Mohs micrographic surgery of rare cutaneous tumours

C. van Lee
S. Flohil
J. Beisenherz
M. Mureau
L. Overbeek
T. Nijsten
R. van den Bos

J Eur Acad Dermatol Venereol 2017;31(8):1285-88

ABSTRACT

Background: Recurrence rates after Mohs micrographic surgery (MMS) for rare cutaneous tumours are poorly defined.

Objective: To investigate the recurrence rate after MMS for rare cutaneous tumours at a university centre.

Methods: Retrospective review of all rare cutaneous tumours treated with MMS at a large university centre between January 2008 and December 2012. To detect all recurrences, patients were linked to The Nationwide Network and registry of histology and cytopathology (PALGA).

Results: In total, 80 patients with 80 tumours were included. Tumour types included dermatofibrosarcoma protuberans (27), atypical fibroxanthoma (22), Merkel cell carcinoma (8), microcystic adnexal carcinoma (9), sebaceous carcinoma (6), extramammary Paget's disease (2) and other (6). Mean follow-up time was 3.7 years (SD 1.4) during which two atypical fibroxanthomas recurred (2.5%).

Conclusion: This large case series shows that MMS is an appropriate treatment for rare cutaneous tumours with a recurrence rate less than 3%. To improve the quality of treatment, MMS for rare cutaneous tumours is preferably performed in centres where multidisciplinary experts work together.

INTRODUCTION

Mohs micrographic surgery (MMS) for the treatment of skin cancer is associated with low recurrence rates and maximal preservation of healthy tissue.[1] Most studies focus on the surgical treatment of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC), as these are the most common cutaneous cancers among Caucasians.[2-5] Studies about the treatment of rare cutaneous tumours are sparse.

Rare cutaneous tumours are commonly treated with wide standard excision, whereby excision margins range from 2 to 5 centimetres. Despite these margins, incomplete excisions and recurrences occur frequently.[6,7] Few studies, which investigated MMS for rare cutaneous tumours, all reported low recurrence rates.[8–10] However, conclusions were based on small numbers of patients and limited information on follow-up. Therefore, large case series with adequate follow-up data are needed to obtain more in-depth information on recurrences after MMS for rare cutaneous tumours.

METHODS

Patient selection

This retrospective case series included all rare cutaneous tumours (i.e. excluding BCC and SCC) treated with MMS at the Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands between 1 January 2008 and 31 December 2012. This time frame was chosen because at the study centre from 2008 and on, rare cutaneous tumours were structurally treated with MMS. Inclusion was stopped after 2012 to set a solid follow-up period. In the study period, all patients with rare cutaneous tumours were preoperatively discussed in a multidisciplinary team (i.e. dermatologist, head and neck surgeon, plastic surgeon, radiologist and a radiation oncologist) where MMS was considered as an appropriate treatment for operable rare cutaneous tumours. Dermatologists certified by the European Society for Micrographic Surgery performed the MMS procedures. Well-trained histotechnicians made MMS fresh frozen slides, which were stained with haematoxylin and eosin and evaluated by the MMS surgeon. Pathologists were available for an intraoperative consultation. For routine quality assurance, a pathologist additionally reviewed all MMS slides within one week after the MMS procedure. In some cases, depending on tumour type and MMS surgeon, an additional margin was excised after the MMS to confirm tumour clearance with immunohistochemical stains (e.g. CD34) on paraffin slides. When tumour clearance was achieved, the MMS surgeon or plastic surgeon reconstructed the defect. For follow-up after treatment, patients were recommended to visit a dermatologist at least once a year during the following five to ten years.

