Yonsei Medical Journal
Vol. 31, No. 3, 1990

Clinical Study of Marjolin's Ulcer

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Marjolin's ulcer is the malignant lesion which develops in a burn scar or chronic fistula. Due to the low prevalence of this lesion, there has been disagreement regarding its clinical features, methods of treatment, and prognosis. We evaluated 19 cases of patients who had been admitted to Severance Hospital from Jan. 1970 to Dec. 1985. The results were as follows: The previous lesion was a burn scar in 52% of the cases and a fistula of chronic osteomyelitis in 32% The mean latent period was 31. 5 years. The initial symptoms were increased pain (74%), discharge with foul odor (68%) and bleeding (58%). Upon histological examination, all of the cases were squamous cell carcinoma. The rate of metastasis at the time of diagnosis was 32%. Of the 16 patients treated by surgery, local recurrence was noted in 4 cases. Three of these cases were patients who had been treated by excision and split thickness skin graft. The time interval for local recurrence ranged from 6 months to 11 months (average 8.8 months). In conclusion, the squamous cell carcinoma of marjolin's ulcer seems to have a worse prognosis than other squamous cell carcinomas and it requires aggressive treatment. The burn scar or chronic fistula that occurs in elderly patients especially requires more adequate treatment and close observation.

Key Words: Marjolin's ulcer

Marjolin's ulcer is a malignant tumor, occurring in scars of long duration or fistulae, and was first reported by J. N. Marjolin in patients who developed malignant ulcers from burn scars in 1828 (Benedict 1931). C. Hawkins reported seven cases of malignant scars which developed from scars resulting from trauma, osteomyelitis, and burns in 1835 (Benedict 1931). There have been further reports of Marjloin's ulcer, but there have been different opinions regarding its clinical characteristics, treatment and prognosis. In this report, the authors describe the results of clinical study of 19 patients with Marjolin's ulcer treated at Severance Hospital, Yonsei University College of Medicine from Jan. 1970 to Dec. 1985.

Received January 15, 1990
Accepted May 1, 1990
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METHODS AND MATERIALS

The study subjects were 19 cases of Marjolin's ulcer treated over a period of 16 years from Jan. 1970 to Dec. 1985. There were fifteen male and four female patients and the average age was 50.2 years (range, twenty-five to seventy-two). All patients were followed for 3.9 years ranging from 5 months to 7 years and 6 months (Table 1).

Table 1. Age and sex distribution

Age (yrs)	Sex		Total
	Male	Female	
20 - 29	0	1	1
30 - 39	2	0	2
40 - 49	6	0	6
50 - 59	5	1	6
60 - 69	2	1	3
70≤	0	1	1
Total	15	4	19

RESULTS

Site of occurrence

Of the 19 total cases, 13 cases (68%) developed lesions in the knee joint and leg areas. There were two cases each in the ankle and foot, and sacral area, and there was one case each in the thigh and forearm (Table 2).

Clinical manifestations

The primary presenting symptoms were acute pain in 74% of patients, foul-smelling pus discharge in 68%, and hemorrhagic lesion in 58%. There were also complaints of increasing pus discharge and increasing lesion size (Table 3).

Previous lesions

Burn scars were the most common causative lesions of Marjolin's ulcer, representing 10 cases (52%). Six cases (32%) were due to fistulae resulting from osteomyelitis. Trauma scar represented 2 cases, and one case resulted from a sore (Table 4).

Table 2. Location of lesion

Location	No.	Percent
Leg & Knee	13	68
Ankle & Foot	2	11
Back (sacral area)	2	11
Thigh & Hip	1	5
Forearm	1	5
Total	19	100

Table 3. Symptoms

Symptoms	No.	Percent
Increased pain	14	74
Foul odor	13	68
Hemorrhage	11	58
Increased drainage	8	42
Enlarged mass	4	21

Table 4. Previous lesions

Previous Lesion	No.	Percent
Burn	10	52
Osteomyelitis	6	32
Traumatic wound scar	2	11
Decubitus ulcer	1	5
Total	19	100

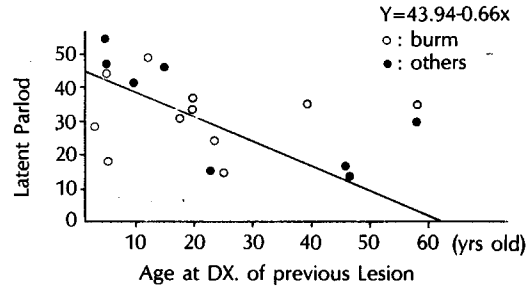

Fig. 1. Relationship of age at diagnosis of previous lesion to latent period.

