

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

- Fortuño Y, Gallego I, Marcoval J. Sarcoidosis cutánea. *Actas Dermosifiliogr.* 2004;95:137–53.
 - Drummond C, Savdie E, Kossard S. Sarcoidosis with prominent giant cells. *Australas J Dermatol.* 2001;42:290–3.
 - Li N, Bajoghli A, Kubba A, Bhawan J. Identification of mycobacterial DNA in cutaneous lesions of sarcoidosis. *J Cutan Pathol.* 1999;26:271–8.
 - Ding XL, Cai L, Zhang JZ. Detection and identification of mycobacterial gene in skin lesions and lymph nodes in patients with sarcoidosis. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao.* 2009;31:20–3.
 - Wong CF, Yew WW, Wong PC, Lee J. A case of concomitant tuberculosis and sarcoidosis with mycobacterial DNA present in the sarcoid lesion. *Chest.* 1998;114:626–9.
 - Mise K, Goic-Barisic I, Puizina-Ivic N, Barisic I, Tonkic M, Peric I. A rare case of pulmonary tuberculosis with simultaneous pulmonary and skin sarcoidosis: A case report. *Cases J.* 2010;3:24.
 - Gupta LK, Luhadia SK, Khare AK, Garg A, Mittal A, Kuldeep CM. Pulmonary and cutaneous sarcoidosis in a treated case of renal tuberculosis. *Indian J Dermatol Venereol Leprol.* 2012;78:229.
 - Ahmad K, Powell FC. Cutaneous sarcoidal reaction in a patient with pulmonary tuberculosis. *Ir Med J.* 2005;98:182.
 - Ganguly S, Ganguly D. Sarcoidosis following sputum positive pulmonary tuberculosis: A rare entity. *Indian J Dermatol.* 2012;57:76–8.
 - Mandal SK, Ghosh S, Mondal SS, Chatterjee S. Coexistence of pulmonary tuberculosis and sarcoidosis: A diagnostic dilemma. *BMJ Case Rep.* 2014:19.
 - Oluboyo PO, Awotedu AA, Banach L. Concomitant sarcoidosis in a patient with tuberculosis: First report of association in Africa. *Cent Afr J Med.* 2005;51:123–5.
 - Papaetis GS, Pefanis A, Solomon S, Tsangarakis I, Orphanidou D, Achimastos A. Asymptomatic stage I sarcoidosis complicated by pulmonary tuberculosis: A case report. *J Med Case Rep.* 2008;2:226.
 - Chokoeva AA, Tchernev G, Tana C, Ananiev J, Wollina U. Sarcoid-like pattern in a patient with tuberculosis. *J Biol Regul Homeost Agents.* 2014;28:783–8.
 - Du SS, Zhao MM, Zhang Y, Zhang P, Hu Y, Wang LS, et al. Screening for differentially expressed proteins relevant to the differential diagnosis of sarcoidosis and tuberculosis. *PLoS One.* 2015;10:e0132466.
- S. de la Fuente-Meira,^{a,*} T. Gracia-Cazaña,^b
I. Pastushenko,^c M. Ara^d
- ^a *Servicio de Dermatología, Hospital Ernest Lluch, Zaragoza, Spain*
^b *Servicio de Dermatología, Hospital de Barbastro, Huesca, Spain*
^c *Interdisciplinary Research Institute (IRIBHM), Université Libre de Bruxelles (ULB), Bruselas, Bélgica*
^d *Servicio de Dermatología, Hospital Clínico Lozano Blesa, Zaragoza, Spain*
- *Corresponding author.
E-mail address: delafuente.sonia@gmail.com
(S. de la Fuente-Meira).