Outcome and data source

The primary outcome was a histologically proven recurrence in or within one centimetre of the MMS scar, in tumours which were completely excised with MMS. Patients who proved inoperable during the MMS procedure were reported separately. In the Netherlands, all histopathology reports from every biopsy, excision or MMS procedure are registered in The Nationwide Network and registry of histology and cytopathology (Dutch acronym: PALGA).[11] To detect recurrences, patient files were reviewed and the included patients were linked (through an encrypted identification code) to PALGA on 11 August 2015, assuming that lesions clinically suspicious of recurrence were histologically verified by biopsy or excision. In addition to this latter assumption, we recorded whether each patient visited a dermatologist for follow-up in the past six months. Vital status was obtained from the Dutch Municipal Population Register (Dutch acronym: GBA) until 18 June 2015. Follow-up duration was determined as the number of years between the MMS procedure and PALGA linkage (11 August 2015) or date of recurrence or date of death. The secondary outcome was the number of MMS stages needed for tumour clearance.

Patient, tumour and MMS characteristics

Patient, tumour and MMS characteristics were derived from electronic patient files including standardized digital MMS files and pathology reports. SPSS 22.0 for windows (SPSS Inc., Chicago, IL) was used for the descriptive summary statistics.

RESULTS

During the study period, a total of 4,258 cutaneous tumours were treated with MMS: 88% BCC, 10% SCC and 2% rare cutaneous tumours. In total, 86 patients with 87 rare cutaneous tumours were treated with MMS. Of these 87 tumours, 92% (n = 80) were completely excised and 8% (n = 7) turned out to be inoperable. The seven inoperable tumours were three extramammary Paget's disease (EMPD), two Merkel cell carcinoma (MCC), one microcystic adnexal carcinoma (MAC), and one trichilemmal tumour. The 80 completely excised tumours were 27 dermatofibrosarcoma protuberans (DFSP), 22 atypical fibroxanthoma (AFX), nine MCC, eight MAC, six sebaceous carcinoma (SEB CA), two EMPD and six other rare cutaneous tumours. In 30 cases, an additional margin was excised after the MMS to confirm tumour clearance with immunohistochemical stains (e.g. CD34 for DFSP) on paraffin slides. This was performed in 23 cases of DFSP, one AFX, two MCC, three MAC and one cutaneous angiosarcoma. In one MAC, there were still tumour cells present on the paraffin slides; however, the outer margins were tumour free.

In Table one, a description is given of the 80 completely excised rare cutaneous tumours. In total, there were 2.5% (n = 2) recurrences, both AFX, during a mean follow-up time of 4 years (SD 1). Overall mean age during time of MMS was 61 years (SD 19). Of all 80 patients, 19% (n = 15) died during the follow-up period, these patients were treated for an AFX (n = 6), SEB CA (n = 4), DFSP (n = 4), MCC (n = 1), MAC (n = 1), and porocarcinoma (n = 1). Of all 65 patients who finished the studied follow-up period, 77% (n = 50) patients had their skin checked in the past six months and 23% (n = 15) patients were lost to follow-up.

The two recurrences were both located on the scalp. Case one was a primary AFX tumour, which was excised in one MMS stage. Case 2 was an AFX which was previously three times incompletely excised. Case two was excised in two MMS stages. Both cases had a final defect of 4 centimetres in diameter and reached on to the skull. In both cases, bone milling was performed additionally to the MMS. The MMS slides were additionally reviewed by a pathologist in concordance with the MMS surgeon. The recurrences occurred three and seven months after the MMS procedure. Remarkably, the histopathology of the two recurrences was unclear, an AFX was considered, but an undifferentiated pleomorphic sarcoma could not be excluded. Case one developed lymphovascular and lung metastasis and died eight months after the MMS procedure. Case two was not additionally treated because of severe comorbidity and died 12 months after the MMS procedure.

Figure one shows an overview of the number of MMS stages needed for tumour clearance in all 80 cases. DFSP was the only rare cutaneous tumour that in certain cases needed six MMS stages, and DFSP had the highest percentage of cases with the largest defect size of more than ten centimetres.

Table 1. Patient, tumour and Mohs procedure characteristics of 80 completely excised rare cutaneous tumours.