Duration of previous lesions

The latent period from the time when the previous lesion began until the time of diagnosis of Marjolin's ulcer ranged from 15 to 55 years (average 31.5 years). If the age of the patient when the previous lesion was found is X and the latent period is Y, the relationship between X and Y is represented by the regression equation $Y=43.94-0.66X$, which shows that age is inversely related to the latent period (Fig. 1).

Metastasis rate at the time of diagnosis

In six cases, there was metastasis to the lymph nodes and other organs. Among the 7 patients with lymph node enlargement, the results of lymph node dissection showed that 4 cases were due to reactive hyperplasia, and that 3 cases were definitely due to metastasis. Among the cases of organ metastasis, 2 cases showed metastasis to the ischium.

Pathologic examination

All 19 cases showed squamous cell carcinoma. One case showed undifferentiated squamous cell carcinoma, while the other cases showed a fair degree of differentiation.

Treatment

In 3 cases in which surgery was impossible or the patient refused surgery, only radiotherapy was conducted. Sixteen of the patients underwent surgery, two of whom underwent a second surgery. Ten cases underwent amputation, 7 cases underwent wide excision and STSG, and one case underwent wide exci-

Table 5. Treatment

Operation	No. of cases
Amputation	10
Wide excision & STSG	7
Wide excision & free flap	1
Radiotherapy	3

Table 6. Recurrence rate

Operation (Cases)	No. of cases	Recurrence rate per operation (%)
Amputation (10)	1	10%
Wide excision & STSG (7)	3	43%

sion and free flap surgery (Table 5).

Follow-up observation

Among the 10 cases of amputation, one case resulted in local recurrence of the lesion at the amputated site. The period of local recurrence in this case was 14 months. The lesion was again amputated after 2 months and the patient underwent chemotherapy. Of the 7 patients who underwent wide excision and STSG, 3 patients had local recurrence. Of the 3 patients, one patient underwent amputation, one patient underwent wide excision and free flap (case 1) and one patient refused surgery and was subject to radiotherapy only. The period of local recurrence was 9.6 months in one case, 9 months in 2 cases, and 11 months in 1 case, representing an average of 8.8 months. The local recurrence of the lesion within 6 months showed that differentiation in pathology was poor (Table 6). Patients treated with radiotherapy expired due to distant metastasis within 2 years.

CASE REPORTS

Case 1. Park, H. M., M/33

This patient suffered from a burn injury of the left foot 28 years ago and thereafter underwent a skin graft. His chief complain was recurrent bleeding from the scar on the lateral aspect of the left ankle. Excision of the lesion and skin grafting were done. But recurrence of the lesion occurred after 9 months and wide excision including the fascia was performed with a scapular free flap. After that there was no recurrence 20 months after operation (Figs. 2~6).

Fig. 2. Case 1. *Photograph showing malignant ulcer at the site burn scar site of the left heel.*

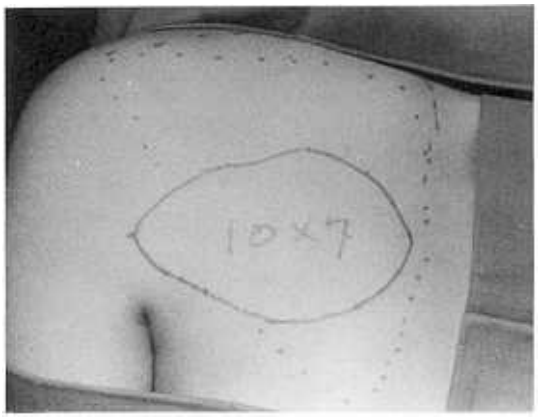

Fig. 3. Case 1. *The donor site for the left free vascularized scapular flap.*

Fig. 4. Case 1. *The free vascularized scapular flap transplantation was performed on the left heel wide excision.*