Benign Cutaneous Plexiform Hybrid Tumor of Perineurioma and Cellular Neurothekeoma[☆]



Tumor benigno cutáneo plexiforme híbrido de perineuroma y neurotecoma celular

Dear Editor:

The benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma (BCPHTPCN) is an entity described by Requena et al.¹ in 2013. It typically presents clinically as a small solitary papule in the perioral region, although other authors have described a lesion on the nose² and another on the left ankle.³ Histology reveals mixed pathological features of perineurioma and of cellular neurothekeoma with a plexiform architecture.^{1,3} Immunohistochemistry, when performed, has been positive for S100A6, microphthalmia-associated transcription factor (MITF), lysosomal membrane-associated glycoprotein

3 (NKI/C3), protein gene product 9.5 (PGP9.5), epithelial membrane antigen (EMA), and neuron-specific enolase (NSE). Expression of CD34, claudin-1, and glucose transporter 1 (GLUT1) has been more variable, weaker, and focal. In addition to the 9 patients in the original study, a further 2 cases have been published. We present a new case of this recently identified lesion. The tumor in our case was positive for CD68 and CD163 in a large number of cells situated between the nests of neoplastic cells, a finding that was only described in a few stromal histiocytes in 2 of the cases in the original series.¹

The patient was a man aged 58 years who presented a well-defined, hard, round, elevated lesion that had been growing slowly on his lower lip for 2 years and measured 5 mm in diameter at the time of first consultation. The surface of the lesion was erythematous and shiny. The patient was otherwise asymptomatic. Curettage was performed. Histology showed a circumscribed, nonencapsulated nodule in the superficial dermis (Fig. 1A). The nodule had a plexiform architecture (Fig. 1B) and did not make contact with the epidermis. Some cells had an epithelioid appearance with abundant eosinophilic cytoplasm, blurred cell borders, vesicular nuclei, and inconspicuous nucleoli. Other cells were delicate and spindle-shaped, with hyperchromatic nuclei. No pleomorphism, mitoses, or necrosis were observed. The stroma was myxoid with areas of collagen

[☆] Please cite this article as: Areán C, Córdoba A, Requena L, Álvarez ML. Tumor benigno cutáneo plexiforme híbrido de perineuroma y neurotecoma celular. *Actas Dermosifiliogr.* 2016;107:607–610.

