Metastatic Adenocarcinoma Histologically Mimicking Fibrohistiocytic Tumors

Jong Min Kim, M.D., Hyong Jin Kim, M.D., Kwang Ho Kim, M.D.,
Hye Rim Park, M.D.*, Eil Soo Lee, M.D.**

Departments of Dermatology and Pathology, College of Medicine, Hallym University,*
*Departments of Dermatology**, Samsung Medical Center*
Seoul, Korea

Cutaneous metastasis from visceral malignancies shows diverse manifestations. Very rarely, cutaneous metastasis mimicks benign mesenchymal tumors. We describe a case in which metastasis from gastric adenocarcinoma mimicked fibrohistiocytic tumors. The diagnosis of cutaneous metastasis was confirmed by the presence of atypical cells and signet-ring cells, positive staining for mucin and positive immunohistochemical stainings for keratins, carcinoembryonic antigen(CEA), and lysozyme within the tumor cells infiltrated in the irregular, intertwining bundles of collagen in the reticular dermis. (Ann Dermatol 8:(1)73~78, 1996).

Key Words : Metastatic adenocarcinoma, Fibrohistiocytic tumor

Cutaneous metastasis from visceral malignancies is unusual and the reported incidence varies from 1.4% to 4.4%[1-4]. Cutaneous metastasis shows diverse manifestations[5-8]. Most commonly, it appears as a solitary or more often multiple, firm, flesh-colored, red or blue nodules. Other manifestations include inflammatory lesions, vascular tumor pattern, cicatricial skin lesions, zosteriform pattern, scarring alopecia, epidermoid cyst-like or condyloma acuminatum-like lesions. In 1991, Hartschuh and Bersch[9] reported a case in which cutaneous metastasis from gastric carcinoma resembled benign mesenchymal tumors.

We describe a 52-year-old male with metastatic gastric adenocarcinoma mimicking fibrohistiocytic tumors histologically.

REPORT OF A CASE

A 52-year-old Korean male visited to the department of dermatology of Hangang Sacred Heart Hospital on May 24, 1993. He presented multiple cutaneous nodules on the scalp, forehead, and back. Biopsy specimens from the cutaneous nodules suggested metastatic tumors and fibrohistiocytic tumors. For a thorough evaluation of whether there was a visceral malignancy or not, this patient was admitted to Kangdong Sacred Heart Hospital on June 19, 1993. Significant in his medical history was a partial gastrectomy for stomach perforation 25 years ago and a cholecystectomy with choledojejunostomy for gallbladder empyema and common bile duct stone in October 1989.

Physical examination revealed a chronically ill appearance, pale face, anemic conjunctivae, and paresthesia on both lower extremities. Skin examination revealed fourteen, asymptomatic, red nodules on the scalp, forehead, and back. The nodules were firm and discrete, however they did not show dimple-like depressions by lateral compression. They varied in size from 3 to 15 mm in diameter(Fig. 1). The number of nodules had increased to eighteen during the next seven days.

Result of esophagogastroduodenoscopic examination showed a mass along the lesser curvature

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Reprint request to: Jong Min Kim, M.D., Departments of Dermatology and Pathology*, College of Medicine, Hallym University, Seoul, Korea

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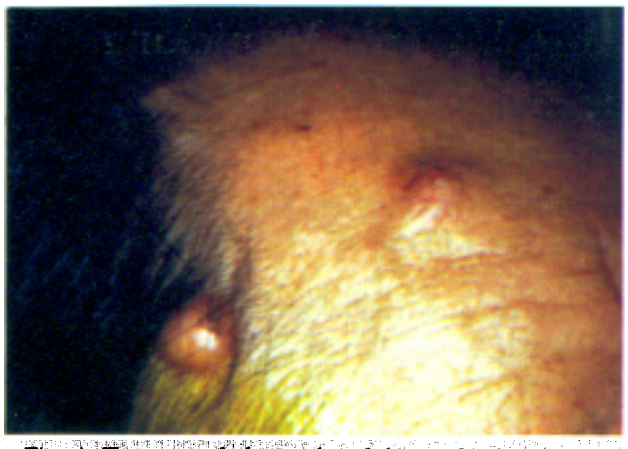

Fig. 1. Two, round,elevated nodules on forehead.

