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Spontaneous regression of Merkel cell carcinoma: A case report and review of the literature

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ABSTRACT

INTRODUCTION: Merkel cell carcinoma (MCC) is a rare and highly aggressive primary cutaneous neuroendocrine carcinoma, most often occurring in the elderly. Recurrence is frequent and in 40% of cases regional and distant metastases develop. Despite this, there have been reports of spontaneous regression. We report the first case of MCC with primary complete spontaneous regression of the nose in an 86-year-old woman following an incisional biopsy.

PRESENTATION OF CASE: An 86-year-old woman presented with a violaceous lump on the left side of the nose measuring 25 × 25 mm. Incisional biopsy of the lesion showed MCC and immunohistochemistry confirmed diagnosis. Following an 8-week period the lesion completely disappeared and histology did not show any residual MCC but immunohistochemistry demonstrated a mixture of T and B cells.

DISCUSSION: Complete spontaneous regression (CSR) is rare. The literature documents 22 similar cases of CSR of MCC. From this case report and previous literature the most likely reason for regression is a T-cell mediated immune response.

CONCLUSION: To the best of our knowledge, this is the first described case of MCC with primary CSR of the nose. Exact mechanism of regression remains unclear. Further research is needed in identifying pathway of immune response and possible immunotherapy as a cure.

1. Introduction

Merkel cells are primarily located in the basal layer of the epidermis and concentrated in touch-sensitive areas of the skin.[1] Their most noticeable ultrastructural characteristics are the dense-core secretory granules accumulated near the nerve fibre junction, which may contribute to its indefinite neuroendocrine function.[2]

Merkel cell carcinoma (MCC) was first described by Toker[3] in 1972 as trabecular carcinoma of the skin. 85% of all MCCs appear on sun-exposed areas[4] with the head and neck region most frequently affected, accounting for 35–47% of these cases.[5,6] The prognosis is poor, with a 5-year survival rate of around 60%[7], owing to the common involvement of regional lymph nodes (10–45%) at initial presentation, of which 50–75% of patients develop regional lymph node metastases at some time.[8–12] Distant metastases commonly affects 50% of patients with common sites being the lymph nodes, liver, bone, brain, lung and skin.[8–10,13,14]

O'Rouke and Bell[15] first described complete spontaneous regression (CSR) of MCC in 1986. Thereafter, 21 additional cases have been reported. This present study presents a case of complete spontaneous regression of MCC with an immunohistochemistry study of the region in which the tumour was located.

2. Presentation of case

An 86-year-old female patient presented with a violaceous lump on the left side of the nose measuring 25 × 25 mm. An incisional biopsy was performed and histology showed a dense infiltrate of small tumour cells with hyperchromatic nuclei and little cytoplasm (Fig. 1). Immunohistochemistry confirmed the diagnosis of MCC, with positive staining for cytokeratin 20 (CK20) (Fig. 2), neuron-specific enolase (Fig. 3), synaptophysin and negative staining for cytokeratin 5/6T, TTF1 and MelanA. The patient attended for an excision 8 weeks after her initial biopsy and showed no presence of lump prior to excision (Fig. 4). Histology of the excised specimen showed severely sun-damaged skin with mild epidermal atrophy. There was a patchy chronic inflammatory cell infiltrate with focal fibrosis and foreign body giant cell reaction with no evidence of any residual MCC. Immunohistochemistry demonstrated a mixture of both T and B cells with positive staining for CD4, CD3, CD5, and

