Imaging Of Cutaneous and Subcutaneous Nodules in Oncology Patient

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Learning objectives

Many patients with tumors either benign or malignant presented with skin and subcutaneous nodules. These lesions are considered as a challenge to the radiologist. We propose these learning objectives:

• To review the imaging findings of skin nodules in oncological patients.
• To increase awareness and recognition of uncommon lesions.
• To illustrate the imaging features of each lesion.

Background

Skin and subcutaneous lesions are frequently encountered by radiologists in clinical practice. These lesions can have etiologies ranging from benign neoplastic and non-neoplastic lesions to primary and metastatic malignant lesions.

The recognition and proper characterization of these lesions can have significant prognostic and management implications in the oncologic patient.

A systematic approach to image interpretation is vital to ensure that these lesions are not overlooked. Unfortunately, despite advances in imaging, characterization of these lesions remains problematic.

Imaging findings OR Procedure details

skin Anatomy

The skin is the body’s largest organ, covering the entire body. It serves as a protective shield against heat, light, injury, and infection. The skin is made up of three layers: the thin outer layer is the epidermis, which consists ofstratum corneum (horny layer), keratinocytes (squamous cells) and basal layer. The epidermis also contains melanocytes that produce melanin. The dermis is the middle layer of skin and contains blood and lymph vessels, hair follicles, sweat glands, collagen bundles, fibroblasts, and nerves. The deepest layer is the subcutaneous layer which consist of a network of collagen and fat cells.

Imaging the Skin
Cutaneous and subcutaneous nodules in oncological patients are not infrequent and can have etiologies ranging from benign to malignant. Unfortunately, the skin is commonly ignored on interpretation of CT and MR images.

**Cutaneous metastases**

Cutaneous metastasis from internal malignancy is uncommon but not rare. It is reported most frequently after the fourth decade of life with a frequency ranging between 0.7% and 10.4% of all patients with cancer. Skin involvement in malignant patients can occur either by direct extension or by lymphatic or hematogenous spread.

The most frequent primary tumors associated with skin metastases are breast cancer in females and lung cancer in males, followed by colorectal cancer in both sexes. In children, neuroblastoma is the most frequent malignancy to cause skin metastases.

Cutaneous metastases may be the primary presentation of an internal malignancy. In these cases, it represents a source of accessible tumor cells for pathological assessment without the need for more invasive procedures. In other cases, detection of cutaneous metastasis is essential in proper staging, and proper management. Metastatic skin lesions may also represent an early sign of recurrent malignancy.

Skin metastases indicate a poor prognosis especially when multiple. (neuroblastoma is an exception to this rule). The treatment of skin metastases depends on their size and location. Surgical excision followed by radiotherapy may occasionally control limited disease, leading to longer survival.

Imaging plays a crucial role not only in the detection of and therapeutic planning for cutaneous metastases, but also in detection of a clinically occult primary cancer.

**Clinical Findings:** The diagnosis of cutaneous metastases requires a high index of suspicion, as the clinical findings, especially in the early stages, may be very subtle. Cutaneous metastases usually present as asymptomatic, firm, rubbery painless nodules. The appearance is nonspecific; however, some can be morphologically distinctive. For example, neuroblastoma skin metastases are firm non-tender, bluish, and randomly distributed all over the body, giving the typical "blueberry muffin baby" appearance.

**Imaging findings**

The skin is commonly overlooked on image interpretation, and special attention is required to detect cutaneous lesions. Most skin metastases appear as a small subcutaneous or intradermal nodular lesions on CT and MRI.

**High-frequency ultrasound (US)** enables examination of tissues close to the skin surface. Skin deposits usually appear as a homogeneously hypoechoic area in
comparison to the surrounding hyperechoic dermis, from which it can be easily distinguished. US also allows differentiation of cystic from solid lesions.

$^{18}$F-FDG PET/CT has higher sensitivity than MRI and CT in detecting skin metastases. The diagnosis of skin metastases using combined PET/CT is relatively straightforward, as most lesions have FDG uptake significantly higher than that of the liver. It can occasionally be difficult to differentiate skin metastases from primary skin carcinomas.

