Ann Dermatol Vol. 26, No. 5, 2014 http://dx.doi.org/10.5021/ad.2014.26.5.624

CASE REPORT

Alopecia Neoplastica due to Gastric Adenocarcinoma Metastasis to the Scalp, Presenting as Alopecia: A Case Report and Literature Review

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Alopecia neoplastica is defined as hair loss secondary to a visceral malignancy that has metastasized to the scalp. The scalp is a relatively common site of cutaneous metastasis, usually presenting as a single or multiple firm scalp nodules. Alopecia neoplastica is a well-recognized but rare presentation, and its pathogenesis is incompletely understood. Atrophy of the hair follicles due to tumor invasion of the scalp plays a role in the development of alopecia. Herein, we describe a 33-year-old woman with gastric adenocarcinoma who developed alopecia neoplastica while receiving cancer chemotherapy. Scalp biopsy revealed metastatic adenocarcinoma cells interspersed between collagen bundles and around hair follicles. Immunohistochemical analysis indicated that the tumor cells originated from the primary gastric adenocarcinoma. Therefore, she was diagnosed with alopecia neoplastica due to gastric adenocarcinoma. The findings from this report may be helpful for understanding the mechanism of alopecia neoplastica. **(Ann Dermatol 26(5) 624～627, 2014)**

-Keywords-
Alopecia neoplastica, Gastric adenocarcinoma, Scalp metastasis

INTRODUCTION

The scalp is a relatively common site of cutaneous metastasis, usually presenting as a single or multiple firm scalp nodules[1,2]. Alopecia neoplastica is a well-recognized but rare presentation that, manifests as a single or multiple areas of cicatricial alopecia. Herein we report a rare case of alopecia neoplastica due to metastatic gastric adenocarcinoma and review the relavant literature.

CASE REPORT

A 33-year-old woman was referred for a subcutaneous nodule on the surface of an erythematous-, hairless patch on the frontal scalp observed 3 months previously, to rule out metastasis from her known gastric adenocarcinoma diagnosed in January 2008. She had undergone total gastrectomy for the gastric carcinoma diagnosed in May 2007; she subsequently underwent 6 cycles of chemotherapy and total abdominal

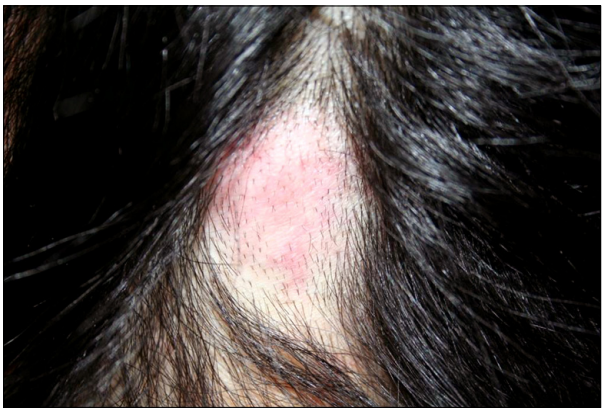

Fig. 1. Subcutaneous nodule covered with erythematous, hairless patch on the frontal scalp.

Received July 16, 2012, Revised October 25, 2012, Accepted for publication October 26, 2012

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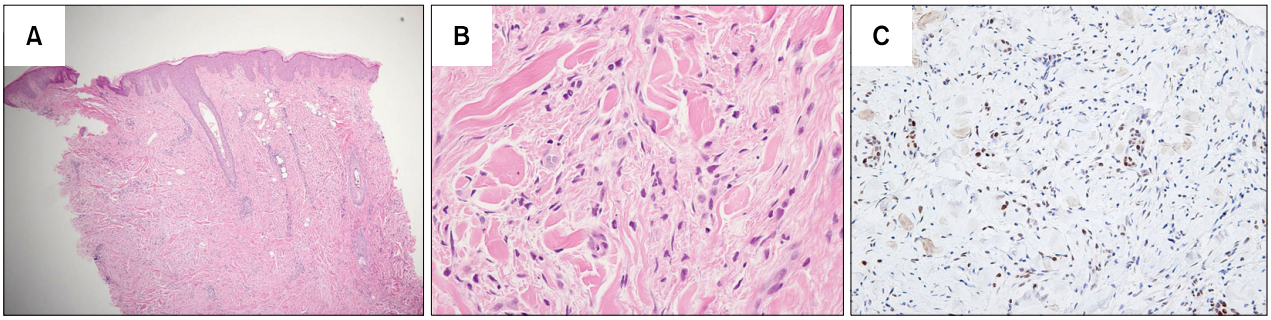