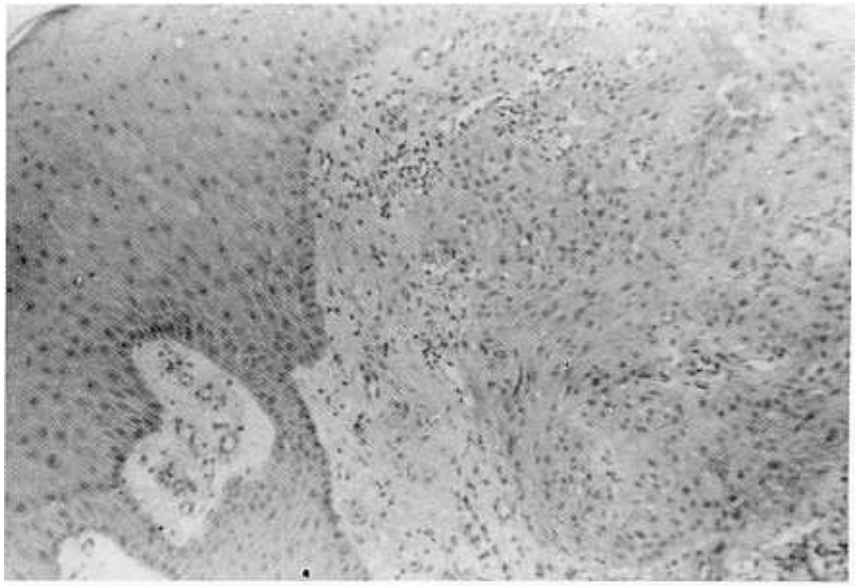

Fig. 5. Case 1. Microscopic section showing squamous cell carcinoma (×100).

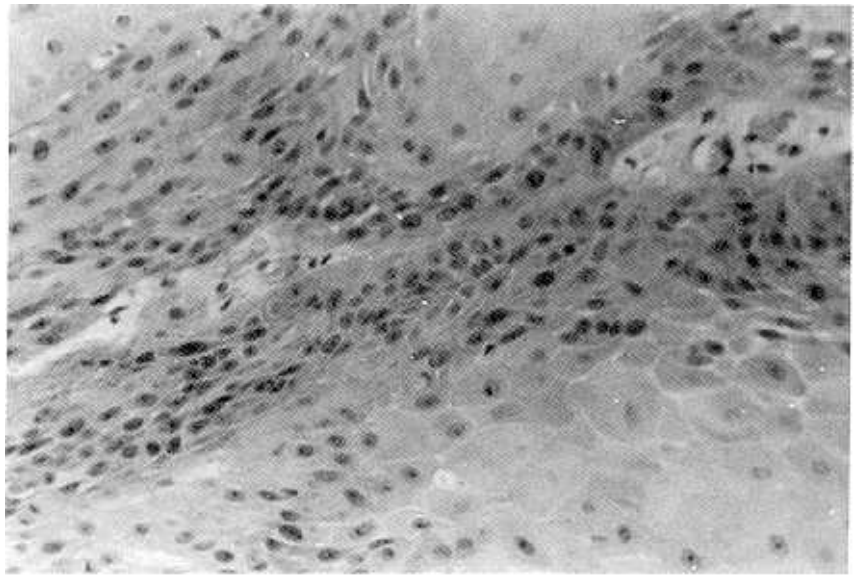

Fig. 6. Case 1. Tumor cells have a large amount of eosinophilic glassy cytoplasm with large pleomorphic nuclei and show frequent mitoses (×400).

Case 2. Kim M. J., M/60

The patient had been diagnosed and treated for osteomyelitis of the left tibia 45 years ago, and complained of foul-smelling pus discharge and pain for the past 8 months. At the time of admission, the physical examination showed that there was a defect and fistula of the anterior aspect of the left leg with foul-smelling pus discharge and hemorrhage. A whole body bone scan showed that there was a lesion of the left ischium

Fig. 7. Case 2. *X-ray showing chronic osteomyelitis of the middle third of the tibia with a marked bony defect.*

Fig. 8. Case 2. *Tc-99m scan showing hot uptake on the tibia and pelvic bone.*

Fig. 9. Case 3. *Photograph showing malignant ulcer at the site of a burn scar in the popliteal area.*

Fig. 10. Case 3. *X-ray showing a lobulated soft tissue mass shadow and the periosteal reaction on the proximal tibia.*

suggesting metastasis. The patient underwent an above knee amputation but expired 5 months after surgery (Figs. 7 and 8).

Case 3. Han, K. S., F/72

At the age of 37 years, the patient suffered from a burn of the left popliteal area, and recently com-

plained of recurrent bleeding and pain. At the time of admission, there was lymph node enlargement in the right inguinal area and a whole body bone scan showed metastatic squamous cell carcinoma, so the patient underwent radiotherapy and heat therapy (Figs. 9 and 10). After radiotherapy and heat therapy, she expired in 12 months.

