

# Atypical Spitz Tumor Arising on a Congenital Linear Plaque-Type Blue Nevus: A Case Report With a Review of the Literature on Plaque-Type Blue Nevus

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**Abstract:** The plaque-type blue nevus (PTBN) is a rare variant of blue nevus, of which only a few reports are described. A nodular growth within a preexistent PTBN should always alert to the possibility of malignant transformation. The authors report the first case of an atypical Spitz tumor arising on a congenital linear PTBN in a 60-year-old woman. The diagnosis of “atypical Spitz tumor” is here used to describe a microscopic “gray zone” in which it is not possible to differentiate with adequate certainty between a Spitz nevus and a spitzoid melanoma. This report adds to and summarizes the small body of literature describing PTBN and discusses diagnostic and clinical implications.

**Key Words:** plaque-type blue nevus, atypical Spitz tumor, combined nevus, subcutaneous nodules, spitzoid melanoma

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## INTRODUCTION

Plaque-type blue nevus (PTBN) is a rare variant of blue nevus that is present at birth or may arise in early childhood.<sup>1</sup> In the setting of “combined nevi,” it has been anecdotally described only in association with a speckled lentiginous and a congenital nevus.<sup>2–6</sup> The development of malignant melanoma within a PTBN has also been reported.<sup>7–9</sup> While reviewing the literature on PTBN, we report the first case of a spitzoid melanocytic neoplasm arising on a PTBN in a 60-year-old woman. Although the clinical presentation raised suspicion about the development of a melanoma, the pathological features lead us to consider the possibility of a combined nevus with features of a Spitz and blue nevus or an atypical Spitz tumor arising within a PTBN.

## CASE REPORT

A 60-year-old woman presented with a congenital linear grayish-blue plaque on her right flank of 7 cm in diameter composed

of multiple macules and papules. In the last year, there had been a progressive growth inside the plaque of a bluish papule with keratotic and crusted surface because of micro traumatism, leading the patient to dermatological consultation (Fig. 1). Dermoscopy of the new growing papule showed a blue homogeneous pattern with overlying scales and crusts, surrounded by an erythematous halo with dotted vessels (Fig. 2). The entire plaque-like lesion was typified by areas of homogeneous blue pigmentation, brownish-blue in the center and steel-blue at the periphery. These areas were either coalescent or separated. The growing papule was removed with a large excision, including the surrounding bluish patch/plaque with some maculopapules inside. The patient was lost to further follow-up.

## PATHOLOGICAL FINDINGS

Histopathology showed a melanocytic lesion that combines features of common blue nevus and a spitzoid melanocytic neoplasm (Figs. 3A, B). The latter was a 5 mm in diameter, nodular, superficial, sharply circumscribed, slightly asymmetrical lesion that was bounded by a collarette (Fig. 3A) and was composed of a junctional and dermal proliferation of spindle-shaped and epithelioid cells arranged in nests or fascicles (Figs. 3C, D). The overlying epidermis showed irregular hyperplasia (Fig. 3A), hyperkeratosis, and parakeratosis, with rare Kamino bodies. The spindle-shaped and epithelioid cells were monomorphic without atypical cytological features. The nodule exhibited a prominent cellularity, and a clear-cut maturation in the reticular dermis was difficult to appreciate (Figs. 3C, D). One typical mitosis was seen in many different serial sections. A peripheral non-brisk lymphocytic infiltrate was also seen. In the deepest part of the reticular dermis corresponding to the linear large plaque-type blue lesion, the spitzoid lesion was combined with multiple foci of dendritic melanocytes, with melanophages and coarse melanocytic pigment consistent with a common blue nevus (Fig. 3E). No necrosis or atypical mitoses were seen in either area. Histopathology of an adjacent macule/papule presenting into the plaque and included into the excision showed features of common and cellular blue nevus (Figs. 4A, B). The melanocytes of both lesions were positive for S100, Melan-A, and HMB45 (Fig. 5). S100 stain was less intense than the Melan-A in the areas of common blue nevus. P16 expression was homogeneous without focal loss (Fig. 5). The Ki67 labeling index was below 2% (Fig. 5). Although the Spitz nevus was included within the margins of the excision, the common blue nevus component extended to all margins. No gains or