Fig. 2. (A) Histologic examination revealed decreased pilosebaceous units and scattered, infiltrated tumor cells around hair follicles, upper and mid-dermis (H&E, ×40). (B) Metastatic adenocarcinoma cells were interspersed between collagen bundles and around hair follicles (H&E, ×200). (C) Tumor cells were positively stained against tumor marker MSH-2 (MSH-2, ×200).

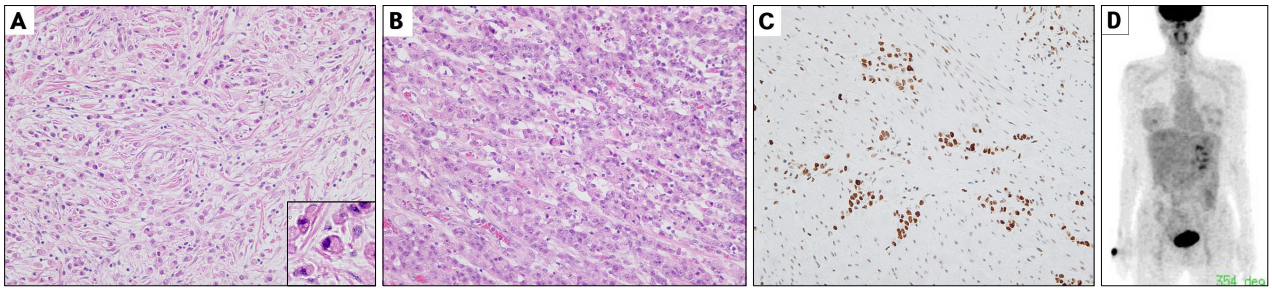

Fig. 3. (A) Total gastrectomy specimen shows many signet ring cells (H&E, ×200). Signet ring cells are magnified in inset (H&E, ×400). (B) There are poorly differentiated tumor cells either (H&E, ×200). (C) Part of poorly differentiated tumor cells were positively stained against tumor marker MSH-2 (MSH-2, ×200). (D) Whole body fusion positron emission tomography scan performed after diagnosed with stomach cancer shows abnormal FDG uptake on stomach and rectosigmoid. Following colonoscopy and colon biopsy revealed no other malignancy.

hysterectomy with bilateral salphingo-oophorectomy after being diagnosed with metastatic adenocarcinoma (Krukenberg cancer) in November 2007.

Examination revealed no abnormalities besides a scalp lesion exhibiting a hard, movable, non-tender subcutaneous nodule covered with a slightly erythematous alopecic patch (Fig. 1). The patient did not report any previous dermatological diseases at the site of alopecia. Routine laboratory test results including full blood count, liver function, renal function, electrolytes, chest radiography and electrocardiogram were all normal. Histopathological examination of the scalp lesion showed decreased hair follicle cells, as well as metastatic adenocarcinoma cells interspersed between collagen bundles and around hair follicles (Fig. 2A, B). Similar to the original gastric cancer, tumor cells stained positively for tumor marker MSH-2, the DNA mismatch repair protein (Fig. 2C). The total gastrectomy specimen showed signet ring cells (Fig. 3A) and poorly differentiated adenocarcinoma cells (Fig. 3B) which stained positive for MSH-2 (Fig. 3C). MSH-2 is a marker of a major mismatch repair gene, MSH-2. Polymorphisms in the MSH-2 gene were recently suggested to modulate an individual's susceptibility to gastric cancer[3]. Although there were no signet ring cells, the scalp specimen showed scattered, poorly differentiated, MSH-2−positive carcinoma cells. Whole body positron emission tomography (PET) scanning showed no other abnormal uptake than in the stomach (Fig. 3D). Following colonoscopy with biopsy also revealed no malignancy. PET scanning performed after total abdominal hysterectomy with bilateral salphingo-oophorectomy in November 2007 revealed no remaining malignancy. Therefore, we concluded the scalp metastasis originated from the gastric cancer. Cutaneous metastasis usually exhibits features consistent with the underlying malignancy. However, the metastasis may exhibit less differentiation and be more anaplastic. Therefore, we can infer that atrophy of the hair follicles and gastric cancer invaded the collagenous stroma, influencing the development of alopecia. On the basis of both clinical and histopathological findings, the patient was diagnosed with alopecia neoplastica due to gastric adenocarcinoma. Despite performing the cancer chemotherapy, no hair regrowth was observed.