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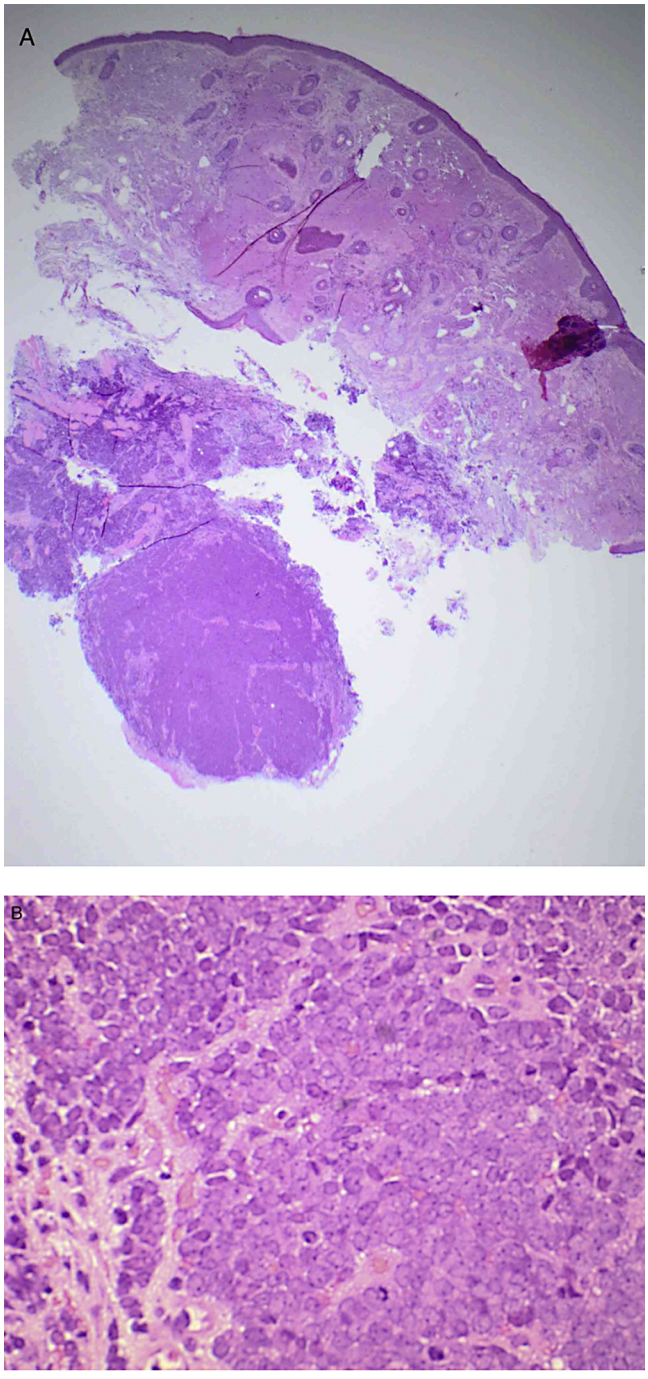

Fig. 1. Histopathological examination showing dense infiltrate of small tumour cells with hyperchromatic nuclei and little cytoplasm. (A) Haematoxylin-eosin, magnification 20×. (B) Haematoxylin-eosin, magnification 400×.

CD8 with CD4 slightly more than CD20 and CD79a. In addition, the specimen revealed admixed macrophages, which stained with CD68.

3. Discussion

Spontaneous regression among all neoplastic diseases has been estimated to be 1 case per 60,000 to 100,000 neoplasms.[16] Complete spontaneous regression (CSR) of MCC is rare and predicted to be 0.0013%.[17] To date, 15 cases of complete MCC regression following incisional biopsy have been reported (Table 1), along with 7 cases of regression occurring after local or regional recurrence of

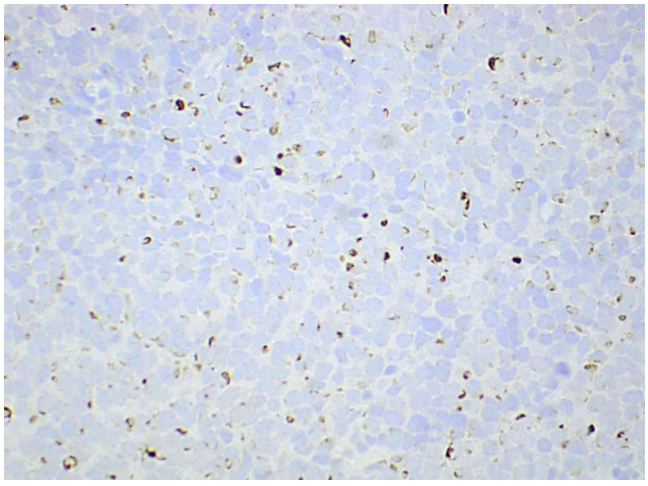

Fig. 2. Positive immunostaining for cytokeratin 20 showing a dot-like pattern (magnification 400×).

