



Skin as a site of metastasis

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Cutaneous metastasis is a rare occurrence but may be the presenting sign of a primary internal malignancy. Skin, breast, lung, gastrointestinal, and kidney are the most common primary malignancies to metastasize to skin. Common regions for cutaneous metastasis include the scalp, abdomen, chest, back, and extremities. The appearance of cutaneous metastasis is a preterminal occurrence and clinically a very poor prognostic sign. Skin cancer was the topic chosen, but it was decided to explore skin as a site of metastasis rather than primary melanoma, squamous cell, or basal cell carcinoma. A search and review of the literature on PubMed was performed to identify cases of cutaneous metastasis caused by a variety of primary sources in adults—mainly breast, lung, skin, gastrointestinal, genitourinary, renal, and thyroid. Inclusion criteria for the review was most common types of cancer in adults, appearance of lesions, and cutaneous metastasis to distant regions rather than direct extension with the exception of breast cancer. Primary malignancies found in children, lymphomas, and leukemias were not included in this review.

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Primary skin cancers such as melanoma, squamous cell carcinoma, and basal cell carcinoma are common. According to the American Cancer Society, approximately 1.6 million new cancer cases will be diagnosed in 2011. Of those new cancer cases, it is estimated that 76,330 will be new skin cancers. This number does not include squamous cell and basal cell carcinomas, which are not reported. In addition, more than 2 million of the skin cancers diagnosed in 2011 could be prevented by avoiding indoor tanning and using protection from the sun's rays; this is two times the estimate for 2010.^{1,2} It is common for the family medicine physician to have patients that present with these lesions for evaluation.

When presented with a skin lesion suspicious for cancer, the first consideration is usually a primary melanoma, squamous cell, or basal cell carcinoma.³ However, metastasis should also be included in the differential diagnosis because the skin lesion could rarely be the presenting sign of an

internal malignancy. Cutaneous metastases account for 2.8% to 4.4% of malignant skin tumors and occur in approximately 10% of patients with cancer.^{4,5}

Even though the incidence of these lesions is rare, it will likely be the family medicine physician who will be faced with detecting and diagnosing these lesions.

Incidence

In approximately 10% of patients with cancer, the skin, breast, stomach, lung, uterus/cervix, large intestines, and kidneys are the most frequent organs to cause cutaneous metastasis. Cancers with the highest incidence of skin metastasis are melanoma (45%), breast (30%), nasal sinuses (20%), larynx (26%), and oral cavity (12%) (Table 1).⁴ Cutaneous metastasis caused by breast cancer is most commonly encountered as a result of the high incidence of breast cancer in clinical practices. The presence of cutaneous metastasis is a sign of diffuse metastatic disease and represents a poor prognosis, regardless of the cell type or

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Table 1 Primary malignancies that metastasize to skin⁴

Primary malignancy	Patients with cutaneous metastases
Melanoma	44.80%
Breast	30%
Nasal sinuses	20%
Larynx	16.30%
Endocrine glands	12.50%
Oral cavity	11.50%
Esophagus	8.60%
Kidney	4.60%
Stomach	2%

organ of origin of the primary cancer. Cutaneous metastasis occurs in less than 10% of visceral carcinomas and is the presenting symptom 0.8% of the time.^{4,6} The most common primary cancers that metastasize to skin are shown in Table 2. Lung cancer, colon cancer, and melanoma are shared between men and women. Primary malignancies that result in cutaneous metastasis in men also include oral, renal, and gastric; for women, ovarian and breast cancer are common primary malignancies that result in cutaneous metastasis.

