Enlightening the Pink
Use of Confocal Microscopy in Pink Lesions

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KEYWORDS

• Reflectance confocal microscopy (RCM) • Dermoscopy • Amelanotic melanoma • Nevi
• Nonmelanoma skin cancer (NMSC) • Pink skin tumors • Noninvasive diagnostics

KEY POINTS

- The differential diagnosis for a solitary pink lesion is broad, ranging from inflammatory to neoplastic and from benign to malignant. Solitary pink tumors show often vague, nonspecific overlapping clinical and dermoscopic features.
- Reflectance confocal microscopy (RCM) allows for in vivo evaluation of skin lesions at the cellular level, and, as such, allows for noninvasive identification of specific diagnostic features previously only visualized on histopathology.
- Incorporating RCM into the clinical examination of solitary pink tumors provides additional information, which increases the likelihood of achieving an accurate specific diagnosis noninvasively.

INTRODUCTION

Pink lesions are a large, heterogeneous group of skin lesions of neoplastic and/or inflammatory origin that are characterized by a conspicuous absence of pigmentation. They often constitute a difficult diagnostic challenge because of the lack of unique observable features using conventional techniques, for example, dermoscopy. Dermoscopy and other related techniques, despite offering advantages over visual inspection of the lesion, have an elevated rate of misdiagnosis. Rapid accurate diagnosis is particularly crucial in the case of amelanotic melanoma, which requires early diagnosis to increase the probability of therapeutic success.

The gold standard in the assessment of dermatologic disease is histologic analysis of a sample of the lesion. However, this implies the collection of a biopsy specimen, which is invasive and can be aesthetically damaging. Dermoscopy is closer to this standard than visual inspection, but it is still far from it in the case of pink lesions. Other techniques, however, offer better resolution while preserving the noninvasive nature of dermoscopy. One of such techniques is reflectance confocal microscopy (RCM), which takes advantage of light scattering by endogenous skin structures, for example, melanin granules, architectural differences between the skin layers. The differential reflection of the light together with sampling and analysis of the affected area in a noninvasive manner underlies the great promise of RCM in the assessment and management of pink lesions.

In this review, the state-of-the-art regarding the use of RCM for the assessment of pink lesions in the dermatology office is summarized.

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A BRIEF CLASSIFICATION OF PINK LESIONS

Pink lesions can be inflammatory in origin or neoplastic. In general, inflammatory pink lesions are clustered or widespread, unlike amelanotic tumors, which are usually solitary and can be either benign or malignant.[1] Examples of benign pink tumors include amelanotic benign nevi, sebaceous hyperplasia (SH), sebaceous adenoma/sebaceoma, trichoepithelioma, seborrheic keratosis (SK), clear cell acanthoma (CCA), dermatofibroma (DF), angioma, and pyogenic granuloma (PG). Examples of malignant pink tumors include amelanotic/hypomelanotic melanoma, mammary and extramammary Paget disease, basal cell carcinoma (BCC), and squamous neoplasia (actinic keratosis [AK], squamous cell carcinoma in situ [SCCIS]/Bowen disease, invasive squamous cell carcinoma [SCC]). Other pink lesions, such as but not limited to, angiosarcoma, Merkel cell carcinoma, and lymphoma as yet have not been well described on dermoscopy or RCM; therefore, these lesions will not be discussed further, but should be considered in lesions that lack features described in this article.

DIAGNOSTIC FLOW OF SKIN LESIONS AT THE DERMATOLOGIST OFFICE

The evolution of imaging techniques such as dermoscopy and RCM has altered the decision and diagnostic trees in the dermatologist's office. Primary visual inspection reveals whether the lesion is inflammatory (usually multifocal) or neoplastic (often solitary), melanotic (contains melanin), or amelanotic/hypomelanotic (not obviously pigmented). Most melanotic lesions are benign nevi, as revealed by dermoscopy and/or RCM. This approach also reveals unique features of malignant melanoma (reviewed elsewhere in this issue); hence, diagnosis has the potential to be efficient and decisive. However, amelanotic/hypomelanotic (pink) lesions are often less easy to distinguish; thus, visual aids and information are required to establish an initial diagnosis. Although the gold standard is histology, a desirable goal (particularly from the patient's point of view) is to obtain information close to the gold standard without resorting to invasive biopsy specimen collection.

THE LIMITS OF DERMOSCOPY IN THE DIAGNOSIS OF SOLITARY PINK LESIONS

Dermoscopy represents a leap over mere visual inspection of solitary pink lesions, particularly in terms of sensitivity. However, it also has severe limitations regarding specificity, which is crucial to determine the course of action to treat the disease. In the following paragraphs, the major dermoscopic observations of a wide range of nonmalignant and malignant pink tumors are outlined with an emphasis on the lack of distinguishing features in many cases.

DERMOSCOPIC FINDINGS OF NONINFLAMMATORY BENIGN PINK TUMORS

Dermoscopy confers a significant advantage over visual inspection alone in the clinical diagnosis of several nonpigmented lesions. Variants of amelanotic nevi include Miescher facial, Unna, Clark (red), and Spitz nevi. The main dermatoscopic feature of Miescher and Unna nevi is the presence of comma-shaped blood vessels, which have great predictive value. Additional features include keratinized crypts. On the other hand, Clark nevi display dotted and comma-shaped vessels arranged regularly against a pink background. Spitz nevi display dotted vessels in a relatively regular arrangement and reticular depigmentation.[2,3]

Dermoscopy varies in its utility for the diagnosis of adnexal tumors. SH is often confused with superficial BCC by visual inspection due to its appearance, which includes yellowish smooth papules on the face. Dermoscopy reveals wreathed and blurred blood vessels and radial telangiectasia. Such radial arrangements are the defining feature that distinguishes SH from BCC, in which telangiectasia are treelike, intense, and very sharp.[4,5] Sebaceous adenoma and sebaceoma show opaque structureless yellow areas surrounded by elongated, radially arranged crown vessels or branching arborizing vessels and a few loosely arranged arborizing vessels.[6] Trichoepithelioma can be very difficult to distinguish from papular variants of BCC clinically and dermoscopically because it also presents as a papule with arborizing telangiectasias. However, because of the characteristic stroma of trichoepithelioma, the tumor lacks the pearliness seen in BCC and has a shiny white background on dermoscopy. Desmoplastic trichoepithelioma closely mimics morpheaform BCC on dermoscopy, appearing as an ivory-white plaque with prominent arborizing telangiectasias.[7]

SK and CCA are benign epithelial tumors that can be confused with SCC or BCC. Dermoscopy of SK reveals lobulated vessels (capillary loops) arranged regularly, but surrounded by whitish halos consistent with keratinized structures. A major distinguishing feature of SK from SCC is that lobulated vessels are irregularly shaped and do not form a pattern in the latter. An exception to this