DISCUSSION

The overall incidence of cutaneous metastasis from visceral

carcinomas ranges from 0.7%～9%[4]. The scalp is a relatively common site of cutaneous metastasis. Brownstein and Helwig[1] report that the scalp is the site of 4% of all skin metastases, usually presenting as single or multiple nodules[5-8]. The most frequent manifestation of scalp metastasis is the occurrence of single or multiple non-tender nodules that usually appear suddenly and grow rapidly[9,10]. Alopecia neoplastica is a well-recognized but rarer manifestation that presents as a single or multiple areas of cicatricial alopecia. To our knowledge, 29 patients with alopecia neoplastica including the one described herein have been reported in the literature (Table 1)[1,8,11-16]. A review of these cases revealed that alopecia neoplastica is usually a presentation of breast cancer metastasis, and other primary sites are extremely rare. Yuen et al.[15] reported a case in which the primary tumor was a placental trophoblastic tumor. Furthermore, metastases from colon and cervical cancer have also been reported. Kohno et al.[14] and Kim et al.[8], each of them reported 2 cases of alopecia neoplastica due to metastasis from gastric carcinoma. Meanwhile, only 3 cases of alopecia neoplastica due to gastric carcinoma, including this case, have been reported, among them 2 cases were alopecia neoplastica due to signet ring cell-type gastric carcinoma. Because of the small number of cases, it remains unclear if the metastatic potential of signet ring cell-type gastric carcinoma is greater to the skin or scalp. However, a recent study about the characteristics of gastric adenocarcinoma shows that signet ring-cell gastric cancers