A primary internal malignancy is usually known before cutaneous metastasis is discovered; however in rare cases, the cutaneous metastasis is the presenting sign of internal malignancy.⁴

Pathogenesis

Cutaneous metastasis may occur by three different mechanisms: direct extension, local invasion, or distant metastasis.⁷ Direct extension occurs as rapidly growing tumors invade the surrounding tissues. For more superficial or rapidly growing lesions, the skin can be a site of tumor extension presenting as a hemorrhagic or ulcerated lesion. Direct extension can also present as a surgical site invasion as a result of seeding of the surgical tract from biopsies or injection therapies. This has been documented in cutaneous metastasis of hepatocellular carcinoma and renal cell carcinoma.^{4,6}

Local invasion can occur through lymphatic spread, which is the initial means of metastasis of cancerous lesions.⁸ The replication of cancerous cells in the lymphatic system and tumor growth that impinges on lymphatic flow can result in nonpitting edema or peau d'orange appearance

Table 2 Most common primary malignancies that result in cutaneous metastases by sex/age^{4,8}

Men	Lung, colon, melanoma, oral, renal, gastric
Women	Breast, colon, melanoma, ovaries, lung
Children	Rhabdomyosarcoma, leukemia, neuroblastoma

noted in inflammatory breast carcinoma.^{4,8} Local invasion or regional spread may also occur through body cavities, in particular the peritoneal cavity.⁴

Distant metastasis occurs through lymphatic and hematogenous spreading, which can be difficult to differentiate because they are interconnected. The scalp is a common site for cutaneous metastasis from a variety of primary internal malignancies because of its high vascularity. Cutaneous metastasis to the scalp will appear as smooth areas of hair loss; smooth flesh-colored nodules; or hemorrhagic, ulcerated lesions.^{4,6}

Types of cutaneous metastasis

Renal

“Almost 30% of patients with renal cell carcinoma already have metastatic disease at the time of diagnosis and 40% of patients with clinically localized disease develop distant metastasis despite elimination of the primary tumor.”⁵ The most common sites of metastasis are lung, liver, and bone, but “about 6% of all cutaneous metastatic tumors are caused by renal cell carcinoma.”⁵

“In most instances, once cutaneous involvement is manifest the disease is widespread and has a poor prognosis. The skin should be examined during tumor evaluation as part of the physical examination and skin lesions in patients with renal cell carcinoma should be evaluated aggressively to rule out cutaneous metastasis.”⁹ Metastatic skin lesions caused by renal cell carcinoma were described as usually solitary well-circumscribed smooth nodules that are either pinkish-red or blue, or a cutaneous horn.

Thyroid

Cutaneous metastases of thyroid carcinoma are rare and when they do occur they are in the region of a locally invasive tumor. Cutaneous metastases have been found in medullary and papillary thyroid carcinoma.¹⁰⁻¹² Appearance varies because it is typically caused by direct tumor extension: solitary or multiple, flesh- or blue-colored nodules or papules that may be tender, pruritic, or ulcerated.¹¹

Malignant melanoma

Metastatic melanoma (Fig. 1) is the most common type of cutaneous metastasis and is the first manifestation of the disease in up to 5% of affected patients.¹³ Most tumors are located on the proximal legs, scalp, or arms and measure 0.8 to 3cm. It can simulate primary melanoma or other benign and malignant neoplasms. It is important to differentiate between metastatic and primary lesions for staging, treatment, and prognostic reasons.¹³

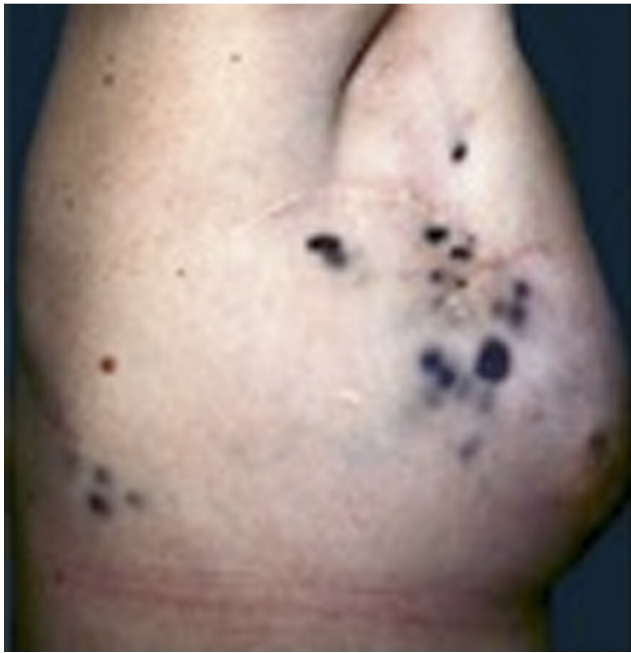


Figure 1 Malignant melanoma. (From Wolff K, Johnson RA: Skin signs of systemic cancers. In *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology*, 6th ed. New York: McGraw-Hill, 2009, pp. 486-503).

