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Milia En Plaque as a Distinct Follicular Hamartoma With Cystic Trichoepitheliomatous Features

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Abstract: Milia en plaque (MEP) is an uncommon disorder characterized by an erythematous plaque containing numerous milia. The pathogenesis of MEP is not clear. The authors report a man with an erythematous plaque on the right retroauricular area, containing numerous white-yellow cysts varying in size. Histological examination showed that multiple cystic structures at various levels of the dermis that were lined by stratified squamous epithelium and contained keratinous material—these findings were consistent with the diagnosis of multiple milia. In addition to epidermal cysts, however, the lesion consisted of a branched proliferation of pale-staining keratinocytes lined with basal keratinocytes budding from the overlying epidermis. Moreover, some cysts were formed within the branched epithelial proliferation, had thicker cyst walls than the ordinary milium, or had irregular or branched projections toward the surrounding dermis. From these findings, the authors conclude that MEP is a distinct follicular hamartoma with cystic trichoepitheliomatous features.

Key Words: milia en plaque, infundibulum

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INTRODUCTION

Milia are small white benign superficial keratinous cysts. Histologically, they resemble epidermal cysts with a wall of stratified epithelium of a few cell layers. They are classified into 2 groups: primary milia and secondary milia, which are caused by trauma, burn scar, bullous dermatoses, or drugs. A milia en plaque (MEP) is an uncommon disorder clinically characterized by an erythematous plaque containing a number of milia.[1] Although the pathogenesis of MEP is unknown, it may be best classified as a primary type of milia.

CASE REPORT

A 40-year-old Japanese man, in good general health, presented with a 1-year history of erythematous and slightly indurated plaque involving his right retroauricular area without any symptoms. His primary care physician treated him with a topical steroid, which was not effective. The patient consulted our hospital because he wanted radical treatment for the lesion. There was no history of any trauma, exposure to radiation therapy, photosensitivity, or any other skin diseases.

On examination, there was an erythematous, slightly indurated and elevated, 30- × 20-mm plaque on the right retroauricular area, containing numerous variously sized white-yellow cysts located in the superficial and deep dermis. There was also an umbilication in the center of the plaque where the papules seemed to be ruptured (Fig. 1A). On dermoscopic examination, there were numerous white or white-yellow cysts, varying in size, which seemed to be present at various levels of the dermis. In addition, there were scattered brown dots and many telangiectatic vessels (Fig. 1B). Histological examination showed multiple cystic structures at various levels of the dermis that were lined by stratified squamous epithelium and contained keratinous material. The cysts were surrounded by a mononuclear cell infiltrate (Figs. 2A–C). In Figure 2A, to obtain a better understanding, we combined multiple pictures using Adobe Photoshop Elements 12. These findings were consistent with the diagnosis of multiple milia. However, this low-magnification view revealed that, in addition to epidermal cysts, the lesion consisted of a branched proliferation of pale-staining keratinocytes lined with basal keratinocytes budding from the overlying epidermis. Moreover, some cysts were formed within the branched epithelial proliferation, had thicker cyst walls than the ordinary milium, or irregular or branched projections toward the surrounding dermis. No milia recurred after the excision.

DISCUSSION

MEP is an unusual and rare type of primary milia. Histopathologically, MEP is characterized by keratin-filled epidermal cysts surrounded by a mononuclear cell infiltrate. MEP was initially described in the retroauricular area in 1903 by Balzer and Fouquet and named by Hubler in 1978.[2,3] Lesions are commonly seen on the head and neck, especially on the periauricular area; they may also be periorbital, on the nasal bridge, or truncal. MEP is associated with pseudoxanthoma elasticum, discoid lupus erythematosus, lichen planus, trauma, drugs such as cyclosporine, and renal transplantation, but also arises in healthy persons.[1] So far, the pathogenesis of MEP has not been precisely defined.

Other than multiple epidermal cysts varying in size and located at various levels of the dermis, our case was histologically characterized by a branched proliferation of lighter staining keratinocytes surrounded by basal cells budding from the overlying epidermis. The lesion showed a silhouette with a horizontal orientation and did not contain sebaceous glands, immunohistologically confirmed by the

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The authors declare no conflicts of interest.