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**FIGURE 1.** Congenital linear grayish-blue plaque on the right flank of 7 cm in diameter composed of multiple macules and papules. Note the growing papule with keratotic and crusted surface inside the plaque.

losses of copy numbers in the Spitz lesion has been detected with the multicolor melanoma fluorescent in situ hybridization (FISH) assay according to the method of Gerami et al<sup>10</sup> using Abbott probes. FISH analyses targeting the 9p21 locus were performed using the LSI p16 (9p21)/CEP 9 dual-color probe (Abbott Molecular Inc, Des Plaines, IL). The case was recorded as FISH-deleted for locus 9p21 when at least 30% of the examined nuclei exhibited the 1 orange and 2 green signal pattern or a number of orange spots were fewer than half of the green spots.<sup>11</sup> The spitzoid lesion was of unaltered 9p21 status.

## DISCUSSION

We report the first case of an atypical Spitzoid melanocytic neoplasm arising on a congenital linear PTBN in a 60-year-old woman.

The first case of a PTBN published in the English literature was the one described by Upshaw et al<sup>12</sup> in 1947. They reported a case of a large blue nevus, measuring 17 × 6 cm on the thorax of a 9-year-old boy, which appeared when the patient was 4 weeks of age. It was characterized by a bluish background in which multiple slightly raised nodules



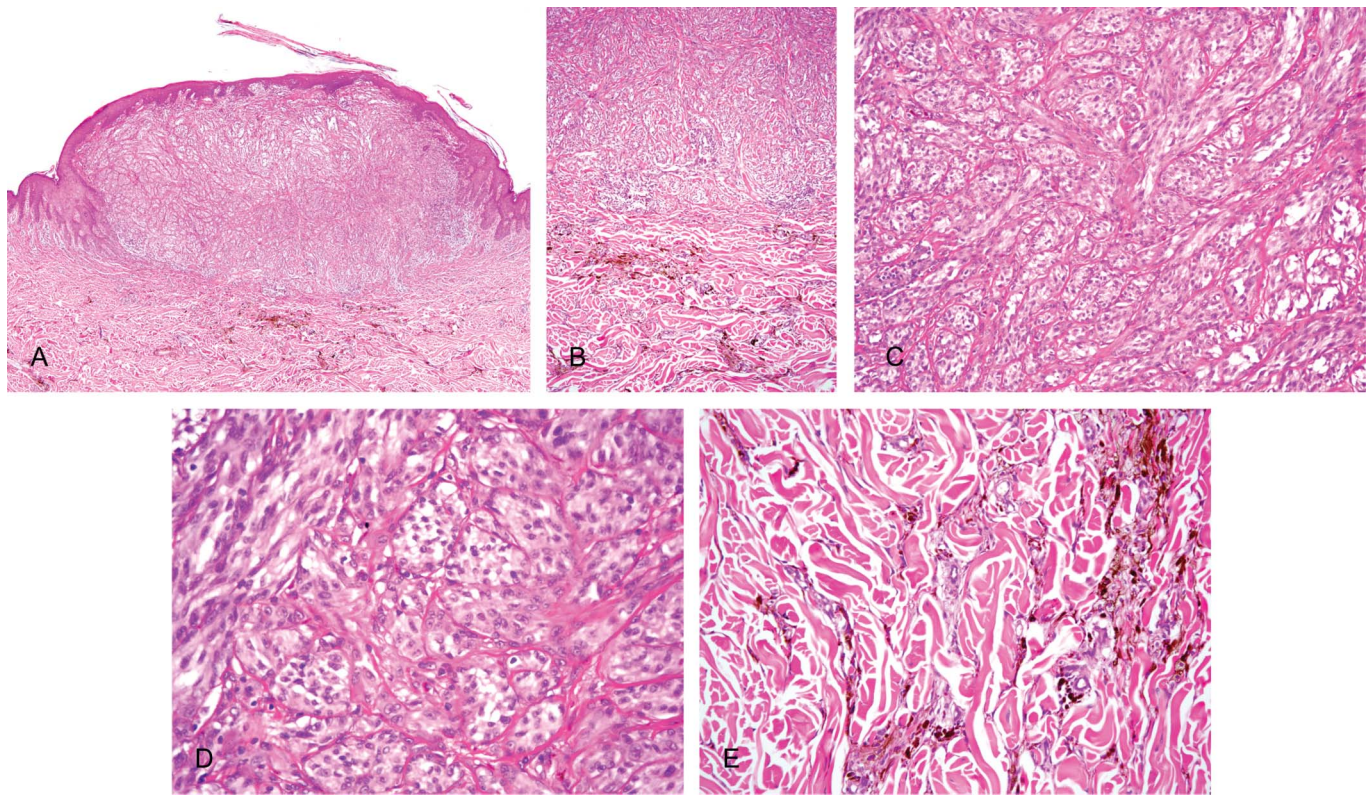
**FIGURE 2.** Dermoscopy of the new growing papule shows a blue homogeneous pattern with overlying scales and crusts, surrounded by an erythematous halo with dotted vessels.