Lung

Cutaneous metastasis from lung cancer can have a zosteriform appearance that is symmetrical along the direction of intercostal vessels usually in the scar from thoracotomy or needle aspiration tract.⁸ Cutaneous metastasis to the scalp from lung cancer appears as a large number of nodules in a short amount of time or thinning hair known as alopecia neoplastica (Fig. 2).⁴ The most common sites of cutaneous metastasis in descending order are the chest, abdomen, back, scalp, neck, face, extremities, and pelvis.⁴ A case was described where bronchial mucoepidermoid carcinoma initially presented as an enlarging nodule beneath the skin of a young male's lower back that progressed to more nodules along the right ribs, left forearm, and left lower leg.¹⁴

Gastrointestinal

Gastrointestinal cancers, particularly stomach and colon, often metastasize to the skin of the abdomen and pelvis as nodules. Metastatic nodules to the umbilicus are referred to as Sister Mary Joseph nodules. It is also noted that colon cancer cutaneous metastasis may present as an inflammatory skin condition in the inguinal or supraclavicular regions or even in the face and neck.^{4,8}

Liver

Cutaneous metastasis of hepatocellular carcinoma develops in approximately 3% of patients affected by the disease.

It usually develops along sites of liver needle biopsy or percutaneous injection therapies. It may mimic pyogenic granuloma in appearance.^{8,15}

Cervix/Vulva

Cutaneous metastasis of cervical cancer occurs in less than 2% of patients but may occur at the initial diagnosis or a decade later. It is a poor prognostic sign. Most common sites of metastasis are the abdomen, chest, vulva, scalp, and umbilicus. The lesions may mimic dermatitis by appearing as a plaque-like pruritic lesion. It may progress to an ulcer over time that has a purulent drainage.^{16,17}

Cutaneous metastasis from vulvar carcinoma is extremely rare but may metastasize to areas close in proximity to the genitalia such as the thigh and lower abdomen, although there have been reports of cutaneous metastasis to the forearm as well.^{18,19}

Breast

Cutaneous metastasis in breast cancer occurs through direct extension and lymphatic and hematogenous spread. Direct extension and lymphatic spread result in a peau d'orange appearance/carcinoma erysipelatoides (Fig. 3), carcinoma telangiectaticum (pinpoint telangiectasis within carcinoma erysipelatoides), or en curiassse metastatic carcinoma (Fig. 4). En curiassse, which is a diffuse induration of the skin that causes the chest to appear as a metal breastplate encasing the chest, also occurs in primary lung, gastrointestinal tract, and kidney cancers.^{4,8}



Figure 2 Alopecia neoplastica (From Helm TN, Lee TC: Metastatic carcinoma of the skin. Available at: eMedicine from WebMD <http://emedicine.medscape.com/article/1101058-overview>. Accessed March 2, 2010).



Figure 3 Carcinoma erysipelatoides (From Wolff K, Johnson RA: Skin signs of systemic cancers. In *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology*, 6th ed. New York: McGraw-Hill, 2009, pp. 486-503).

Testicle/Prostate/Bladder

Cutaneous metastasis caused by testicular, prostatic, or bladder cancer is extremely rare. Individual cases are reported next that show the variability in the appearance of the skin lesions.