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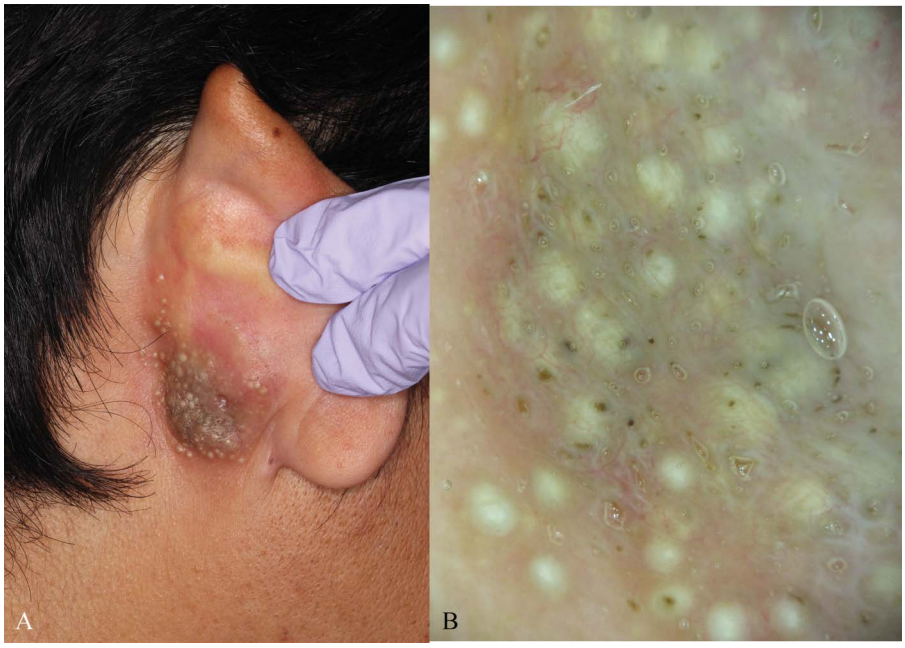

FIGURE 1. Clinical and dermoscopic features. A, The patient presented with an erythematous, slightly indurated and elevated, 30- × 20-mm plaque on the right retroauricular area, containing numerous white-yellow cysts. B, Dermoscopic examination revealed numerous white or white-yellow cysts, scattered brown dots, and many telangiectatic vessels.