	DFSP (%)	AFX (%)	MCC (%)	MAC (%)	SEB CA (%)	EMPD (%)	Other[a] (%)
Total number of tumours	27	22	9	8	6	2	6
Men	15 (56)	16 (73)	4 (44)	4 (50)	5 (83)	1 (50)	3 (50)
Mean age at MMS, years (SD)	44 (15)	72 (9)	74 (9)	68 (15)	74 (10)	65 (4)	58 (25)
Mean follow-up time, years (SD)	4 (1)	3 (2)	4 (1)	4 (1)	3 (2)	3 (1)	4 (1)
Recurrence[b]	0	2 (9)	0	0	0	0	0
Tumor location							
Head or neck	8 (30)	22 (100)	8 (89)	6 (75)	6 (100)	0	2 (33)
Trunk	10 (37)	0	0	1 (13)	0	0	1 (17)
Extremities	8 (30)	0	0	1 (13)	0	0	2 (33)
Hands or feet	0	0	0	0	0	0	1 (17)
Genital region	1 (4)	0	1 (11)	0	0	2 (100)	0
Pre-treatment							
None	10 (37)	15 (68)	4 (44)	6 (75)	5 (83)	2 (100)	3 (50)
Incompletely excised or recurrence	16 (59)	6 (27)	5 (56)	2 (25)	1 (17)	0	3 (50)
Radiotherapy	0	1 (5)	0	0	0	0	0
Imatinib	1 (4)	0	0	0	0	0	0
Defect size after 1st MMS stage							
0-2 cm	4 (15)	6 (27)	3 (33)	3 (38)	5 (83)	0	0
2.1-5 cm	5 (19)	13 (59)	5 (56)	1 (13)	1 (17)	1 (50)	5 (83)
5.1-10 cm	15 (56)	3 (14)	1 (11)	3 (38)	0	1 (50)	1 (17)
10.1-20 cm	3 (11)	0	0	1 (13)	0	0 (0.0)	0
Final defect size							
0-2 cm	2 (7)	5 (23)	3 (33)	2 (25)	5 (83)	0	0
2.1-5 cm	5 (19)	14 (64)	5 (56)	1 (13)	1 (17)	0	5 (83)
5.1-10 cm	11 (41)	3 (14)	1 (11)	1 (13)	0	1 (50)	1 (17)
10.1-20 cm	9 (33)	0	0	4 (50)	0	1 (50)	0
Final defect depth							
Subcutaneous fat	9 (33)	0	5 (56)	1 (13)	3 (50)	1 (50)	3 (50)
Muscle	14 (52)	12 (55)	2 (22)	3 (38)	3 (50)	1 (50)	2 (33)
Cartilage or bone	4 (15)	10 (46)	2 (22)	4 (50)	0	0	1 (17)
Mean number of MMS stages (SD)	2.6 (1.4)	1.5 (0.5)	1.6 (1.0)	2.1 (0.4)	1.3 (0.8)	2.5 (0.7)	1.3 (0.5)
Margin for histochemistry after MMS	23 (85)	1 (5)	2 (22)	3 (38)	0	0	1 (17)
Reconstruction							
Noncomplex[c]	16 (59)	14 (64)	6 (67)	1 (13)	5 (83)	0	3 (50)
Complex[d]	11 (41)	8 (36)	3 (33)	7 (88)	1 (17)	2 (100)	3 (50)

Table 1. (continued)

	DFSP (%)	AFX (%)	MCC (%)	MAC (%)	SEB CA (%)	EMPD (%)	Other[a] (%)
Reconstruction by							
Dermatologist	20 (74)	20 (91)	9 (100)	4 (50)	6 (100)	1 (50)	4 (67)
Plastic surgeon	7 (26)	2 (9)	0	4 (50)	0	1 (50)	2 (33)
Adjuvant treatment[e]	4 (15)	6 (27)	6 (67)	2 (25)	0	0	2 (33)

Percentage were rounded.

AFX, atypical fibroxanthoma; cm, centimeter; DFSP, dermatofibrosarcoma protuberans; EMPD, extramammary Paget's disease; MAC, microcystic adnexal carcinoma; MCC, Merkel cell carcinoma; MMS, Mohs micrographic surgery; SEB CA, sebaceous carcinoma; SD, standard deviation.