arose. Since then, about 25 cases of large PTBN have been described as single case reports.<sup>1,13–24</sup> Clinically, the lesion appears as a congenital or less frequently acquired blue-gray pigmented single patch/plaque without palpable lesions or is composed by a confluence of multiple macules, papules, or nodules on a blue-gray background (papular or agminate PTBN). Evolution may be fast (eruptive). PTBN measures from 1 to 25 cm and has a predilection for the trunk or extremities, but also the face<sup>14,21</sup> or the oral cavity<sup>16</sup> are occasionally involved. An unusual hypertrichotic variant<sup>18</sup> and an association with meningeal melanocytoma<sup>15</sup> have been reported. The histological features of PTBN are characterized by a multifocal dermal and subcutaneous proliferation of spindle-shaped and dendritic pigmented melanocytes reminiscent of common blue nevus, dermal melanocytoses, and cellular blue nevus. Additional histological variants of PTBN include the combination of blue nevi with a speckled lentiginous nevus in 4 patients<sup>3–6</sup> and with a congenital nevus in 1 patient.<sup>7</sup>

Recently, a variant of PTBN on the trunk, named “large PTBN with subcutaneous cellular nodules,” has been described, in which multiple nodules with histopathologic features of cellular blue nevus and common blue nevi developed secondarily many years later and extend deeply into underlying soft tissues such as the fascia or breast.<sup>25–27</sup>

The biologic behavior and prognosis of PTBN is difficult to establish because it is based only on a small number of anecdotal case reports with scarce follow-up data. Most of these patients seem to have a good prognosis, but 6 patients had developed melanoma in the setting of PTBN. Four patients developed metastatic disease,<sup>7,8,28,29</sup> whereas 1 patient was alive 6 years after the excision of the melanoma.<sup>9</sup> In 2 patients whose clinicopathologic picture was that of large “PTBN with subcutaneous cellular nodules,” comparative genomic hybridization showed chromosomal aberrations typical of melanoma, and both patients are alive at about 1 year of follow-up.<sup>30</sup> In a further case classified as “large PTBN with subcutaneous nodules,” the subcutaneous cellular nodule that had rapid growth with an area of striking nuclear atypia and a mitotic index of 2/10 high-power field was considered as not a melanoma but an atypical blue nevus. The clinical course was characterized by repeated recurrent nodules within the PTBN over 11 years and absence of lymph node metastasis.