DISCUSSION

Malignant tumors occurring from fistulae resulting from previous burn scars or ulcers, or from chronic osteomyelitis are defined as Marjolin's ulcer. When first reported by Marjolin (1828), the definition only meant warty ulcer resulting from a burn scar. Smith and Dubin (1963) discovered that this warty ulcer was a form of malignant ulcer, and Dacosta (1963) discovered that this warty ulcer was a form of malignant ulcer, and Dacosta (1963) defined ulcers arising from burn scars as Marjolin's ulcer. As in other malignant tumors, the pathogenesis of Marjloin's ulcer is not fully known, and due to the low incidence, there exist different opinions regarding the clinical manifestation and prognosis. Marjolin's ulcer usually develops from fistulae resulting from chronic osteomyelitis, chronic ulcers, and burn scars. According to Lee *et al.* (1976), 44% are due to trauma scars. Cruickshank *et al.* (1963) reported that 55% are due to varicose ulcers. According to Coburn (1970), the most common causes were chronic fistulae and burn scars. This study showed that chronic fistulae and burn scars were the most frequent causes (84%).

As the incidence of this disease is very low, Traves and Pack (1930) reported that among 2465 cases of squamous cell and basel cell carcinomas, 28 cases were due to carcinoma arising from burn scars. The precise incidence of Marjolin's ulcer resulting from osteomyelitis is not definite, but Hobart and Miller (1939) reported that 1.5% of all osteomyelitis patients developed Marjolin's ulcer. Treves and Pack (1930) reported that 2% of burn scar patients developed Marjolin's ulcer, and Arons (1966) reported that experimentation with animals showed that 0.77% of burn scars became malignant. With regard to the pathogenesis, Menkin (1960) reported that this was due to the combination of the growth promoting factor included in the inflammation transudate and carcinogenic hydrocarbons to act as co-carcinogens. On the other hand, Treves and Pack (1930) suggested that the mechanism which caused burn scars to become malignant was due to the continuing external aggravation of tissue along with the decreased blood supply and decreased regenerative capacity of the burn scar tissue. Recently there have also been theories which suggest an immunologic pathogenesis. Overall, the pathogenesis of Marjolin's ulcer is as yet uncertain, but generally a concept is accepted that the osteomyelitis or burn is not in itself carcinogenic, but these facors cause the tissue to become increasingly susceptible to other carcinogens, thus acting as co-carinogens.

With regard to the time of the development of the tumor, Gilbin *et al.* (1976). suggested that the latent period of the scar rather than the age of the patient is mored important and that the average latent period is 34 years. Various reports on the latent period are: Kim and Koh (1977) 3.3 years; Moon *et al.* (1986) 28 years; and Seldin and Flemming (1963) 30.5 years (average of 90 cases). This study also showed an average latent period of 31.5 years. However, Treves and Pack (1930) reported that the latent period in 6 acute cases averaged 0.3 years, but as yet, there have been no cases reported in korea where the latent period was less than one year. According to Lawrence (1953), the latent period of ulcers originating from burn scars was inversely proportional to the age at which the burn scar occurred. The results of this study showed that this was also true not only for burn scars but also for osteomyelitis originating ulcers, and although there was no statistical significance because of the small number of cases, this could be clearly seen in cases other than patients with burn scars. Therefore, caution should be stressed for the old age patients with burns, osteomyelitis, or trauma scars.

The majority of Marjolin's ulcers are squamous cell carcinoma as reported by Lawrence (90%) (1935). McCally and Dockerly (1946) and Bower and Young (1960) reported that all Marjolin's ulcers are squamous cell carcinoma. In this study also, all cases were squamous cell carcinomas with low malignant character which do not easily invade other organs, and the progression was relatively good. This is reflected in a report by Epstein (1968) where the rate of metastasis at the time of diagnosis was less than 2%. However, once the tumor had metastasized to another organ, the 5-year survival rate was reported as 25.1%. According to Bowers and Young (1960), squamous cell carcinoma of Marjolin's ulcer showed no metastasis at the time of diagnosis and the prognosis was excellent. On the other hand, McCally and Dockerty (1949) reported a 22% metastasis rate, and ours was a relatively high 31.5%. This high rate is seen to be due to the late recognition of the lesion because of delayed visits to the hospital by the patients. Therefore, it is thought that the squamous cell carcinomas of Marjolin's ulcers have a relatively high rate of metasteasis compared to other squamous cell car-

cinomas.

