

# 陰囊線狀基底細胞癌

—病例報告—

甯中柱<sup>1&2</sup> 趙曉秋<sup>1</sup>

國立成功大學附設醫院皮膚部<sup>1</sup> 沙鹿童綜合醫院皮膚科<sup>2</sup>

## Linear Basal Cell Carcinoma of the Scrotum

—A Case Report—

Chung-Chu Ning<sup>1&2</sup> Sheau-Chiou Chao<sup>1</sup>

Although basal cell carcinoma (BCC) is the most common human malignancy, only 34 cases involving the scrotum have been previously reported. The linear type BCC is also an uncommon morphologic variant and was never reported over the scrotum. We describe a very rare case of linear BCC of the scrotum.

A 70-year-old man noted an asymptomatic linear pigmented lesion over the scrotum for 4-5 years. As a resident of the blackfoot endemic area (Township Peimen), he reported to have been drinking high-arsenic artesian well water for more than forty years and no history of sexually transmitted disease, previous trauma or radiotherapy to the scrotum. A skin biopsy revealed that was a mixed type BCC. The lesion was excised completely with a free margin of 0.6 cm of normal skin. There was no evidence of recurrence after a 4 months follow up.

We did not detect any somatic mutation in *PTCH* gene. (Dermatol Sinica 20 : 57-62, 2002)

*Key words:* Linear, Basal cell carcinoma, Scrotum, Arsenic, *PTCH* gene

雖然基底細胞癌是人類最常見的癌症，但發生在陰囊上的只有34個病例曾被報導過。線狀基底細胞癌同樣是少見且未曾被報導發生於陰囊。在此，報告一罕見之陰囊線狀基底細胞癌個案。

70歲男性在其陰囊上發現一逐漸擴大無症狀線狀斑塊已歷五年。此病人居住在北門鄉曾飲深井水達四十餘年。病灶未曾受傷過且無性病史或做放射線治療。病理切片結果為混合型基底細胞癌。此病灶被切除並留有0.6公分之安全邊緣。追蹤四個月並無復發的跡象。

在*PTCH*基因上未偵測到任何的體突變(somatic mutation)。(中華皮誌20 : 57-62, 2002)

From the Department of Dermatology, National Cheng-Kung University Hospital<sup>1</sup>, and Shalu Tungs' memorial Hospital<sup>2</sup>

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Reprints requests: Sheau-Chiou Chao, M.D., Department of Dermatology, National Cheng-Kung University Hospital, 138 Sheng-Li Road, Tainan, Taiwan, R.O.C. TEL: 886-6-2766180 FAX: 886-6-2766180 E-mail: joly@mail.ncku.edu.tw

## INTRODUCTION

Basal cell carcinoma (BCC) is the most common human malignancy. Although many different factors have been implicated in the pathogenesis of BCCs, UV light exposure is the most common predisposing factor. Therefore, it is not surprising that 85% of all BCCs occur on the head and neck.<sup>1</sup> BCC can also occur in sun-protected areas including the rare occurrence on the scrotum. There have been only 34 previously reported cases of scrotal BCC.<sup>2-4</sup> Linear type of BCC is also an uncommonly morphologic variant and was first described by Lewis in 1985.<sup>5</sup> Subsequently, twenty-nine cases of linear BCC were reported and none of them were located over the scrotum.<sup>6</sup>

We describe a rare case of linear BCC of the scrotum. We also perform the somatic mutation screening over *PTCH* gene.

## CASE REPORT

A 70-year-old man noted an asymptomatic linear lesion over the scrotum for 4-5 years. He reported no history of sexually transmitted disease, previous trauma or radiotherapy to the scrotal area. As a resident of the blackfoot endemic area (Township Peimen), he reported to have been drinking high-arsenic artesian well water for more than forty years.

Physical examination revealed a 1.0x5.5cm<sup>2</sup> slightly ulcerated hyperpigmented plaque with a well-defined raised pearly border on the left side of the scrotum (Fig. 1A). No enlarged inguinal lymph nodes or other skin tumor were noted. Mild "raindrop" sign over the back and one single 0.1-0.2cm punctate keratosis over soles were noted in our patient. The clinical impression was BCC.

A biopsy specimen demonstrated many aggregates of hyperchromatic basaloid cells with peripheral palisading within a fibrotic and desmoplastic stroma in the dermis. (Fig. 2A) At the deeper part of the lesion, the basaloid cells are arranged in cords and strands with irregular, spiky outlines. (Fig. 2B) Melanin pigment is also present within nests and stroma. In other sections, many small rounded nests of basaloid cells were

also noted. Mixed type (micronodular and infiltrative) BCC was diagnosed. Removal was accomplished by fusiform excision under local anesthesia, with a lateral margin of 0.6cm, followed by primary closure. There was no evidence of recurrence after a 4 months follow up (Fig. 1B).