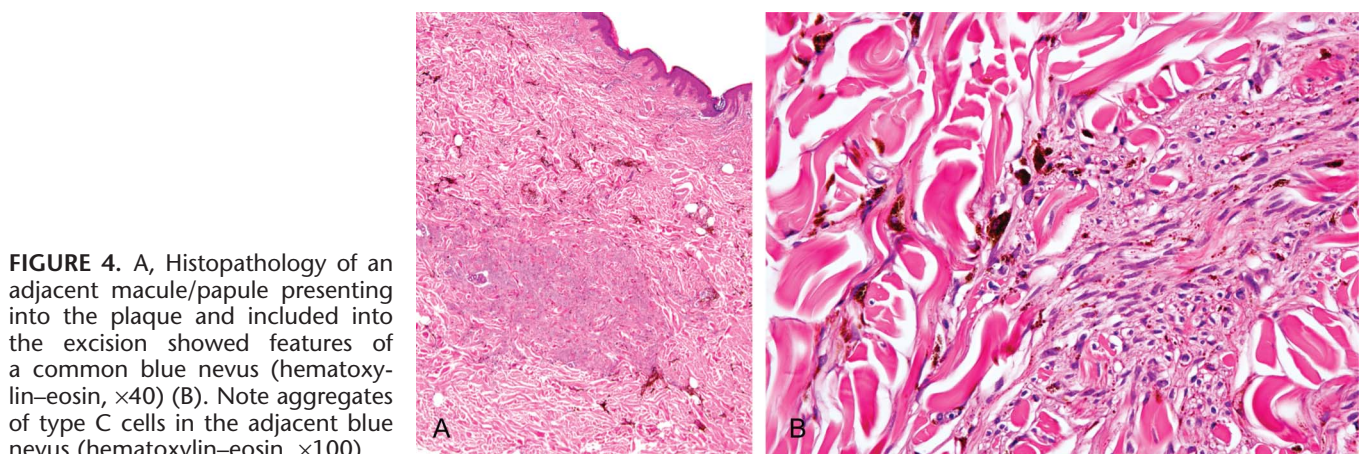
In our patient, although the clinical presentation such as the age of 60 years and the recent development of a new nodular lesion in a long-lasting stable congenital blue nevus raised a suspicion about the development of a melanoma, the pathological features led us to discuss the possibility of a Spitz nevus versus an atypical Spitz tumor. The latter belongs to a subset of problematic and diagnostically challenging melanocytic neoplasms variably labeled as atypical Spitz nevus, atypical Spitz tumor, Spitz-like lesion in the borderline category of indeterminate malignant potential, and diagnostically controversial spitzoid melanocytic neoplasms.<sup>31,32</sup> Although diagnostic parameters and a grading system for risk stratification for atypical Spitz tumors have been proposed,<sup>33</sup> there is no single technique that unequivocally discriminates among these borderline lesions. In this particular case, the slight asymmetry of the nodule, the presence of a prominent cellularity made of spindle-shaped and epithelioid cells, the