For the treatment of Marjolin's ulcer, Coburn (1970) reported a number of methods including 1)wide excision, 2) amputation, and 3) radiotherapy, but he also reported that the effect of radiotherapy was questionable because of the poor vascular supply surrounding the ulcer tissue. Results reported by Benedict (1963) or Bowers and Young (1960) showed that wide excision followed by skin grafting gave good results, but McCally and Dockerty (1949) reported that amputation was eventually required after excision or curettage. In addition, Seldin and Flemming (1963) regarded amputation, in principle, to be the best treatment.

In this study, excision and skin graft were conducted in seven cases, after which local recurrence occurred in 3 cases. There was no statistical significance but it is thought that the recurrence rate was higher compared to the amputation cases. Therefore, the standard treatment of Marjolin's ulcers is thought to be amputation. If excision is done, however, it is thought that the excision boundary should include 3-4cm of surrounding normal skin tissue including the muscle fascia, as suggested by Coburn (1970). Different opinions also exist regarding the excision of enlarged lymph nodes. McCally and Dockerty (1949) proposed that lymph node excision should also be done, but Fitzgerald (1976) suspested that lymph node excision should be done only if there is no decrease in the size of the lymph node 3 months after excision of the ulcer lesion. In this study, all seven cases where lymph node enlargement was present underwent excision, and metastasis was confirmed in 3 cases. Therefore, it is believed by the authors that better results would be obtained if excision of enlarged lymph nodes is conducted along with excision of the lesion. During the follow-up observation period, this study showed that all 4 cases of local recurrence of ulcers occurred from 6 months to 1 year after treatment. According to Seldin and Flemming (1963), most cases of local recurrence occur within 18 months after initial diagnosis, and good prognosis can be foreseen if there is no local recurrence after 3 years of follow-up observation. Consequently, it can be seen that careful follow-up observation. Consequently, it can be seen that careful follow-up observation and study after treatment contribute significantly to the determination of the prognosis of the patient.

There are several authors who suggest that the prognosis of Marjolin's ulcer is relatively good (Benedict 1931; Bower and Young 1960; Hobert and Miller 1939), and there are others who see the prognosis as poor (Gillis and Lee 1951; Seldin and Flemming 1963). Gillis and Lee (1951) reported 13 cases of 24 where the patients expired of the cancer, and Seldin and Flemming (1963) reported that 19 of 22 cases of lymph node metastasis expired, and therefore, as mentioned above, the high rate of metastasis of squamous cell carcinoma of Marjolin's ulcer can be seen to present a relatively poor prognosis. Pathologically, basal cell carcinomas are reported to present relatively better prognosis compared to squamous cell carcinoma (Treves and Pack 1930). There have been no reports regarding the prognosis based on the degree of differentiation of squamous cell carcinoma, but in this study, even though there was no lymph node involvement at the time of diagnosis with regard to differentiated squamous cell carcinoma, and despite vigorous radiotherapy and hip disarticulation, the expiration of the subject 20 months after diagnosis gave the authors the impression that the prognosis of undifferentiated squamous cell carcinoma is poor.

SUMMARY AND CONCLUSION

Marjolin's ulcer is the malignant lesion which develops in a burn scar or chronic fistula. Due to the low prevalence of this lesion, there has been disagreement regarding its clinical features, methods of treatment, and prognosis.

We evaluated 19 patients who had been admitted to Severance Hospital from Jan. 1970 to Dec. 1985. The results were as follows:

1. The previous lesion was a burn scar in 52% of the cases, and a fistula of chronic osteomyelitis in 32%.
2. The mean latent period was 31.5 years.
3. The initial symptoms were increased pain (74%), discharge with foul odor (68%) and bleeding (58%).
4. Upon histological examination, all of the cases were squamous cell carcinoma.
5. The rate of metastasis at the time of diagnosis was 32%.
6. Of the 16 patients treated by surgery, local recurrence was noted in 4 cases. Three of these cases were patients who had been treated by excision and split thickness skin graft.
7. The time interval for local recurrence ranged from 6 months to 11 months (average 8.8 months).

In conclusion, the squamous cell carcinoma of Marjolin's ulcer seems to have a worse prognosis than other squamous cell carcinomas and it requires aggressive treatment. The burn scar or chronic fistula that occurs in elderly patients especially requires more adequate treatment and close observation.

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