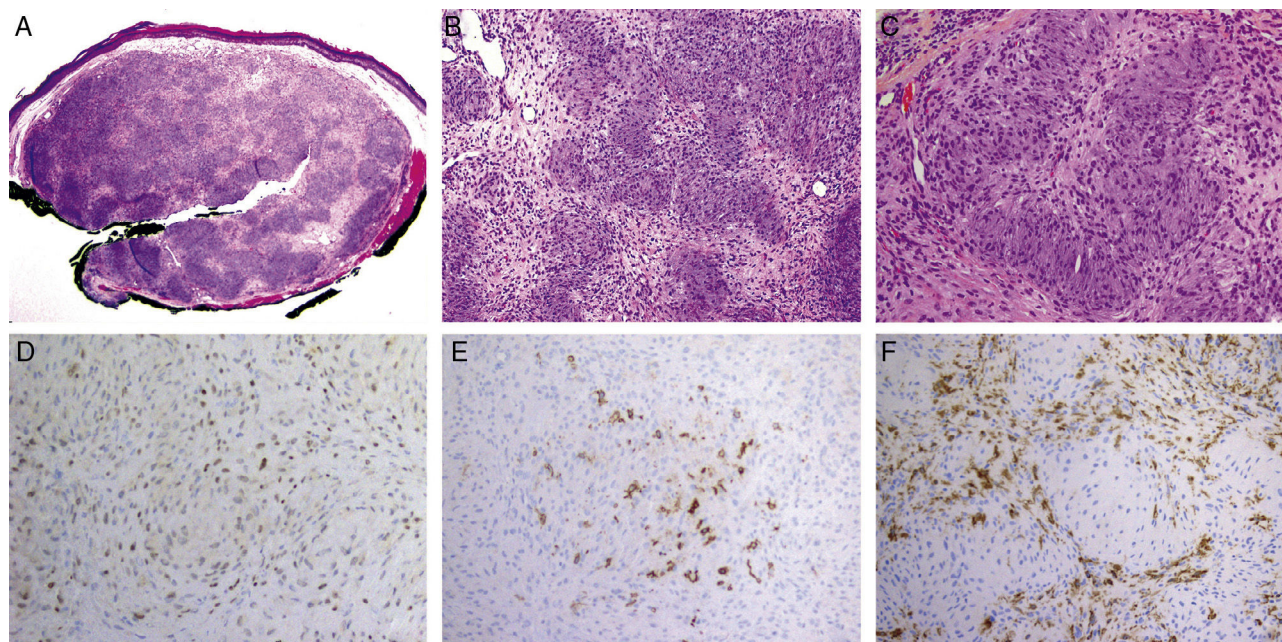


Figure 1 A, In the superficial dermis, a circumscribed nonencapsulated nodule is observed that does not make contact with the epidermis. Hematoxylin and eosin (H&E), original magnification $\times 2$. B, Plexiform architectural pattern. The neoplastic cells form round and irregular nests in a predominantly myxoid stroma. No neural or vascular structures are visible within these nests. H&E, original magnification $\times 10$. C, The majority of the neoplastic cells have ovoid nuclei with inconspicuous nucleoli and eosinophilic cytoplasm with poorly defined borders. These cells are intimately associated with distinct spindle-shaped cells with delicate, elongated, hyperchromatic nuclei. D, Diffuse positivity for MiTF in the nuclei of the neoplastic cells. Original magnification $\times 10$. E, Focal positivity for claudin-1 in the neoplastic cells. Original magnification $\times 10$. F, Positivity for CD163 in numerous interstitial cells between the nests. Original magnification $\times 10$.

Table 1 Summary of the Main Differential Diagnoses.

Lesion	Site Affected	Size	Capsule	Histology	Immunohistochemistry
Solitary circumscribed neuroma	Face, oral cavity, penis	< 1 cm	Yes (incomplete, only around the basal and lateral walls of the nodule)	Eosinophilic spindle-shaped cells with poorly defined cytoplasm and hyperchromatic nuclei. Artfactual clefts are observed between the cells	S100 in Schwann cells present among numerous neurofilament-positive axons. The incomplete capsule is positive for EMA
Neurofibroma	Variable. Upper trunk	Variable	None (poorly defined)	Wavy, spindle-shaped cells with relatively poorly defined pale cytoplasm among nerves fibers and mast cells. Fibromyxoid matrix. Mix of fibroblasts, perineural cells, and Schwann cells	S100 positive in 30% to 50% of cells
Schwannoma	Cranial nerves, bone, digestive tract, deep soft tissues, muscle	< 5 cm	Yes	Antoni A areas (densely cellular, made up of palisaded Schwann cells in a collagen stroma, forming Verocay bodies). Antoni B areas (paucicellular, made up of Schwann cells with inconspicuous cytoplasm and nuclei that appear to be suspended in a myxoid material). Mitoses may be observed (< 5 in 10 HPF)	S100 diffusely and strongly positive. EMA in the capsule of perineural cells

Table 1 (Continued)

Lesion	Site Affected	Size	Capsule	Histology	Immunohistochemistry
Cellular neurothekeoma	Head and upper limbs	< 1 cm	None (poorly defined tumor borders)	Lobulated or micronodular pattern. Epithelioid or spindle-shaped cells separated by collagen or in a myxoid stroma. No connection with the epidermis. Some osteoclast-like giant cells. The majority of lesions show some degree of cellular atypia	NKI/C3, neuron-specific enolase, smooth muscle actin (focally), and CD68 (focally)
Perineurioma	Limbs and trunk	< 5 cm	None (but tumor is circumscribed)	Bipolar spindle-shaped cells with pale eosinophilic cytoplasm and hyalinized or myxoid stroma. Formation of onion bulb-like whorls	EMA, claudin-1 (20% to 25% of cases). CD34 (50%). S100 focally in a few cases
BCPHTPCN	Lips, nose, ankle	< 1 cm	None (but tumor is circumscribed)	Plexiform pattern. No contact with epidermis. The majority of the cells are oval or spindle-shaped and have vesicular nuclei with inconspicuous nucleoli, pale eosinophilic cytoplasm, and unclear cell borders. These cells are intermixed with other delicate, elongated bipolar cells. No vascular or neural structures in the center of the whorls	Positive for S100A6, MiTF, NKI/C3, PGP9.5, EMA, and neuron-specific enolase. Variable focal staining for CD34, claudin-1, and Glut-1. S100 negative