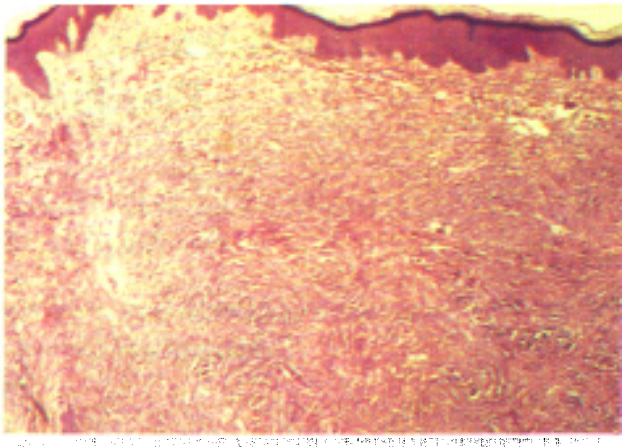

Fig. 2. Histology of the nodule on forehead showes ill-defined fascicles of collgen bundles, and cellular infiltration in the dermis(Hematoxylin-eosin stain ; × 20).

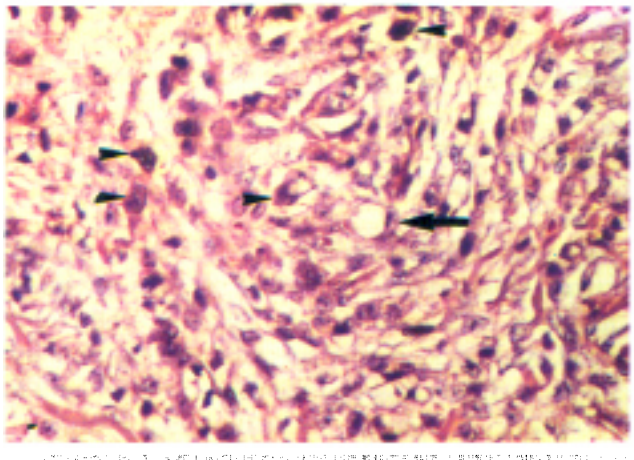

Fig. 3. Magnifying view of Fig. 2. Dermal infiltrate consisting of atypical tumor cells(arrowheads), signet ring cells(arrow), spindle cells and inflammatory cells (Hematoxylin-eosin stain ; ×200).

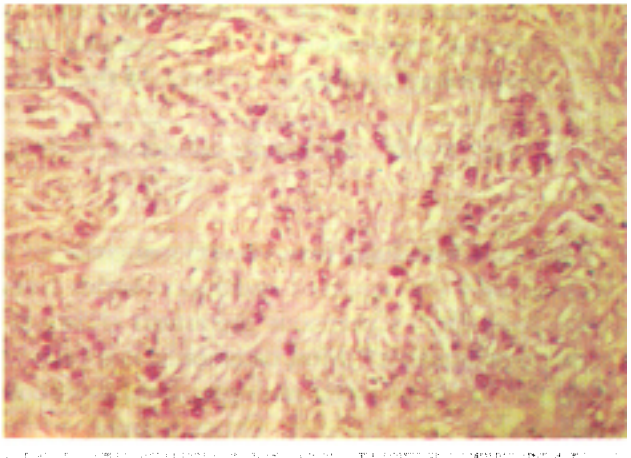

Fig. 4. Many tumor cells contained mucin (PAS stain, after diastase treatment ; ×200).

on the anastomotic site of the previous surgery. The mass was confirmed as poorly differentiated adenocarcinoma by biopsy. A computerized tomographic scan of the abdomen showed a 2 cm-sized round low density lesion at the retrogastric area, ill-defined diffuse low density lesions at the peripancreatic area and pancreatic head area, and small bowel wall thickening and dirty mesenteric fat sign with omental mass, suggesting metastatic lesions. A chest roentgenogram demonstrated old pulmonary tuberculosis with pleural thickening on the right upper lung field with no evidence of metastasis. Simple abdominal x-ray and sigmoidoscopic examination were normal. Other laboratory findings were as the followings: hemoglobin, 8.9 gm/dl(normal, 13-17 gm/dl); total protein, 6.0 gm/dl(normal, 6.5-8.0 gm/dl); albumin, 3.3 gm/dl(normal, 3.7-5.2 gm/dl). Serum iron was 51 ug/dl(normal, 20-70 ug/dl) and total iron binding capacity was 291 ug/dl(normal, 250-400 μg/dl). A peripheral blood smear revealed iron deficiency anemia. After diagnosis of gastric adenocarcinoma, he refused to have an the operation for the gastric tumor and cutaneous nodules and died 5 months later.

Microscopic studies

Two biopsy specimens from the cutaneous nodules(one from the scalp and the other from the back) and one biopsy specimen from the gastric mass were formalin-fixed and paraffin-embedded and they were stained with hematoxylin and

Table 1. Immunohistochemical findings

Tumor \ Marker	CAM 5.2	34βE12	CEA	S-100 protein	Vimentin	Lysozyme	CD68
Gastric Mass							
Atypical cells	+	−	+	−	−	+	ND
Signet-ring cells	+	−	+	−	−	−	ND
Histiocytes	−	−	−	−	−	+	ND
Cutaneous nodules							
Atypical cells	+	−	+	−	−	+	−
Signet-ring cells	+	−	+	−	−	−	−
Histiocytes	−	−	−	−	−	+	+
Spindle shaped cells	−	−	−	−	+	−	−

*ND; not done.