[a] Others included one trichilemmal carcinoma, one cutaneous angiosarcoma, one porocarcinoma, one nerve sheath myxoma, one granular cell tumour, one spiradenocarcinoma.

[b] Number of recurrences after MMS; this means that aborted MMS were excluded from this study and number of recurrences.

[c] Noncomplex reconstructions included primary closure or healing by secondary intention.

[d] Complex reconstructions included all noncomplex reconstructions, e.g. skin grafts, flaps.

[e] Adjuvant treatments included bone milling, radiotherapy, chemotherapy, imatinib or an combination of these treatments.

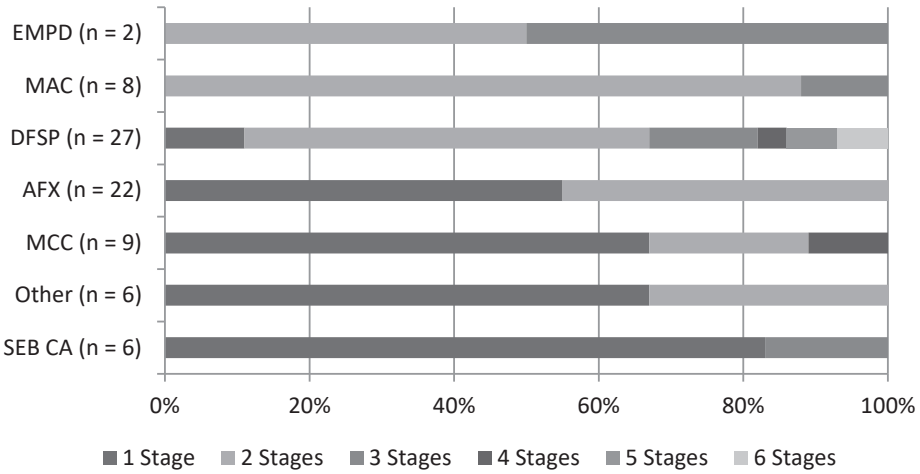

Figure 1. Number of Mohs micrographic surgery stages needed for tumour clearance in 80 rare cutaneous tumours.

AFX, atypical fibroxanthoma; DFSP, dermatofibroma sarcoma protuberans; EMPD, extramammary Paget's disease; MAC, microcystic adnexal carcinoma; MCC, Merkel cell carcinoma; n, number; SEB CA, sebaceous carcinoma.

Other included one trichilemmal carcinoma, one cutaneous angiosarcoma, one porocarcinoma, one nerve sheath myxoma, one granular cell tumour, one spiradenocarcinoma.

DISCUSSION

This Dutch case series showed that MMS for rare cutaneous tumours is an appropriate treatment, because only two of the 80 cases had a recurrence during our mean follow-up period of four years. This percentage is extremely low in comparison with standard excision, as for the latter recurrence rates up to 89% are reported.[8,12] In this study, most rare cutaneous tumours occurred at older age (except for DFSP) and men were relatively more often affected than women (except for MCC), which has also been observed by others.[8,9,13] Our study was limited by retrospective data and selection bias. Our observed low recurrence rate is in accordance with a study of the Geisinger Medical Center in Pennsylvania where only 4% of rare cutaneous tumours recurred after MMS during a mean follow-up period ranging from 11 to 39 months.[13] The three recurrences were MAC, the tumours which did not recur were 39 DFSP, 23 MAC, 10 EMPD. [13] Others also report low recurrence rates after MMS.[6,8,9,13-15]

The risk of missing recurrences during our follow-up period was low because patients were linked with PALGA. The two tumours that recurred were diagnosed as AFX based on the pre-MMS biopsy. The recurrences were classified as undifferentiated pleomorphic sarcoma, which must in retrospection already have been the initial diagnosis. These tumours have a very aggressive behaviour and a poor prognosis, wherefore MMS might be a less appropriate treatment.