Abbreviations: BCPHTPCN, benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma; EMA, epithelial membrane antigen; GLUT-1, glucose transporter 1; HPF, high-power fields; MiTF, microphthalmia-associated transcription factor; NKI/C3, lysosomal membrane-associated glycoprotein 3; S100, protein S100.

appearance (Fig. 1 C). The epidermis showed mild hyperpigmentation of the basal layer, hyperkeratosis, and pagetoid dyskeratosis.

Immunohistochemistry was diffusely positive for vimentin and MiTF (Fig. 1D) and focally positive for claudin-1 (Fig. 1E). The tumor cells were negative for S100, Melan-A, NSE, EMA, GLUT1, actin, and CD34. Numerous CD68⁺ and CD163⁺ cells were observed between the nests (Fig. 1F). A diagnosis of BCPHTPCN was made.

Perineurioma is a tumor formed of perineural cells arranged in whorls in a hyalinized or myxoid collagen stroma. Although immune expression of EMA is typical, these tumors are frequently positive for claudin-1, GLUT1, and CD34, and almost always negative for protein S100.³ Cellular neurothekeoma is a tumor of uncertain histogenesis, with a lobulated architectural pattern. It is formed of epithelioid and/or spindle-shaped cells in a predominantly myxoid stroma. It is usually positive for vimentin, NKI-C3, NSE, MiTF1, and PGP9.5, and sometimes for actin and CD68 (Table 1).^{4,5} In 2013, Requena et al.¹ described BCPHTPCN as a tumor with mixed features of perineurioma and cellular neurothekeoma, with a plexiform architectural pattern. The original series consisted of 9 cases in which the perioral region was affected, as found in our case. However, Yamada et al.² subsequently reported a case affecting the

nose, and Linos et al.³ described one on the left ankle. To date, all reported patients have been adults aged between 30 and 76 years, with no gender difference. Clinically the tumor presents as a solitary papule or nodule covered by skin of normal appearance¹⁻³; the histopathology findings have also been similar in all the lesions, with the exception of the case presented by Linos et al.,³ in which the plexiform architecture was not observed.

The tumor in our patient showed all the typical morphological characteristics and was diffusely positive for MiTF1 (specific to neurothekeoma) and focally positive for claudin-1 (commonly observed in perineurioma). However, other markers frequently used for the diagnosis of these tumors—NSE, S100, EMA, GLUT1, actin, and CD34—were negative. Staining for CD68 and CD163 was positive in numerous cells distributed between the nests of the tumor. This finding was described in 2 of the cases presented by Requena et al.,¹ but only affected a few stromal histiocytes. In all cases of BCPHTPCN published to date (including our case), protein S100, melanoma markers (HMB45, Melan-A, SOX10), and smooth muscle markers (actin, desmin) have been negative. MiTF1, S100A6, and PGP9.5 have been strongly positive in those cases in which they were studied. NKI/C3, EMA, NSE, CD34, claudin-1, GLUT1, and CD68 have shown more variable results in BCPHTPCN.