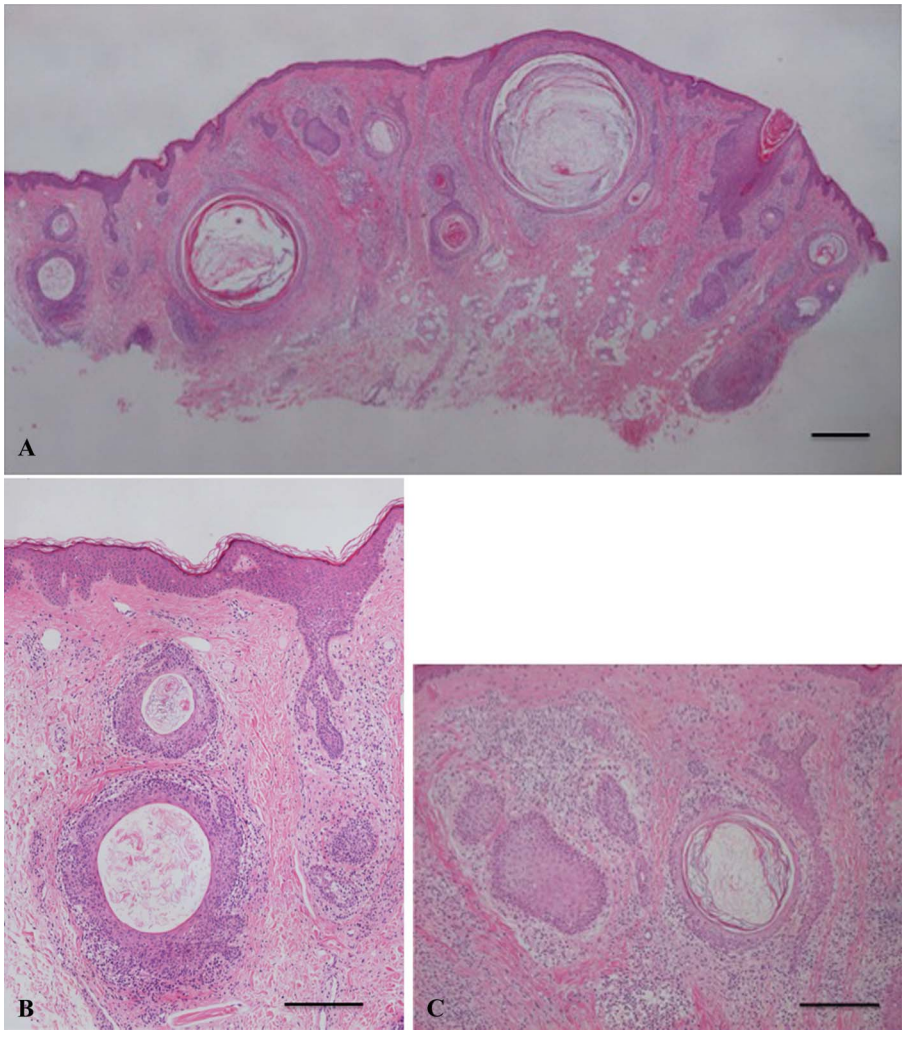

FIGURE 2. Histological features. A, Histological examination showed multiple cystic structures at various levels of the dermis that were lined by stratified squamous epithelium and contained keratinous material. The cysts were surrounded by a mononuclear cell infiltrate (hematoxylin–eosin [H&E], original magnification ×50, scale bar = 500 μm). B, High-power magnification of one of the cystic structures and surrounding infiltrate. C, branched epithelial structures (H&E, original magnification, ×200, scale bar = 200 μm).

TABLE 1. Summary of Previous Case Reports

Number	References	Age (yrs) and Sex	Location	Clinical Findings	Histological Features	Journals
1	Hubler et al[3]	49 F, 43 F	PAA	EPMM	MEC, BEP, II (49 F)a	*Cutis*. 1978;22:67–70
2	Fujita et al[7]	39 F	Forehead	EPMM	MEC, BEP, IIa	*J Dermatol*. 2008;35:39–41
3	Ishiura et al[8]	44 M	Right temple and submandibular area	EPMM	MEC, BEP, IIa	*Br J Dermatol*. 2007;157:1287–9
4	Alsaleh et al[4]	35 M	Right anterior nasal fold	EPMM	MEC, BEP, IIa	*Int J Dermatol*. 2000;39:614–5
5	Stork[10]	49 F	Bilateral PAA	EPMM	MEC, BEP, IIa	*Dermatology*. 1995;191:260–1
6	Cota et al[6]	12 F, 9 F, 9 F	Periorbital (12 F, 9 F), left cheek (9 F)	EPMM	MEC, BEP (9 F), IIa	*Pediatr Dermatol*. 2009;26:717–20
7	Samlaska et al[9]	39 F	PAA	EPMM	MEC, BEP, IIa	*J Am Acad Dermatol*. 1989;21:311–3
8	Combemale et al[5]	42 M	Supraclavicular area	EPMM	MEC, BEP, IIa	*Dermatology*. 1995;191:262–3
9	van Lynden-van Nes et al[40]	60 F	Mandibular ridge	EPMM	MEC, IIa	*Dermatol Surg*. 2005;31:1359–62, discussion
10	Stefanidou et al[38]	35 F	Unilateral periorbital area	EPMM	MECa	*Dermatol Surg*. 2002;28:291–5
11	Garcia Sanchez et al[21]	84 F	Bilateral submandibular region	Groups of globoid skin colored papules	MECa	*Clin Exp Dermatol*. 1998;23:227–9
12	Cho et al[17]	36 F	PAA	EPMM	MEC, IIa	*J Cutan Pathol*. 1997;24:61–3
13	Losada-Campa et al[28]	59 F	Bilateral preauricular areas	EPMM	MECa	*Br J Dermatol*. 1996;134:970–2
14	Keohane et al[24]	50 M, 49 M	Ear lobe	EPMM	MEC, IIa	*Clin Exp Dermatol*. 1996;21:58–60
15	Voth et al[41]	32 F	Periocular area	Multiple small yellowish papules	MEC, IIa	*J Cosmet Laser Ther*. 2011;13:35–7
16	Pozo et al[33]	12 M, 50 F, 13 F, 30 F	Left inner cantum, forehead, thorax, right wrist	EPMM	MECb	*J Cosmet Laser Ther*. 2010;12:191–4
17	Zhang et al[44]	65 F	The end points of bilateral auricular canals	EPMM	MEC, IIa	*Indian J Dermatol Venereol Leprol*. 2012;78:122
18	Sandhu et al[36]	37 M	Left PAA	EPMM	MECb	*J Dermatolog Treat*. 2003;14:253–5
19	Noto et al[32]	32 F	Bilateral PAA	EPMM	MECb	*Acta Derm Venereol*. 2001;81:370–1
20	Calabrese et al[16]	62 F	PAA and auricle	EPMM	MECa	*Acad Dermatol Venereol*. 1999;12:195–6
21	Boehm et al[13]	43 F	Face	Multiple milia in a plaque-like aggregation	MEC, IIa	*Br J Dermatol*. 1997;137:649–51
22	Lee et al[26]	14 M	Right PAA	EPMM	MECa	*J Am Acad Dermatol*. 1994;31:107
23	Quist et al[34]	67 F	Periauricular and intraauricular area	EPMM	MECa	*Acta Derm Venereol*. 2010;90:445–7
24	Barzegar et al[11]	4 F	Right nasal ala area	EPMM	MECa	*Int J Dermatol*. 2013
25	Munoz-Martinez et al[30]	53 F	Right helix and ear lobe	EPMM	MEC, IIa	*Actas Dermosifiliogr*. 2013;104:638–40
26	Lee et al[27]	22 F	Left inner canthus to the tip of nose	EPMM	MEC, IIa	*J Dermatol*. 2012;39:936–7
27	Boggio et al[14]	16 F	Bilateral upper eyelids	EPMM	MEC, IIa	*Dermatol Online J*. 2012;18:11
28	Martins et al[29]	32 M	Left PAA	EPMM	MEC, IIa	*An Bras Dermatol*. 2010;85:895–8

