluorescent in situ hybridization and array-based comparative genomic hybridization, in our patient.

Results: Genomic testing of OM showed 34 genomic alterations, with most of the genomic losses being on chromosome 11. Array-based comparative genomic hybridization showed the deletion of 11p15.4, which harbors *STIM-1*, 11q14.2 (RP-11 292E14), which harbors the *Cathepsin C* gene, 11q14 (RP11-281F10-RP11-265F24), and 11q21 (RP11-203F8 and RP11 183A22).

Limitations: This work is an initial approach to a genome-wide study of this tumor. Further studies (with more cases) must be conducted to pinpoint possible candidate genes for the development of OM.

Conclusions: Array-based comparative genomic hybridization showed important genomic alterations in OM, especially genomic losses. Most genomic losses affected the chromosome 11 in our patient. The *STIM-1* and the *Cathepsin C* genes might play a role in the development of OM. (J Am Acad Dermatol 2011;64:573-8.)

Key words: comparative genomic hybridization arrays; nail tumors; onychomatricoma.

Onychomatricoma (OM) is a rare benign tumor of the nail matrix. It was first described in 1992 by Baran and Kint,[1] who called it "onychomatrixoma" because of its clinical appearance. The most widely used term, "onychomatricoma," was first used in 1995 by Haneke and Fränken.[2] A new nomenclature, based on histology, has been proposed to further extend the understanding of this entity. This includes the terms "unguioblastoma," "unguioblastic fibroma," and "atypical unguioblastic fibroma,"[3] although more recent articles have not included these terms.

Abbreviations used:

aCGH:	array-based comparative genomic hybridization
BAC:	bacterial artificial chromosome
CEP:	centromere-specific probe
CGH:	comparative genomic hybridization
FFPE:	formalin-fixed paraffin-embedded
FISH:	fluorescent in situ hybridization
OM:	onychomatricoma

From the Department of Dermatology,[a] Department of Pathology,[b] and Laboratory 12, Cancer Research Center-CSIC (Consejo Superior de Investigaciones Científicas), Campus Miguel de Unamuno,[c] University Hospital of Salamanca.

Funding sources: None.
Conflicts of interest: None declared.

Reprint requests: Javier Cañueto, MD, Department of Dermatology, University Hospital of Salamanca, Paseo San Vicente 58-182, 37007, Salamanca, Spain. E-mail: jcanueto@yahoo.es.

Published online August 6, 2010.
0190-9622/$36.00

doi:10.1016/j.jaad.2009.07.051

To date, 44 cases of OM in 42 patients have been described and almost all have been diagnosed in Europe. OM affects both men and women and is much more common in Caucasians (only one African American patient has been identified).[4] Regarding the time of its appearance, the age range is fairly broad, but the tumor is unusual in children; nevertheless, one case of OM has been reported in a pediatric population.[5] Despite this, it was proposed that this case, which affected a 4-year-old child, may have been a reactive hyperplastic process caused by onychomycosis.[6] Because this tumor is typically asymptomatic, most cases are treated years after its initial appearance.

CAPSULE SUMMARY

- Onychomatricoma is a rare benign tumor of the nail matrix in which genome-wide analyses have never been performed.
- We carried out fluorescent in situ hybridization and array-based comparative genomic hybridization.
- Genomic testing showed 34 genomic alterations, with most of the genomic losses located on chromosome 11.
- This work is an initial approach to a genome-wide study of this tumor.

Clinically, OM is characterized by an increased transversal curvature of the nail plate, a yellowish discoloration in a longitudinal pattern, and splinter hemorrhages. Once the nail plate has been removed, fingerlike projections appear through the proximal nailfold.[1] Four clinical features have been proposed to be sufficient to allow diagnosis: (1) the presence of a longitudinal yellowish band of varying thickness; (2) the appearance of splinter hemorrhages involving the proximal portion of the nail plate; (3) prominent longitudinal ridging associated with a tendency to transverse curvature; and (4) fingerlike projections emerging from the nail matrix.[7] Most cases reported to date have involved the typical clinical appearance described originally. Nevertheless, some atypical cases have also been described. Thus, it has been reported that OM may be a rare cause of nail bleeding,[8] melanonychia,[9] cutaneous horn,[10] and pterygium.[7,11] OM is slightly more common on the fingers than on the toes, although this observation may be biased because hands are more visible and important in interpersonal relationships.

The differential diagnosis of OM includes onycholemmal horn, malignant proliferating onycholemmal cyst, subungual keratoacanthoma, subungual squamous cell carcinoma, subungual and periungual porocarcinoma, subungual exostoses, subungual osteochondroma, and, above all, subungual and periungual warts,[2] ungual Bowen disease,[12] and fibrokeratoma of the nail bed.[13] Complete surgical excision is the recommended treatment to avoid recurrences.[14] Histopathology seems to be the most reliable tool to differentiate OM from other clinically similar entities.

Histologically, OM is a fibroepithelial tumor. It comprises two portions: the proximal zone corresponds to the base of the pedunculated lesion, whereas the distal zone is composed of multiple fingerlike fibroepithelial projections. Its stroma is organized in two layers: one of them is superficial and highly cellular and is made of fibrillary collagen, and the other one is deeper, with thicker collagen bundles but fewer fibroblasts. It has a keratogenous zone and the thick nail plate exhibits woodworm-like holes.[10] Some authors have noted the presence of numerous stromal mast cells in OM.[13] Immunohistochemical analyses have demonstrated a pattern of expression of cytokeratins and integrins in OM identical to that observed in a normal nail matrix; however, the AE13 antibody specific to Ha 1-4 trichocystic keratins could potentially be a useful marker of OM.[15] Recently, a study of adhesion proteins in OM has demonstrated the absence of beta-catenin expression in comparison with other matrix tumors.[16] On electron microscopy, the basal cells apparently contain decreased numbers of tonofilaments and desmosomes of nonuniform evolution.[17] Because the nail plate is not always analyzed in histologic studies, the keratogenous zone may not be visualized. Magnetic resonance imaging may also be useful in some cases, because the lesion appears with a Y shape in the proximal portion of the nail plate, with holes transversally.[18] The prognosis seems to be good despite the lack of series with long follow-up.[19]

OM is considered to be the result of a disturbed differentiation of the nail matrix and electron microscopy findings seem to support this theory.[17] Fig 1 depicts the mechanisms through which OM develops. It appears to be the only tumor that actively produces a nail plate.[2] Some authors have suggested that OM may arise from a structure of the nail apparatus other than the matrix (proximal nailfold in its distal part, near the cuticle), although it seems to produce the same tissue structure wherever it develops. Nevertheless, to date the causes of OM have not been recognized. Trauma has been proposed to be a related inducing factor, but has only been identified in 3 cases.[11,20]