In conclusion, BCPHTPCN is a recently described tumor that shows a preference for the perioral region, and whose pathology findings are a hybrid between perineurioma and cellular neurothekeoma. Immunohistochemistry is variable, but important findings include positivity for S100A6, MiTF, NKI/C3, PGP9.5, EMA, and NSE. In our case, we draw particular attention to the presence of numerous CD68⁺ and CD163⁺ cells between the tumor nests. This peculiar trait has been reported previously in 2 patients, but as a less intense feature.¹ Given the variability of the immunohistochemistry findings and, in general, the low levels of expression of typical neural markers in this neoplasm, we consider the clinical and morphological features to be key elements in reaching the diagnosis.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors would like to thank the Dermatology Department and the technicians of the Pathology Department of Complejo Hospitalario de Navarra.

References

1. Requena L, Sitthinamsuwan P, Fried I, Kaddu S, Schirren C, Schärer L, et al. A benign cutaneous plexiform hybrid tumor

of perineurioma and cellular neurothekeoma. *Am J Surg Pathol.* 2013;37:845–52.

2. Yamada S, Kitada S, Nabeshima A, Noguchi H, Sasaguri Y, Hisaoka M. Benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma arising from the nose. *Diagn Pathol.* 2013;8:165.
3. Linos K, Stuart L, Goncharuk V, Edgar M. Benign cutaneous biphasic hybrid tumor of perineurioma and cellular neurothekeoma: A case report expanding the clinical and histopathologic features of a recently described entity. *Am J Dermatopathol.* 2015;37:319–22.
4. Hornick J, Fletcher C. Cellular neurothekeoma: Detailed characterization in a series of 133 cases. *Am J Surg Pathol.* 2007;31:329–40.
5. Fetsch J, Laskin W, Hallman J, Lupton G, Miettinen M. Neurothekeoma: An analysis of 178 tumors with detailed immunohistochemical data and long-term patient follow up information. *Am J Surg Pathol.* 2007;31:1103–14.

C. Areán,^{a,*} A. Córdoba,^a L. Requena,^b M^a.L. Álvarez^a

^a Servicio de Anatomía Patológica, Complejo Hospitalario de Navarra, Pamplona, Navarra, Spain

^b Departamento de Dermatología, Fundación Jiménez Díaz, Universidad Autónoma, Madrid, Spain

* Corresponding author.

E-mail address: carolina.arean.cuns@navarra.es (C. Areán).

Majocchi Granuloma of the Breast: A Rare Clinical Entity



Granuloma de Majocchi: Una rara entidad

Dear Editor,

Deep penetration of the skin by dermatophytic agents may provoke a granulomatous inflammatory skin reaction. This was first described by Majocchi.¹ Majocchi granuloma is characterized clinically by papular, pustular, or nodular inflammatory lesions occurring typically on the limbs or face,² though isolated cases affecting the vulva or scrotum have been published.³ We report a unique presentation of Majocchi granuloma in the breast; there are no previous reports of involvement of this location.

A 28-year-old female presented with a slightly painful, raised reddish lesion that had developed in her left breast over the previous 3 months. She gave no history of trauma and did not describe constitutional symptoms. The lesion had increased in size after the repeated application of mud to the area over 2 months. Treatment with a potent topical corticosteroid (betamethasone valerate, 0.122% wt/wt) was then applied twice daily for a month.

Clinical examination revealed a single erythematous plaque with areas of scarring. A yellowish discharge emanated from multiple openings in an area beneath the left nipple measuring approximately 5 × 4 cm (Fig. 1). On

palpation the plaque was firm and indurated and was slightly tender; there was no underlying breast lump. Diascopy findings were nonspecific. Gram stain of the discharge showed the presence of gram-positive cocci and abundant neutrophils. No acid-fast bacilli (AFB) were seen on direct smear. Potassium hydroxide (KOH) mount and fungal culture of skin scrapings and of the discharge was negative. Ultrasonography of the breasts was normal, though a single lymph



Figure 1 Papular-pustular plaque on the left breast with central scarring and a purulent discharge visible at the periphery.