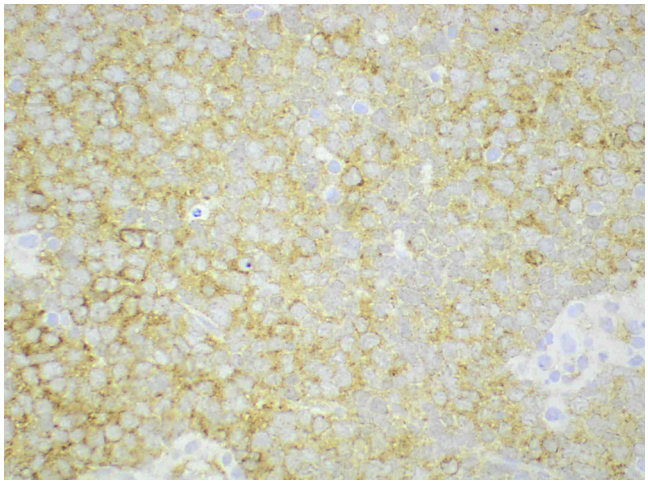

Fig. 3. Positive immunostaining for neurone-specific enloase (magnification 400×).

the carcinoma (Table 2). In the group of MCCs with primary CSR most neoplasms were located on the cheek. In contrast, none of the cases of MCCs with CSR after local recurrence or metastasis were primarily located on the cheek. In both groups of patients the majority were female (15 cases) and the mean age was 79 years old. Our patient presented the typical characteristics of patients with primary CSR of MCC i.e. female sex, elderly and regression after incisional biopsy.

The histopathologic study of the biopsy following CSR in our patient demonstrated results similar to other reports.[18–20] The biopsy showed accumulation of chronic inflammatory cells, mainly T cells. Other studies of both primary and secondary MCC demonstrated infiltration by CD4+, CD8+ and CD3+ T lymphocytes and foamy macrophages.[17–21] The mechanism of CSR remains unclear, however, along with our findings, it suggests that T-cell-mediated immunity plays an important role in tumour regression. This could be attributed to the initial incisional biopsy of MCC (15 cases), which may have triggered tumour regression via stimulation of the immune system. In addition, the majority of patients were elderly with poor health status and various co-morbidities, which may suggest other unknown mechanisms, could be involved.

Table 1
Cases reported with primary complete spontaneous regression of Merkel cell carcinomas.

Author	Sex/age	Co-morbidities	Tumour Site	Treatment	Immunological study after regression	Disease free period
Kayashima et al.[18]	F/68		Forehead	Biopsy	CD3 and CD5 (pan-T cells) cells heavily infiltrated and few CD19 cells (B cells). CD4 cells were in the majority. CD1 (langerhans) cells also present	11 years
Kayashima et al.[18]	F/86	Hypertension Cerebral atherosclerosis, IDDM	Cheek	Biopsy	Infiltrates of inflammatory cells (chiefly lymphocytes)	36 months
Djilali-Bouzina et al.[22]	F/83		Cheek	Biopsy		1 year
Duncan and Tschen[23]	M/79		Scalp	Biopsy		28 months
Tanita et al.[24]	F/75		Cheek	Biopsy		1 year
Satoh et al.[25]	M/87		Cheek	Biopsy		2 months
Maruo et al.[19]	F/82	Cervical spinal cord injury and complete paresis, Cerebral atherosclerosis and Neurosis	Cheek	Biopsy	Large number of KP-1+ foamy cells (macrophages). Infiltration of lymphocytes, numerous lymphoid follicles and T cells	1 year
Connelly et al.[26]	F/71		Cheek	Biopsy		11 months
Sais et al.[27]	F/78		Thigh	Biopsy		40 months
Junquera et al.[28]	F/79		Cheek	Biopsy	Dense cluster of lymphocytes and fibrosis	6 years
Vesely et al.[20]	F/67		Cheek	Biopsy	Prominent lymphocytic infiltrate	6 months
Missotten et al.[16]	M/90		Eyelid	Biopsy	Granulomatous inflammation consisting of many histiocytes and lymphocytes	18 months
Missoten et al.[6]	F/81		Eyelid	Biopsy		2 years
Ciudad et al.[7]	F/86		Cheek	Biopsy	Moderate lymphocytic infiltrate. Most lymphocytes were T cells	18 months
Ciudad et al.[17]	M/92	High blood pressure, Diabetes mellitus, Parkinson's Disease, Glaucoma, Dementia	Scalp	Biopsy		23 months
Present Study	F/86	Osteoarthritis, COPD, Hypertension, AF, PPM (pacemaker)	Nose	Biopsy	Lymphocyte infiltrate staining for CD4+, CD3+, CD5+ with CD4+ slightly more than CD20+ and CD79a. Also admixed macrophages present staining for CD68	

Table 2
Cases reported with complete spontaneous regression of recurrences or metastasis of Merkel cell carcinomas.