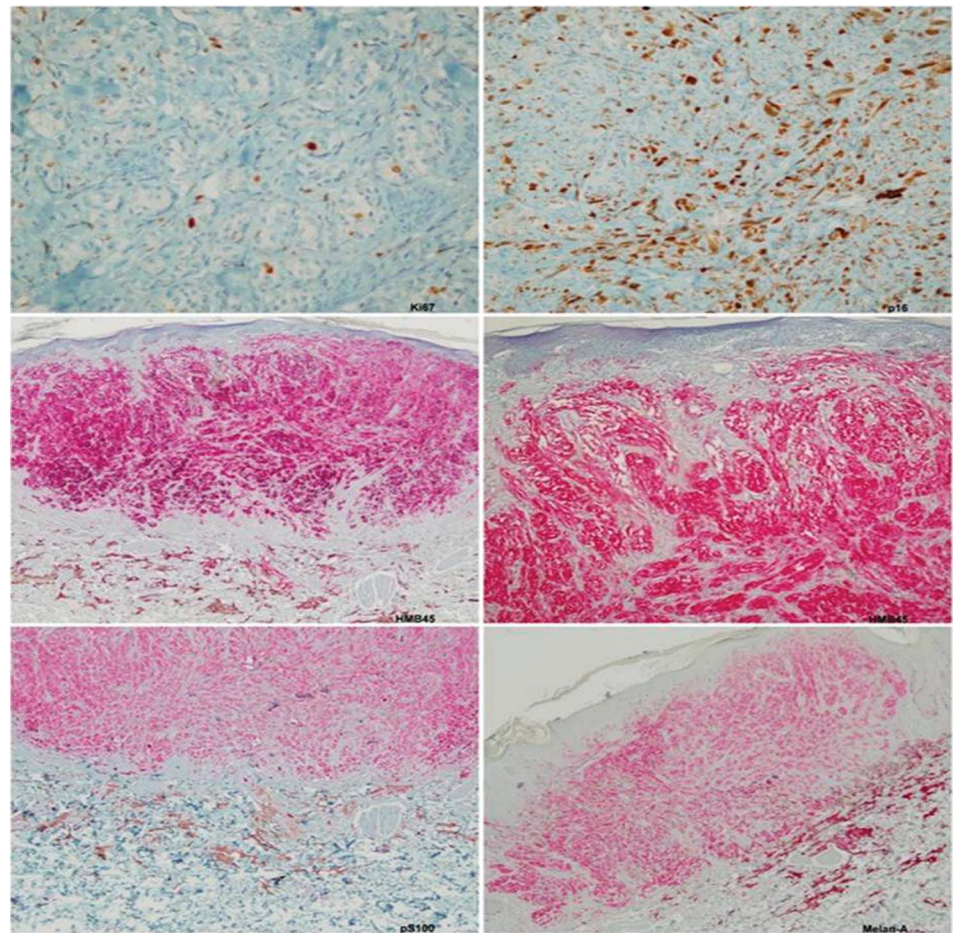
**FIGURE 3.** Histopathology shows a melanocytic lesion that combines features of Spitz nevus and blue nevus. A, A 5 mm in diameter, nodular, superficial, symmetrical lesion with well-defined borders that was bounded by a collarette with underlying multiple foci of dendritic melanocytes with melanophages and coarse melanocytic pigment consistent with a common blue nevus. B, A superficial melanocytic nodule with an underlying blue nevus. C, The melanocytic nodular lesion is composed of a proliferation of spindle-shaped and epithelioid cells arranged in nests or fascicles and showed slight maturation in the reticular dermis. D, The spindle-shaped and epithelioid cells were monomorphic without atypical cytological features. E, In the deepest part of the reticular dermis corresponding to the linear large plaque-type blue lesion, multiple foci of dendritic melanocytes with melanophages and coarse melanocytic pigment consistent with a common blue nevus are seen under the Spitz lesion.

evidence of dermal mitotic activity, and the diffuse expression of HMB45 all play in favor of an atypical Spitz tumor in the setting of PTBN. The possibility of a combined nevus associating features of Spitz and blue nevus was also considered. In fact, significant atypical features characterized by increased cellularity and loss of symmetry are observed in nearly 50%

of combined nevi that contain Spitz elements.<sup>34</sup> However, the clinical context, the absence of dermal sclerosis, and the presence of deep mitoses, although rare and typical, make it perilous to posit that this lesion is a conventional banal Spitz nevus. Despite the absence of prominent malignant features, a low proliferation index, a homogeneous expression of P16,



**FIGURE 4.** A, Histopathology of an adjacent macule/papule presenting into the plaque and included into the excision showed features of a common blue nevus (hematoxylin–eosin,  $\times 40$ ) (B). Note aggregates of type C cells in the adjacent blue nevus (hematoxylin–eosin,  $\times 100$ ).