Table 1. Review of the previously reported cases of alopecia neoplastica

	Age of Ca diagnosis (yr)	Age of AN diagnosis (yr)	Primary cancer (histology of primary tumor)	The pattern of alopecia			Ref.
				n	Site	CP	
1	69	69	Breast Ca (Adenocarcinoma)	NA	NA	Pa-Pl	Conner and Cohen[11] (2009)
2	46	48	Breast Ca (Adenocarcinoma)	NA	NA	NA	Conner and Cohen[11] (2009)
3	41	41	Breast Ca (Adenocarcinoma)	NA	NA	Pl	Conner and Cohen[11] (2009)
4	41	42	Breast Ca (Ductal adenocarcinoma)	6	NA	Pl/E	Cohen et al.[16] (1961)
5	62	65	Breast Ca (Ductal adenocarcinoma)	1	O	Pl/E	Conner and Cohen[11] (2009)
6	43	46	Breast Ca (Ductal adenocarcinoma)	NA	NA	Pl/E	Brownstein and Helwig[1] (1972)
7	69	89	Breast Ca (Ductal adenocarcinoma)	1	NA	Pl/E	Haas and Hauptmann[12] (2004)
8	50	55	Breast Ca (Ductal adenocarcinoma)	2	NA	Pl/E	Conner and Cohen[11] (2009)
9	43	53	Breast Ca (Ductal carcinoma)	1	FP	Pa	Conner and Cohen[11] (2009)
10	42	42	Breast Ca (Lobular carcinoma)	1	F	Pa	Conner and Cohen[11] (2009)
11	51	53	Breast Ca (Lobular carcinoma)	7	NA	D	Conner and Cohen[11] (2009)
12	75	78	Breast Ca (Scirrhous type)	NA	NA	NA	Cohen et al.[16] (1961)
13	50	56	Breast Ca (Scirrhous type)	1	FP	Pl	Conner and Cohen[11] (2009)
14	52	54	Breast Ca (NA)	1	V	Pl/E	Archer and Smith[19] (1990)
15	52	63	Breast Ca (NA)	1	V	Pa	Conner and Cohen[11] (2009)
16	58	60	Breast Ca (NA)	NA	NA	Pl	Conner and Cohen[11] (2009)
17	66	68	Breast Ca (NA)	NA	O,	Pl/E	Conner and Cohen[11] (2009)
18	45	45	Breast Ca (NA)	NA	NA	Pl	Conner and Cohen[11] (2009)
19	46	47	Breast Ca (NA)	3～4	NA	NA	Conner and Cohen[11] (2009)
20	41	43	Breast Ca (NA)	NA	NA	Pa	Brownstein and Helwig[1] (1972)
21	39	40	Breast Ca (NA)	1	F	Pl	Conner and Cohen[11] (2009)
22	69	89	Breast Ca (NA)	NA	O	Pa/E	Haas and Hauptmann[12] (2004)
23	46	54	Breast Ca (NA)	1	V	Pl/E	Choi et al.[13] (2005)
24	31	31	Trophoblastic tumor	NA	F/V/O	Pl/E	Yuen et al.[15] (1998)
25	45	53	Cervix Ca (squamous cell carcinoma)	2	NA	Pl/E	Conner and Cohen[11] (2009)
26	46	46	Colon Ca (Adenocarcinoma)	2	FP	Pa	Conner and Cohen[11] (2009)
27	36	36	Gastric Ca (Signet ring cell type)	2	NA	Pa-Pl/E	Kim et al.[8] (1999)
28	37	38	Gastric Ca (Adenocarcinoma)	1	F	E	Kohno et al.[14] (1983)
Present case	32	33	Gastric Ca (Signet ring cell type)	1	F	No/E	

Ca: cancer, AN: alopecia neoplastica, CP: clinical presentation, NA: information not available, Pa-Pl: both patch and plaque, Pl: plaque, E: erythema, O: occipital, FP: frontoparietal, Pa: patch, F: frontal, D: diffuse, V: vertex, No: nodule.

are more differentiated and less aggressive than non-signet ring-cell gastric adenocarcinoma[17]. Nevertheless, the mechanism of alopecia neoplastica is uncertain. Histopathological examination of the scalp in alopecia neoplastica demonstrates metastatic carcinoma cells in a dense collagenous stroma, which is observed in the dermis and subcutaneous tissue with a loss of pilosebaceous units[18]. However, most malignant tumors evoke a stromal response, which is usually in the form of fibroplasia. Moreover, it is unclear if fibrosis or the release of cytokines from tumor cells leads to the disappearance of hair follicles. It is difficult to explain the complete disappearance of pilosebaceous units, but a loss of hair follicles may be the result of fibrosis; Cohen et al.[16] consider this to be the major mechanism. In particular, lobular breast carcinoma, which accounts for 10% of invasive breast carcinomas, usually elicits reactive fibrosis, which leads to cicatricial alopecia. Factors independent of fibrosis, such as tumor invasion of the hair sheaths, may play a role in the development of alopecia, because hair may be regrown in alopecic areas after effective cancer treatment[19,20]. In the present case, metastatic adenocarcinoma cells were interspersed between collagen bundles and around hair follicles. Immunohistochemical staining was positive, which explains tumor cell infiltration around hair follicles. These findings corroborate the hypothesis that dermal infiltration of cancer cells causes the disappearance of hair follicles. Furthermore, infiltration of metastatic cancer cells into the dermis and subcutaneous tissue may put pressure on and destroy hair follicles, eventually causing alopecia.

In summary, we report a case of alopecia neoplastica due to gastric adenocarcinoma, which is a well-recognized but extremely rare manifestation of cancer metastasis to the skin. This report may be helpful for understanding the mechanism of alopecia neoplastica. Regardless, further study is needed to elucidate the specific pathologic mechanism of this disease.

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