Author	Sex/age	Co-morbidities	Tumour site	Treatment	Metastasis	Immunological study after regression	Disease free period
O'Rourke and Bell[15]	F/90	Cerebral atherosclerosis, SCC upper sternum	Pre-auricular area	Surgery	Skin		18 months
Bayrou et al.[29]	F/69		Temple	Surgery, radiotherapy, chemotherapy	Cervical lymphadenopathy and Skin		15 years
Yanguas et al.[30]	M/65	Dilated cardiomyopathy, Mitral insufficiency, Hypertension, Atrial fibrillation, Transient ischaemic attacks, Chronic renal failure, Abdominal aortic aneurysm	Ear	Surgery	Cervical lymphadenopathy and Skin		18 months
Connelly and Kowalcyk[31]	M/85		Forehead	Surgery	Intraparotid lymphadenopathy and Skin		50 months
Brown et al.[32]	M/85		Scalp	Surgery	Cervical lymphadenopathy and Skin and Bone		33 months
Richetta et al.[33]	F/76		Eyebrow	Surgery	Regional lymph nodes and Skin	Fibrosis, vascular congestion and modest lymphocytic infiltrate	13 months
Wooff et al.[21]	F/94		Eyebrow	Surgery	Regional lymph nodes	Extensive fibrosis with accumulation of foamy macrophages and other chronic inflammatory cells including many T lymphocytes	