**FIGURE 5.** Immunohistochemical panel. The Ki67 labeling index was below 2% (immunoperoxidase,  $\times 100$ ). P16 expression was positive with some focal loss in Spitz lesion (immunoperoxidase,  $\times 100$ ). The melanocytes of both lesions were positive for HMB45 (immunoperoxidase,  $\times 40$  and  $\times 100$ ), positive for pS100 (immunoperoxidase,  $\times 40$ ), and positive for Melan-A (immunoperoxidase,  $\times 40$ ).

and negative genetic test results, a diagnosis of spitzoid melanoma cannot be formally ruled out as sometimes patients with melanoma may reveal no cytogenetic abnormalities.<sup>7</sup>

It is also difficult to establish the best treatment for PTBN. As the lesion involves a large area and has uncertain malignant potential, a close observation with follow-up has been recommended and any new lesions that appear should be biopsied.<sup>2,25</sup> Other authors agree that removal of the lesion should be performed if the size permits it.<sup>19,25</sup> In our patient, because of the size and location of the lesion, we chose to maintain a close follow-up with dermoscopy every 6 months and to biopsy any new lesions that might occur inside PTBN. Unfortunately, we are unable to provide further details as the patient was lost to follow-up.

In conclusion, a nodular growth within a preexistent melanocytic neoplasm with features of PTBN should always alert to the possibility of malignant transformation. However, based on our clinicopathologic features, the current lack of knowledge about the biological nature of spitzoid lesions, and how these lesions will behave with long-term follow-up, the current neoplasm has been best classified as an atypical spitzoid melanocytic neoplasm with indeterminate or uncertain malignant potential.

As the potential for development of both benign and malignant cellular nodules within PTBN theoretically exists

and malignant transformation within PTBN appears not to be so rare every new nodule formed in a PTBN should be carefully examined, including FISH and comparative genomic hybridization, as it is a separate diagnostic challenge.

## REFERENCES

- Pittman JL, Fisher BK. Plaque-type blue nevus. *Arch Dermatol.* 1976; 112:1127–1128.
- Ishibashi A, Kimura K, Kukita A. Plaque-type blue nevus combined with lentigo (nevus spilus). *J Cutan Pathol.* 1990;17:241–245.
- Marchesi L, Naldi L, Parma A, et al. Agminate blue nevus combined with lentigo. A variant of speckled lentiginous nevus? *Am J Dermatopathol.* 1993;15:162–165.
- Betti R, Inselvini E, Palvarini M, et al. Agminate and plaque-type blue nevus combined with lentigo, associated with follicular cyst and eccrine changes: a variant of speckled lentiginous nevus. *Dermatology.* 1997; 195:387–390.
- Park YM, Kang H, Cho BK. Plaque-type blue nevus combined with nevus spilus and smooth muscle hyperplasia. *Int J Dermatol.* 1999;38: 775–777.
- Aroni K, Georgala S, Papachatzaki E, et al. Coexistence of plaque-type blue nevus and congenital melanocytic nevi. *J Dermatol.* 1996;23: 325–328.
- Yeh I, Fang Y, Busam KJ. Melanoma arising in a large plaque-type blue nevus with subcutaneous cellular nodules. *Am J Surg Pathol.* 2012;36: 1258–1263.
- Held L, Metzler G, Eigentler TK, et al. Recurrent nodules in a periauricular plaque-type blue nevus with fatal outcome. *J Cutan Pathol.* 2012; 39:1088–1093.