## PCR amplification and heteroduplex analyses

DNA was extracted from the tumor mass and the attached free marginal normal skin. DNA samples were then subjected to mutation screening by amplification of segments of *PTCH*, spanning all 23 exons of the gene using primers synthesized on the basis of intronic sequences.<sup>7,8</sup>

For PCR amplification, approximately 200 ng of genomic DNA, 12.8pmol of each primer, 10  $\mu$ mole dNTP and 1.25 U of AmpliTaq Gold (Perkin Elmer, Roche Molecular Systems, Inc., Branchburg, New Jersey, USA) were used in a total volume of 50  $\mu$ l. The amplification conditions were 94°C for 12 minutes, followed by 35 cycles of 94°C for 45 seconds, annealing temperature for 45 seconds and 72°C for 45 seconds, and extension at 72 for 10 minutes. The PCR products were visualized under UV light after electrophoresis on 2% agarose gel containing Ethidium bromide. Direct automated sequencing (377 ABI Advanced Biotechnologies, Columbia, Md.) of the PCR products from the extracted DNA of tumor mass. We can't detect any somatic mutation in *PTCH* gene and only find three reported polymorphism: 1503-8 T+C, 2560+9 G+C, 3583 A+T and one new polymorphism: 3141 T+G (1047 Leu→Leu).

## DISCUSSION

Basal cell carcinoma (BCC) is the most common human malignancy. UV light exposure is the most common predisposing factor. The other predisposing factors for developing BCC are known to include radiation therapy,<sup>9</sup> arsenical compounds,<sup>10</sup> scar from vaccination,<sup>11</sup> burns<sup>12</sup> and chronic dermatitis. It has also been found that the prevalence rate of skin cancer, including BCC, in the blackfoot endemic area was as high



**Fig. 1**  
Clinical appearance of the linear basal cell carcinoma located on the scrotum A. Before operation. B After operation for 3 months

as 1.06 per 1,000.<sup>13</sup> Symptoms of chronic arsenic intoxication include general pigmentation and focal "raindrop" pigmentation of the skin and the appearance of punctate keratosis of the palms and sores.<sup>14</sup>

In our patient, living in blackfoot endemic area and drinking high-arsenic artesian well water for more than forty years may be the predisposing factor.

The cases of scrotal BCC are rare. To our knowledge, only 34 cases of scrotal BCC have been reported (Table I).<sup>2-4</sup> The average age of patients with scrotal BCC is 67 years (range, 42-82 years) and the most common clinical presen-

tation is nodule or ulcer form.

Although metastatic BCC is rare (reported incidence, 0.0028-0.55%),<sup>15</sup> metastases occurring in 8.8% (three of 34) cases of scrotal BCC has been reported. This high incidence of metastasis of BCC on scrotum suggests its invasiveness and higher metastasis rate compared with BCC located on other areas. Giving the scant number of cases reported, the biological behavior of scrotal BCC can not be determined definitively.

Linear basal cell carcinoma is also an uncommonly recognized morphologic variant. Paper review by Katherine in 1999 revealed only 29 reported instances. The distributions were

recognized on the head (13 cases), neck (12), trunk (3), and inguinal area (1).<sup>6</sup> Trauma through physical injury or operation has been proposed to play a role in the development of linear basal cell carcinoma.<sup>16</sup> Most of the linear tumors were aligned along relaxed skin tension lines.<sup>6</sup> In the reticular dermis of the normal adult human, skin tension lines have an anatomical counterpart consisting of a preferential parallel orientation and a straightening of thin collagen bundles and elastic fibers.<sup>17</sup> BCC depends on stromal interactions for progression and growth. The relationship between linear BCC and relaxed skin tension lines need further evaluation. Our case also shows alignment along relaxed skin tension lines.