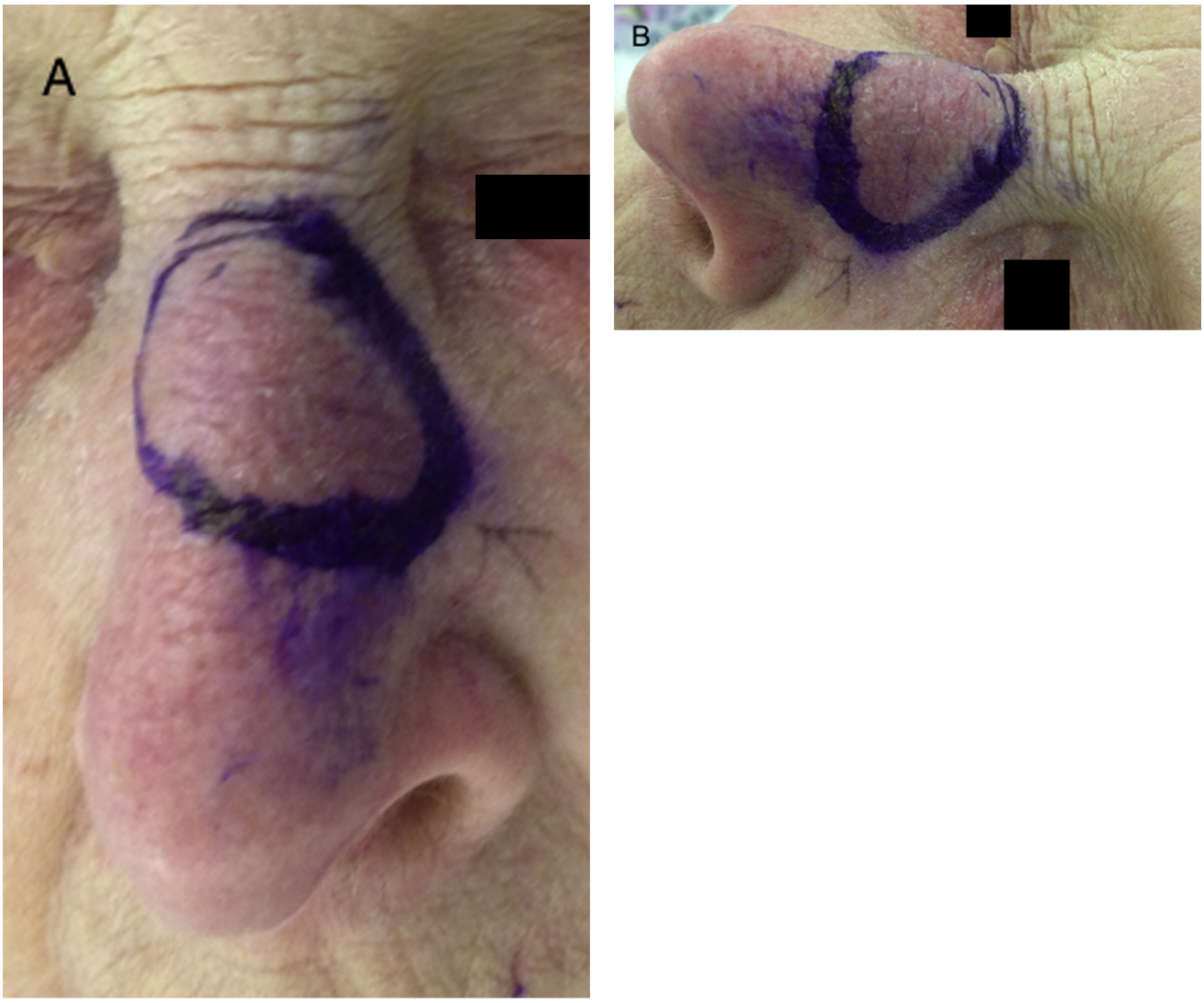

Fig. 4. (A and B) Spontaneous regression of Merkel cell carcinoma after incisional biopsy.

4. Conclusion

In summary, we report one patient with CSR of MCC. To the best of our knowledge, this is the first described case of MCC with primary CSR of the nose. The findings are in concordance with many other studies most notably an incisional biopsy before regression and an infiltrate of T cells after regression. Although, this is only a proposed mechanism it certainly is an area that requires further research with the possibility of developing immune modulating therapy in treating such cancers.

Conflict of interest

None.

Funding

None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contributions

Calver Pang – data collection, data analysis, writing; Deepika Sharma – histopathological and immunohistochemistry studies including figures; Thangasamy Sankar – study design, patient details.

Key learning points

- Merkel cell carcinoma is a rare disease with a high metastatic rate and poor prognosis.
- Spontaneous regression of Merkel cell carcinoma is an extremely rare event.
- In this case report, regression occurred following incisional biopsy.
- Biopsy showed mainly T cells suggesting immunity plays an important role in tumour regression which may be attributed to the incision which triggered an immune response.
- Mechanism of regression is still unclear but research into immune modulating therapy may help in managing such cancers.