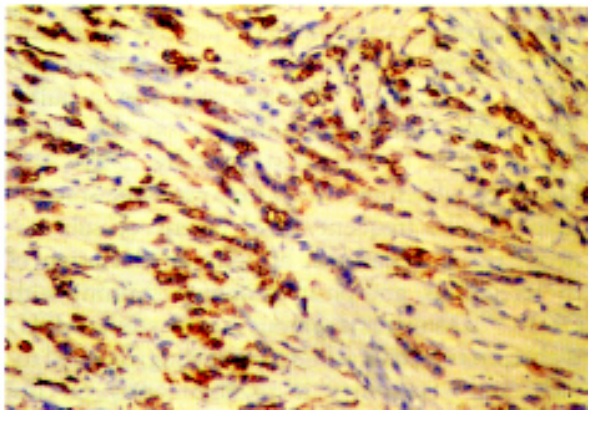

Fig. 5. Numerous tumor cells are stained with CAM5.2(× 100).

eosin(H & E), periodic acid-Schiff(PAS) reagent, with and without diastase digestion, and alcian blue(at pH 2.5 and pH 0.5). Immunohistochemical studies were performed with standard avidin-biotin complex immunoperoxidase technique on paraffin-embedded sections with monoclonal and polyclonal antibodies to low molecular weight keratins(CAM 5.2, Becton-Dickinson, Mountain view, CA), high molecular weight keratins(34β E12, Enzo Diagnostics, N.Y., NY), carcinoembryonic antigen(CEA, Biomeda, Foster, California), S-100 protein(Biomeda), vimentin(DAKO, Glostrup, Denmark), lysozyme(Biomeda), and CD68 (DAKO, Glostrup, Denmark).

RESULTS

Histologic findings

Two biopsy specimens from the cutaneous nodules showed similar features on H & E stain(Fig. 2). They showed irregular, intertwining bundles of collagen from the upper reticular dermis to the lower reticular dermis. At the lateral and upper margins, the tumors revealed poor circumscription with the surrounding normal stroma. Several foci revealed storiform patterns. In addition to spindle-shaped cells of the fascicles of collagen bundles, atypical cells with pleomorphic, hyperchromatic nuclei and a few signet-ring cells were also found(Fig. 3). Definite glandular structures and foamy cells were not observed. The epidermis showed mild acanthosis and elongation of rete ridges, but basal hyperpigmentation was not present. The gastric mass showed typical features of adenocarcinoma including well-developed glandular structures. The lumina of the glandular structures were lined by cells with large, hyperchromatic nuclei.

Histochemical and immunohistochemical findings

Tumor cells of both gastric adenocarcinoma and cutaneous nodules contained mucin. The mucin was PAS-positive, and diastase-resistant(Fig. 4), but did not stain with alcian blue both at pH 2.5 and at pH 0.5, indicating neutral mucopolysaccharides. The result of immunohistochemical stainings is summarized in Table 1. The majority of the tumor cells of both gastric adenocarcinoma and cutaneous nodules labelled with CAM 5.2(Fig. 5), but none of the tumor cells labelled with 34βE12. Most tumor cells of the gastric adenocarcinoma revealed strong positivity for CEA, but only a few scattered tumor cells of the cutaneous nodules re-

vealed positivity for CEA. A few tumor cells of both the gastric adenocarcinoma and cutaneous nodules showed positivity for lysozyme. None of the tumor cells of both the gastric adenocarcinoma and cutaneous nodules showed positivity for S-100 protein, vimentin, and CD68.

DISCUSSION

In the present case, the cutaneous nodules showed histologically irregular, interwoven fascicles and storiform pattern of collagen bundles, suggesting fibrohistiocytic tumors. The infiltrating cells in the dermis included atypical cells and signet ring cells in addition to spindle-shaped cells, lymphocytes and histiocytes. The atypical tumor cells contain mucin(neutral mucopolysaccharides), like those of the primary gastric adenocarcinoma. Of the metastatic tumors, tumors that are low molecular weight keratin(LK) positive, high molecular weight keratin(HK) negative, and CEA strongly positive, tend to be from the gastrointestinal tract, particularly from the colon and stomach[11]. In the present case, the tumor cells of the cutaneous nodules, like those of the the gastric adenocarcinoma, showed positive staining with CAM 5.2(specificity for LK8,18), negative staining with 34βE12(specificity for HK1,5,10,11) and strong CEA positivity. These features further supported the theory that the cutaneous nodules originated from the stomach. A few tumor cells of both the gastric adenocarcinoma and cutaneous nodules also expressed lysozyme. Capella et al[12] reported that cells containing lysozyme were demonstrated in 34.9% of 83 gastric carcinomas, in none of 30 breast carcinomas and in only 1 of 27 cases of colorectal neoplasm. And they suggested that cells containing lysozyme may be an abortive expression of Paneth cell and lysozyme may represent a useful tumor marker for carcinomas of gastric origin.