9. Sanada S, Higaki K, Torii Y, et al. Malignant melanoma arising in a plaque-type blue nevus. *Pathol Int*. 2012;62:749–753.
10. Gerami P, Jewell SS, Morrison LE, et al. Fluorescence in situ hybridization (FISH) as an ancillary diagnostic tool in the diagnosis of melanoma. *Am J Surg Pathol*. 2009;33:1146–1156.
11. Cesinaro AM, Schirosi L, Bettelli S, et al. Alterations of 9p21 analysed by FISH and MLPA distinguish atypical spitzoid melanocytic tumours from conventional Spitz's nevi but do not predict their biological behaviour. *Histopathology*. 2010;57:515–527.
12. Upshaw BY, Ghormley RK, Montgomery H. Extensive blue nevus of Jadassohn-Tieche; report of a case. *Surgery*. 1947;22:761–765.
13. Agusti-Mejias A, Messegueur F, García R, et al. Plaque-type blue nevus on the palm. *Int J Dermatol*. 2013;52:1405–1407.
14. Spring P, Perrier P, Erba P, et al. Large agminated cellular “plaque-type” blue nevus surrounding the ear: a case and review. *Dermatology*. 2013;227:21–25.
15. Zeiler FA, Kreck JP. Plaque-type blue nevus with meningeal melanocytomas. *Can J Neurol Sci*. 2012;39:117–120.
16. Fistarol SK, Itin PH. Plaque-type blue nevus of the oral cavity. *Dermatology*. 2005;211:224–233.
17. Bevona C, Tannous Z, Tsao H. Dermal melanocytic proliferation with features of a plaque-type blue nevus and neurocristic hamartoma. *J Am Acad Dermatol*. 2003;49:924–929.
18. Algermissen B, Toppe F, Henz BM, et al. Hypertrichotic plaque-type blue naevus—a novel type of dermal melanocytosis: report of an unusual case. *Acta Derm Venereol*. 2002;82:61–62.
19. Wen SY. Plaque-type blue nevus. Review and an unusual Case. *Acta Derm Venereol*. 1997;77:458–459.
20. Simis DR, Peris Barbo ML, Baz AC, et al. Papular plaque-type blue nevus [in French]. *Ann Dermatol Venereol*. 1996;123:572–573.
21. Hsiao GH, Hsiao CW. Plaque-type blue nevus on the face: a variant of Ota's nevus? *J Am Acad Dermatol*. 1994;30:849–851.
22. Heymann WR, Yablonsky TM. Congenital appearance of plaque-type blue nevi. *Arch Dermatol*. 1991;127:587.
23. Pfaltz M, Schnyder UW. Follow-up and ultrastructure of plaque-type blue nevus. *Hautarzt*. 1989;40:355–357.
24. Tsoitis G, Kanitakis C, Kapetis E. Multinodular plaque-type blue nevus, superficial and neuroid. *Ann Dermatol Venereol*. 1983;110:231–235.
25. Busam KJ, Woodruff JM, Erlandson RA, et al. Large plaque-type blue nevus with subcutaneous cellular nodules. *Am J Surg Pathol*. 2000;24:92–99.
26. Zattra E, Salmaso R, Montesco MC, et al. Large plaque type blue nevus with subcutaneous cellular nodules. *Eur J Dermatol*. 2009;19:287–288.
27. Skowron F, Balme B. Large plaque-type blue naevus with subcutaneous cellular nodules. *Clin Exp Dermatol*. 2009;34:e782–e784.
28. Pathy AL, Helm TN, Elston D, et al. Malignant melanoma arising in a blue nevus with features of pilar neurocristic hamartoma. *J Cutan Pathol*. 1993;20:459–464.
29. Wlotzke U, Hohenleutner U, Hein R, et al. Malignant infiltrating blue nevus of the plaque type. Case report and literature review. *Hautarzt*. 1995;46:860–864.
30. North JP, Yeh I, McCalmont TH, et al. Melanoma ex blue nevus: two cases resembling large plaque-type blue nevus with subcutaneous cellular nodules. *J Cutan Pathol*. 2012;39:1094–1099.
31. Kapur P, Selim MA, Roy LC, et al. Spitz nevi and atypical Spitz nevi/tumors: a histologic and immunohistochemical analysis. *Mod Pathol*. 2005;18:197–204.
32. Miteva M, Lazova R. Spitz nevus and atypical spitzoid neoplasm. *Semin Cutan Med Surg*. 2010;29:165–173.
33. Spatz A, Calonje E, Handfield-Jones S. Spitz tumors in children: a grading system for risk stratification. *Arch Dermatol*. 1999;135:282–285.
34. Baran JL, Duncan LM. Combined melanocytic nevi: histologic variants and melanoma mimics. *Am J Surg Pathol*. 2011;35:1540–1548.