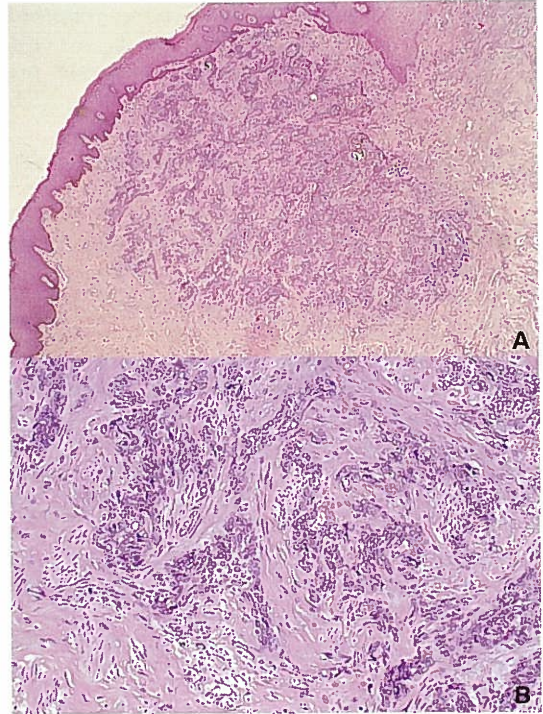
The percentage of aggressive histological subtypes (38%) of linear BCC was higher compared with that in a general population (6%).<sup>6</sup> Wider surgical excision alone is usually considered curative for basal cell carcinoma of the scrotum. The lesion was excised with a 0.6cm free margin.

Germline mutations in the human *homolog of the Drosophila* patched gene, *PTCH*, were demonstrated in individuals with nevoid basal cell carcinoma syndrome.<sup>7,18</sup> Subsequently, somatic mutations in the *PTCH* gene were identified in 20-30% of the sporadic BCC studied.<sup>7,18-20</sup> In this case, we did not find any somatic mutation after sequencing all the exons of *PTCH* gene.

To our knowledge, this is the first case of linear BCC of the scrotum being reported. The linear distribution, location (scrotum) and histopathological pattern (micronodular and infiltrative subtype) indicated poorer prognosis for our patient. Close long-term follow up is indicated in this case.

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**Fig. 2**

Basal cell carcinoma. A. Many aggregates of hyperchromatic basaloid cells within a fibrotic stroma in the dermis. B. At the deeper part of the lesion, the basoloid cells are arranged in cords and strands with irregular, spiky outlines. (Hematoxylin-eosin stain, magnification A. x46 B. x460)

Table I. Scrotal basal cell carcinomas reported in the literature

Author and year	Age (years)	Clinical presentation	Metastasis	Treatment
Richter, 1957	68	Superficial erosion	Pleura	XRT
Godan, 1962				
Case 1	42	NA	NO	XRT
Case 2	75	NA	NO	Excision
Case 5	71	NA	NO	Excision, XRT
Case 4	59	NA	NO	XRT
Case 5	68	NA	NO	XRT
Casal <i>et al.</i> , 1965	77	Nodule	NO	Excision, XRT
Kickham and Dufresne, 1967				
Case 1	NA	NA	NO	NA
Case 2	NA	NA	NO	NA
Hughes, 1973	47	Ulcer	Trunk and scalp	Excision, XRT
ChT				
McEleney, 1976	60	Plaque	NO	Excision
Ray and Whitmore, 1977	NA	NA	NO	Excision
Rahbari and Mehregan, 1979	NA	NA	NO	NA
Grossman and Sogani, 1981	55	Nodular ulcer	NO	Excision
Greider and Vernon, 1982	75	Flat erythematous	NO	Excision
McDonald, 1982				
Case 1	NA	NA	NO	Excision
Case 2	NA	NA	NO	Excision
Case 3	NA	NA	NO	Excision
Esteban and Cruces Prado, 1983	58	Pigmented papule	NO	Excision
Cieplinski, 1984 <sup>14</sup> and Staley, 1983 <sup>15</sup>	58	Indurated ulcers	Pleura	Excision, IT ChT
Gerber, 1985	NA	NA	NO	NA
Parys, 1991 <sup>17</sup> ,				
Case 1	70	Indurated ulcer	NO	Excision
Case 2	72	Nodular ulcer	NO	Excision.
Nahass <i>et al.</i> , 1992				
Case 1	61	Ulcerated plaque	NO	Mohs surgery
Case 2	82	Pigmented papule	NO	Excision
Case 3	80	Ulcer	NO	Excision
Ho <i>et al.</i> , 1995	64	Nodular ulcer	NO	Excision
Schleicher <i>et al.</i> , 1997	66	Nodule	NO	Excision
Esquivias <i>et al.</i> , 1999 <sup>2</sup>	80	Nodule	NO	Excision
Vandeweyer <i>et al.</i> , 1999 <sup>3</sup>	70	Ulcer	NO	Excision
Vandeweyer <i>et al.</i> , 2000 <sup>4</sup>				
Case 1	66	Ulcer	NO	Excision
Case 2	71	Ulcer	NO	Excision
Case 3	58	Nodular	NO	Excision
Case 4	74	Ulcer	NO	Excision
Present case	70	Linear	NO	Excision

NA: information not available; XRT: radiotherapy; ChT: chemotherapy; IT: immunotherapy

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