The first case presented with progressively enlarging upper abdominal skin lesions and scalp nodules for 3 months that were “stony hard with mild bleeding.” Excisional biopsy revealed metastatic germ cell carcinoma.²⁰

A second case presented as a sudden onset of multiple, red, angiomatous, “berry-like” nodules that grew rapidly in a dermatographic distribution and was found to be cutaneous metastasis from prostatic adenocarcinoma. Cutaneous metastasis from the prostate is rare but will most commonly be found on the lower abdomen, genitalia, groin, or thigh and will have genital swelling associated with the skin lesions.²¹

Finally, an isolated skin nodule was noted a few weeks after micropapillary bladder carcinoma excision and was



Figure 4 En curiassie metastatic carcinoma (From Mordenti C, Peris K, Concetta Farnoli M, et al: Cutaneous metastatic breast carcinoma. *Dermatovernerologica* 9, 2000. e-edition.)

Table 3 Common sites of cutaneous metastasis

Common cutaneous metastasis sites	Probable primary sites
Scalp	Breast, lung, kidney
Neck	Oral squamous cell carcinoma
Face	Oral squamous cell carcinoma, renal cell carcinoma, lung
Extremities	Malignant melanoma, breast, lung, renal, intestine
Chest	Breast, lung, malignant melanoma
Abdomen	Colon, lung, stomach, breast, ovary
Umbilicus	Stomach, pancreas, colon, ovary, kidney, breast
Pelvis	Colon, lung, stomach, breast, ovary
Back	Lung

found to be a metastatic lesion from the rare variant of transitional cell carcinoma.²²

Regions and appearance of cutaneous metastasis

Common sites of cutaneous metastasis include the scalp, abdomen, chest, trunk, upper and lower extremities, face, neck, and eye. Because of the high vascularity of the scalp, it is a common location for cutaneous metastasis. Cutaneous metastasis is the third most common malignancy of the scalp behind basal cell carcinoma and squamous cell carcinoma, representing 12.8% of cases.⁶ Wieselthier and White described a case of ocular malignant melanoma presenting as blue nevi on the nasolabial fold, forehead, upper arms, and upper occipital scalp with painful blue/gray axillary nodules.²³ Table 3 describes common cutaneous metastatic sites and probable primary malignancy sites.⁴

“Clinically, the lesions do not have a uniformly characteristic appearance.”²⁴ Cutaneous metastasis may mimic primary skin tumor or dermatosis. Some metastases, especially single skin lesions, look like benign cysts, keratoacanthoma, basal cell carcinoma, or melanoma.²⁴

As described previously, cutaneous metastasis may appear as subcutaneous nodules that are flesh-colored or faintly erythematous, or as dermal lesions that are firm and have a visible pigment. Both may evolve to pink/erythematous lesions that can ulcerate. There can also be an inflammatory component caused by lymphatic congestion resulting in erythema and pitting or nonpitting edema.^{4,6,8}

Palpation of these nodules may reveal a variety of sensations. They may be smooth, firm, solitary nodules palpated in the subcutaneous tissues that may or may not be visualized but only palpated or a rough cutaneous horn or smooth hair loss. In advanced stages they may ulcerate and hemorrhage. Lesions may be nontender to palpation, tender, or pruritic.^{4,6,8}



Figure 5 Scalp nodule (From Koca R, Ustundag Y, Kargi E, et al: A case with widespread cutaneous metastases of unknown primary origin: grave prognostic finding in cancer. *Dermatology Online J* 11:16, 2005).

Prognosis

The appearance of cutaneous metastasis is typically preterminal in most cases despite being the first presentation of malignancy in some.² It is a very poor prognostic sign.^{4,9,13,15,16,18,21}

Conclusion

Cutaneous metastasis is a rare occurrence but may be the presenting sign of a primary internal malignancy. The lesions may have a benign appearance such as hair loss or flesh colored nodules on the scalp (Fig. 5), which may progress to ulcerated, hemorrhagic lesions. Some lesions may not be visualized at first but are instead easily palpated. It is important to remove all hair pieces and examine the scalp thoroughly both visually and with palpation when there is a high index of suspicion for cutaneous metastasis.⁶ Skin, breast, lung, gastrointestinal, and kidney are the most common primary malignancies to metastasize to skin.⁵ Common regions for cutaneous metastasis include the scalp, abdomen, chest, back, and extremities.⁴ The appearance of cutaneous metastasis is a preterminal occurrence and clinically a very poor prognostic sign.

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