The metastatic tumor from visceral malignancies rarely manifests features of fibrohistiocytic tumors. In 1981, Hartschuh and Bersch[9] reported a case of cutaneous metastasis in a 46-year-old male with gastric carcinoma. The cutaneous nodules of the scalp and eyelid of the patient mimicked benign soft tissue tumor clinically and histologically and were confirmed as metastatic tumors only by electron microscopic examination.

The differential diagnosis of cutaneous nodules of the present case includes dermatofibroma, dermatofibrosarcoma protuberans(DFSP), malignant fibrous histiocytoma, atypical fibroxanthoma, plexiform fibrohistiocytic tumor, and sclerotic fibroma which mostly show stromal changes of fascicles of collagen bundles with storiform pattern. Dermatofibroma is the main differential diagnosis. It occurs predominantly on the extremities and often show dimple-like depression by lateral compression in the overlying skin of nodules. Histologically, dermatofibroma can be distinguished by a more polymorphic infiltration, the absence of signet-ring cells, the absence of sulfomucin, the presence of notable epidermal hyperplasia and basal hyperpigmentation, and positive immunostaining for factor XIIIa and negative staining with CAM 5.2[13-15]. DFSP is characterized by a bulky, protuberant mass predominantly on the trunk, and is larger in size. Histologically, DFSP is a highly cellular tumor with uniform large spindle-shaped cells, frequent involvement of subcutaneous tissue, occasional atrophy or ulceration of the epidermis, and positive immunostaining with CD34[15-17]. Malignant fibrous histiocytoma(MFH) is characterized by a solitary, protruding, rounded tumor, and occurrence is predominantly on the thigh or buttock with the occasional presence of preceding radiodermatitis or chronic ulceration. The histology of MFH is very variable, but usually shows highly cellular tumor with marked pleomorphic appearance, location in the subcutaneous tissue or deeper area, and immunoreaction with antibodies specific for fibroblasts and negative immunostaining for keratin[18-21]. Atypical fibroxanthoma(AFX) usually occurs as a raised, nodular lesion in a sun-exposed area of an elderly person. Histologically, AFX is distinguished by a highly cellular dermal infiltrate with marked cellular polymorphism and pleomorphism, a rare storiform pattern, the absence of signet-ring cells, positive immunoreactions with α-1-antitrypsin, α-1-antichymotrypsin, and lysozyme, but negative staining for keratin[21-23]. Plexiform fibrohistiocytic tumor (PFT) is characterized by a slowly growing, poorly demarcated dermal or subcutaneous mass, occurrence in adolescence or young adults, and favoring the upper extremity. Histologically, PFT shows a multinodular or plexiform proliferation of histiocyte- and fibroblast-like cells, the absence of a

storiform pattern, and positive immunostaining with α-1-antitrypsin and α-1-antichymotrypsin, but negative immunostaining for cytokeratin and lysozyme[24,25]. Scleotic fibroma, also known as hypocellular fibroma or circumscribed storiform collagenoma, can be distinquished by a solitary, translucent, white, flesh-colored or waxy papule in adults, no predilection sites, a well demarcated nodule with hypocellular, hyalinized, thick collagen bundles, a whorl-like or vague storiform pattern, prominent clefts between the collagen bundles, and mucin deposits within the clefts, positive immunostaining for vimentin, but negative staining for keratin and CEA[26-28]. Other fibrohistiocytic tumors such as dermatomyofibroma, low-grade fibromyxoid sarcoma, and cutaneous inflammatory pseudotumor also should be included in the differential diagnosis. As described above, fibrohistiocytic tumors have their distinct clinical and histologic features and they usually label so-called "fibrohistiocytic" markers such as α-1-antitrypsin, α-1-antichymotrypsin, lysozyme, MAC-387, KP-1, and anti-factor XIIIa, but they do not label anti-keratin antibodies(markers for epithelial lineage) immunohistochemically[29].

As illustrated in this case, cutaneous metastatic tumor may mimick fibrohistiocytic tumors histologically, but the tumor cells of the metastatic nodules of the present case contain sulfomucin, CEA, lysozyme and low molecular weight keratins like those of the primary gastric adenocarcinoma. Based on our findings, fibrohistiocytic tumors can easily be excluded by proper histochemical and immunohistochemical stainings.

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