References

1. Boulais N, Misery L. Merkel cells. *J Am Acad Dermatol* 2007;**57**(1):147–65.
2. Polakovicova S, Seidenberg H, Mikusova R, Polak S, Pospisilova V. Merkel cells – review on developmental, functional and clinical aspects. *Bratisl Lek Listy* 2011;**112**(2):80–7.
3. Toker C. Trabecular carcinoma of the skin. *Arch Dermatol* 1972;**105**:107–10.
4. Marks ME, Kim RY, Salter MM. Radiotherapy as an adjunct in the management of Merkel cell carcinoma. *Cancer* 1990;**65**:60–4.
5. Suarez C, Rodrigo JP, Ferlito A, Devaney KO, Rinaldo A. Merkel cell carcinoma of the head and neck. *Oral Oncol* 2004;**40**:773–9.
6. Metz KA, Jacob M, Schmidt U, Steuhl KP, Leder LD. Merkel cell carcinoma of the eyelid: histological and immunohistochemical features with special respect to differential diagnosis. *Graefes Arch Clin Exp Opthalmol* 1998;**236**:561–6.
7. Schrama D, Ugurel S, Becker J. Merkel cell carcinoma: recent insights and new treatment options. *Curr Opin Oncol* 2012;**24**(2):141–9.
8. Haag ML, Glass LF, Fenske NA. Merkel cell carcinoma. Diagnosis and treatment. *Dermatol Surg* 1995;**8**:669–83.
9. Ratner D, Nelson BR, Brown MD, Johnson TM. Merkel cell carcinoma. *J Am Acad Dermatol* 1993;**29**:143–56.
10. Yiengpruksawan A, Coit DG, Thaler HT, Urmacher C, Knapper WK. Merkel cell carcinoma. Prognosis and management. *Arch Surg* 1991;**126**(12):1514–9.
11. Goepfert H, Remmler D, Silva E, Wheeler B. Merkel cell carcinoma (endocrine carcinoma of the skin) of the head and neck. *Arch Otolaryngol* 1984;**110**(11):707–12.
12. Tai PT, Yu E, Winquist E, Hammond A, Stitt L, Tonita J, et al. Chemotherapy in neuroendocrine/Merkel cell carcinoma of the skin: case series and review of 204 cases. *J Clin Oncol* 2000;**18–12**:2493–9.
13. Gollard R, Weber R, Kosty MP, Greenway HT, Massullo V, Humberson C. Merkel cell carcinoma: review of 22 cases with surgical, pathologic, and therapeutic considerations. *Cancer* 2000;**88**(8):1842–51.
14. Marks ME, Kim RY, Salter MM. Radiotherapy as an adjunct in the management of Merkel cell carcinoma. *Cancer* 1990;**65**(1):60–4.
15. O'Rourke MG, Bell JR. Merkel cell tumor with spontaneous regression. *J Dermatol Surg Oncol* 1986;**12**:994–6.
16. Missotten GS, de Wolff-Rouendaal D, de Keizer RJ. Merkel cell carcinoma of the eyelid. Review of the literature and report of patients with Merkel cell carcinoma showing spontaneous regression. *Ophthalmology* 2008;**115**:195–201.
17. Ciudad C, Aviles A, Alfageme F, Lecona M, Suarez R, Lazaro P. Spontaneous regression in Merkel cell carcinoma: report of two cases with a description of dermoscopic features and review of the literature. *Dermatol Surg* 2010;**36**:687–93.
18. Kayashima K, Ono T, Johno M, Kojo Y, Yamashita N, Matsunaga Q. Spontaneous regression in Merkel cell (neuroendocrine) carcinoma of the skin. *Rach Dermatol* 1991;**127**:550–3.
19. Maruo K, Kayashima KI, Ono T. Regressing Merkel cell carcinoma – a case showing replacement of tumour cells by foamy cells. *Br J Dermatol* 2000;**142**:1184–9.
20. Vesely MJJ, Murray DJ, Neligan PC, Novak CB, Gullane PJ, Ghazarian D. Complete spontaneous regression in Merkel cell carcinoma. *J Plast Reconstr Aesthet Surg* 2008;**61**:165–71.
21. Wooff JC, Trites JR, Walsh NM, Bullock MJ. Complete spontaneous regression of metastatic Merkel cell carcinoma: a case report and review of the literature. *Am J Dermatopathol* 2010;**32**:614–7.
22. Djilali-Bouzina F, Cribier B, Heid E. Regressive neuroendocrine carcinoma after partial biopsy. *Nouv Dermatol* 1992;**11**:767–70.
23. Duncan WC, Tschen JA. Spontaneous regression of Merkel cell (neuroendocrine) carcinoma of the skin. *J Am Acad Dermatol* 1993;**29**(4):653–4.
24. Tanita M, Tabata N, Kato T. Merkel cell cancer and natural withdrawing. Merkel cell cancer causing natural withdrawing. *Skin Cancer* 1996;**11**(2):214–6.
25. Satoh M, Kikkawa Y, Iwatsuki K. Spontaneous regression of Merkel cell tumour after biopsy. *Hifuka No Rinsho* 1997;**29**:449–1451.
26. Connelly TJ, Cribier B, Brown TJ, Yanguas I. Complete spontaneous regression of Merkel cell carcinoma: a review of the 10 reported cases. *Dermatol Surg* 2000;**26**(9):853–6.
27. Sais G, Admella C, Soler T. Spontaneous regression in primary cutaneous neuroendocrine (Merkel cell) carcinoma: a rare immune phenomenon? *J Eur Acad Dermatol Venereol* 2002;**16**(1):82–3.
28. Junquera L, Torre A, Vicente JC, Garcia-Consuegra L, Fresno MF. Complete spontaneous regression of Merkel cell carcinoma. *Ann Otol Rhinol Laryngol* 2005;**114**(5):376–80.
29. Bayrou O, Avril MF, Charpentier P, Caillou B, Guillaume JC, Prade M. Primary neuroendocrine carcinoma of the skin: clinico-pathologic study of 18 cases. *J Am Acad Dermatol* 1991;**24**:198–207.
30. Yanguas I, Goday JJ, Gonzalez-Guemes M, Oleaga JM, Lozano M, Soloeta R. Spontaneous regression of Merkel cell carcinoma of the skin. *Br J Dermatol* 1997;**137**(2):296–8.
31. Connelly TJ, Kowalcyk AP. Another case of spontaneous regression of Merkel cell (neuroendocrine) carcinoma. *Dermatol Surg* 1997;**23**(7):588–90.
32. Brown TJ, Jackson BA, MacDarlane DF, Goldberg LH. Merkel cell carcinoma: spontaneous resolution and management of metastatic disease. *Dermatol Surg* 1999;**25**(1):23–5.
33. Richetta AG, Mancini M, Torroni A, Lore B, Lannetti G, Sardella B, et al. Total spontaneous regression of advanced Merkel cell carcinoma after biopsy. Review and a new case. *Dermatol Surg* 2008;**34**:815–22.