TABLE 1. (*Continued*) Summary of Previous Case Reports

Number	References	Age (yrs) and Sex	Location	Clinical Findings	Histological Features	Journals
29	Hallaji et al[22]	35 F	Bilateral PAA	EPMM	MEC, IIa	*Dermatol Online J.* 2010;16:12
30	Belhadjali et al[12]	42 M	Cheek, bridge of nose, and chelitis on the lip	EPMM	MEC, IIa	*Clin Exp Dermatol.* 2009;34:e356–7
31	Kautz et al[23]	57 F	From inner canthus to the chin with a gap between the alar of the nose and corner of the mouth	EPMM	MEC, IIa	*Eur Acad Dermatol Venereol.* 2009;23:1335–6
32	Rose et al[35]	56 F	PAA	EPMM	MEC, IIa	*Clin Exp Dermatol.* 2008;33:715–7
33	Kouba et al[25]	44 F	Chin	EPMM	MEC, IIa	*Br J Dermatol.* 2003;149:424–6
34	Ergin et al[20]	62 F	Left infraorbital area	EPMM	MEC, IIa	*J Eur Acad Dermatol Venereol.* 2000;14:47–9
35	Wong et al[43]	39 M	Upper and lower eyelids	EPMM	MEC, IIa	*Clin Exp Dermatol.* 1999;24:183–5
36	Bridges et al[15]	10 F	Bilateral upper eyelids	EPMM	MEC, IIa	*Pediatr Dermatol.* 1998;15:282–4
37	Sharma et al[37]	25 M, 38 M	Left PAA	Multiple milia	MECa	*Indian J Dermatol Venereol Leprol.* 1995;61:365–6
38	Al-Mutairi et al[46]	55 M	Bilateral upper eyelids and infraorbital lesion	EPMM	MEC, IIa	*J Cutan Med Surg.* 2006;10:193–6
39	Wollina[42]	28 M	Upper and lower eyelid	EPMM	MEC, IIb	*Dermatol Surg.* 2010;36:406–8
40	Nambudiri et al[31]	7 M	Nose	EPMM	Not performed	*Pediatrics*. 2014;133: e1373–6
41	Tenna et al[39]	21 F	Eyelid	Multiple milia	Not performed	*Dermatol Ther*. 2014;27:65–7
42	Zhang et al[45]	6 M	Bilateral PAA	EPMM	Not performed	*Pediatr Dermatol.* 2012;29:504–6
43	Dogra et al[18]	5 M	Right upper eyelid	EPMM	Not performed	*J Eur Acad Dermatol Venereol*. 2005;19:263–4
44	Dogra et al[19]	56 M	Right lower limb	EPMM	Not performed	*Int J Dermatol.* 2002;41:897–8
45	Our case	40 M	Right PAA	EPMM	MEC, BEP, IIa	—