DFSP was associated with many MMS stages and large defect sizes. This is probably explained because DFSP mainly grows in the reticular dermis and subcutis often sparing superficial dermis and epidermis whereby the clinical visible part of the DFSP is often much smaller than its microscopically spread.[16]

The seven cases which turned out to be inoperable had bone invasion or were limited by local anaesthesia. Even when adequate imaging has been performed (e.g. CT, MRI), it might be difficult to predict the extent of the tumour preoperatively. To prevent aborted MMS procedures, research should focus on instruments that will be perfectly able to assess tumour extent preoperatively. MMS seems an appropriate treatment for rare cutaneous tumours given the low recurrence rate observed in our case series and should definitely be considered in cases where a wide local excision could mutilate the patient (such as in the head and neck area). To improve the quality of treatment, it is recommended that MMS for rare cutaneous tumours is performed in centres where multidisciplinary experts work together.

REFERENCES

1. Nehal K, Lee E. Mohs surgery. UpToDate www.uptodate.com/contents/mohssurgery?source=machineLearning&search=mohs+micrographic+surgery&selectedTitle=1%7E46&sectionRank=1&anchor= H1574000248#H1574000248 (cited May 2016).
2. Flohil SC, Seubring I, van Rossum MM, Coebergh JWW, de Vries E, Nijsten T. Trends in basal cell carcinoma incidence rates: A 37-year Dutch observational study. J Invest Dermatol 2013;133:913-18.
3. Hollestein LM, de Vries E, Nijsten T. Trends of cutaneous squamous cell carcinoma in the Netherlands: Increased incidence rates, but stable relative survival and mortality 1989–2008. Eur J Cancer 2012;48:2046-53.
4. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. Brit J Dermatol 2012;166:1069-80.
5. Holterhues C, de Vries E, Louwman MW, Koljenovic S, Nijsten T. Incidence and trends of cutaneous malignancies in the Netherlands, 1989-2005. J Invest Dermatol 2010;130:1807-12.
6. Bogucki B, Neuhaus I, Hurst EA. Dermatofibrosarcoma protuberans: A review of the literature. Dermatol Surg 2012;38:537-51.
7. Randle HW. The other skin cancers (non-melanoma, non-basal cell carcinoma, non-squamous cell carcinoma). Curr Probl Derm-Us 2001; 13: 123–129.
8. Boyer JD, Zitelli JA, Brodland DG, D'Angelo G. Local control of primary Merkel cell carcinoma: Review of 45 cases treated with Mohs micrographic surgery with and without adjuvant radiation. J Am Acad Dermatol 2002;47:885-92.
9. Bae JM, Choi YY, Kim H et al. Mohs micrographic surgery for extramammary Paget disease: A pooled analysis of individual patient data. J Am Acad Dermatol 2013;68:632-637.
10. Davis JL, Randle HW, Zalla MJ, Roenigk RK, Brodland DG. A comparison of mohs micrographic surgery and wide excision for the treatment of atypical fibroxanthoma. Dermatol Surg 1997;23105-10.
11. Casparie M, Tiebosch ATMG, Burger G et al. PALGA, the nationwide histo- and cytopathology data network and archive. A role for digital pathology?. Cell Oncol 2008;30:369.
12. Lemm D, Mugge LO, Mentzel T, Hoffen K. Current treatment options in dermatofibrosarcoma protuberans. J Cancer Res Clin 2009;135:653-65.
13. Thomas CJ, Wood GC, Marks VJ. Mohs micrographic surgery in the treatment of rare aggressive cutaneous tumors: The Geisinger experience. Dermatol Surg 2007;33:333-39.
14. Bichakjian CK, Lowe L, Lao CD et al. Merkel cell carcinoma: Critical review with guidelines for multidisciplinary management. Cancer 2007;110:1-12.
15. Wollina U, Scho€nlebe J, Ziemer M et al. Atypical fibroxanthoma: a series of 56 tumors and an unexplained uneven distribution of cases in southeast Germany. Head Neck 2015;37:829-34.
16. Barnhill RL, Crowson AN, Margo CM, Piepkorn MW. DFSP: Histopathologic features. Dermatopathology, 3rd edn. 2010:786-87.