a and b indicate that the article presented histological pictures (a) or not (b) to evaluate the histological characteristics, respectively.
BEP, branched epithelial proliferation; EPMM, erythematous plaque with multiple milia; F, female; II, inflammatory infiltrate; M, male; MEC, multiple epidermal cysts; PAA, postauricular area.

lack of epithelial membrane antigen (data not shown) or eccrine ducts.

We reviewed the previous literature searching the term "Milia en plaque" at PubMed (http://www.ncbi.nlm.nih.gov/pubmed/). There were 44 articles available in English containing 52 cases of MEP.[3–46] Our case was the 53rd case (Table 1). The age of the patients at the time of diagnosis as MEP ranged from 4 to 84 years (mean, 38.7 years old). Of the patients, 20 were males (37.7%) and 33 were females (62.3%). The clinical findings of MEP were mainly a unilateral or bilateral erythematous plaque with multiple milia on periauricular, perieyelid, or other facial parts. The histological features mostly included multiple epidermal cysts with or without an inflammatory infiltrate. Furthermore, we found that some cases had other histological features. There were 8 cases that showed a silhouette with a horizontal orientation and branched epithelial structures in connection with epidermal rete ridges.[3–10] Therefore, we believe that these 2 histopathological findings also characterize MEP.

Milia are believed to be derived from or to mimic the infundibular portions of a vellus hair follicle. There are several follicular tumors differentiating mainly toward follicular infundibulum or follicular hair bulge of the outer root sheath, such as trichofolliculoma, trichoadenoma, trichoepithelioma, and tumor of follicular infundibulum (TFI). Trichofolliculoma usually presents as a solitary papule or tumor on the head and neck, usually the face. Histologically, there are one or several dilated follicles from which numerous small follicles of varying degrees of maturity radiate. The follicles that branch off the central follicle may in turn give rise to

secondary or even tertiary follicles. Trichoadenoma (of Nikolowski) is a rare tumor with hair follicle–like differentiation; it is found as a nodular lesion, particularly on the face and buttocks. Trichoadenoma shows, histopathologically, a well-defined dermal tumor composed of epithelial islands, most of which have a central cystic cavity containing keratinous material. The multilayered squamous epithelium reveals epidermoid keratinization toward the central cavity. Trichoepithelioma is regarded as a poorly differentiated hamartoma of the hair germ. It is composed of branching nests of uniform basaloid cells, sometimes showing peripheral palisading. Its epithelial structures may resemble hair papillae or abortive hair follicles.[47]

TFI, which was initially reported as a kind of benign adnexal tumor by Mehregan and Butler,[48] usually presents as a solitary keratotic papule on the face or scalp of elderly people. Histologically, the tumor shows a plate-like subepidermal epithelial tumor, distinguished from the overlying epidermis by the light staining of its cells and the absence of pigment. The tumor consists of 2 types of cells. The squamous cells, with much lighter staining than those of the epidermis and containing as much periodic acid-schiff-positive material as the outer root sheath, are surrounded by basal cells. Afterward, Ackerman added the distinctive silhouette with a horizontal orientation as one of the crucial findings for the histopathologic diagnosis of TFI.[49] Recently, Abbas and Mahalingam[50] have reported their own 50 cases of TFI and reviewed 41 reported cases. In their article, they also described a plate-like proliferation of bland epithelial cells extending parallel to the epidermis with multiple epidermal connections as a characteristic finding of TFI.

As we already described, MEP also has 2 histological characteristics other than multiple epidermal cysts, such as a silhouette with a horizontal orientation and branched epithelial structures in connection with epidermal rete ridges. Therefore, these characteristics seem to position MEP close to TFI, although it is difficult to conclude this speculation only by observing the histological slide. Therefore, we finally diagnosed this case as a distinct follicular hamartoma with cystic trichoepitheliomatous features. Further immunohistological study and/or gene analysis may be needed for better understanding the origin of this rare tumor.

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