**Lymphoma and leukemia**

Cutaneous infiltration by lymphoma and leukemia is relatively common. It may be difficult to differentiate primary and metastatic cutaneous lymphoma. Primary cutaneous lymphoma is the second most common group of extra-nodal non-Hodgkin lymphomas, but skin involvement is very rare in Hodgkin lymphoma. Skin lesions in leukemia are most commonly located on the scalp and rarely in the extremities. Thirty percent of these lesions are seen in patients with acute myelocytic leukemia (AML), and only 1% in patients with acute lymphocytic leukemia (ALL).

**Clinical Findings:** A broad spectrum of skin lesions can be detected in patients with hematological malignancies including plaques and patches and bullous, erythrodermic, follicular, subcutaneous, granulomatous, hyperkeratotic, hyper- or hypopigmented lesions. The most common presentation of skin involvement with hematological malignancies are nodules or tumors without scaling or ulceration. These lesions may be solitary or multiple.

**Imaging findings**

High resolution US may serve as a highly sensitive, non-invasive tool for assessment of skin lesions, but is not specific enough to replace the pathological assessment. The common presentation of cutaneous lymphoma and leukemia on US is a well-defined hypo-echoic nodule.

MRI provides exquisite anatomic detail and is useful in tumor staging. New techniques, such as whole-body MRI, also help in early detection of asymptomatic skin involvement. Proper local staging of cutaneous lesions, their relation to underlying fascia and muscles can be easily evaluated by MRI.

$^{18}$F-FDG -PET as a functional imaging modality can help to exclude extra-cutaneous disease. As the prognosis of the cutaneous lymphoma is generally good compared to systemic disease. It also helps in proper staging in secondary lymphoma cases and in assessment of response to therapy.
Primary skin cancer

The primary skin cancers may be categorized into 2 major groups: melanoma and non-melanoma (keratinocytic tumors) skin cancers. The latter group consists primarily of basal cell carcinomas and squamous cell carcinomas.

Cutaneous malignant melanoma

Melanoma represents 5% of all diagnosed cancers in the United States, 15% of which prove to be fatal. Tumor depth is the most important prognostic indicator for melanoma, thus careful early radiological assessment is helpful in better therapy.

Imaging findings

Accurate staging is the main factor in therapeutic planning. Other effective factors in are depth of invasion of the primary tumor, and the presence, site, and extent of metastases. Whole body images by PET-CT or MRI have been advocated as an accurate and reliable imaging technique for detecting metastatic melanoma.

The common type of melanoma (pigmented melanotic type) has a characteristic appearance on MRI: high signal on T1- and low signal on T2-weighted images. The amelanotic type is less common (less than 2% of cases) and has a nonspecific appearance: low signal on T1-weighted images and high signal on T2-weighted images pose difficulty in radiological diagnosis.

Squamous cell carcinoma

Squamous cell carcinoma is more common in older, fair-skinned individuals, and is a result of chronic ultraviolet (UV) light exposure (80% of squamous cell carcinomas occur on sun-exposed areas of the body). Immunosuppression in solid organ transplanted patients is a risk factor for squamous cell carcinoma. Some chronic inflammatory lesions such as chronic venous ulcers, discoid lupus erythematosus, erosive lichen planus, and lymphedema may also result in keratinocyte transformation to squamous cell carcinoma.

Lesions of squamous cell carcinoma may vary from a small, pink, erythematous, scaly papules to large, ulcerated, and indurated plaques. If the squamous cell carcinoma is large enough, patients may note pain, bleeding. Peripheral neural symptoms may be seen with perineural spread.

The main role of imaging is the evaluation of the local extension of the lesion to the underlying tissue (muscles, bones). Metastatic lymph nodes may show central necrosis. CT is the modality of choice in local and nodal staging. Perineural spread, especially in the head and neck region, is an important factor in therapeutic planning. MRI is the most useful modality in the detection of perineural spread in the head and neck.
Basal Cell Carcinoma

Basal cell carcinomas most commonly occur in the head and neck, but may also be found in non-sun-exposed areas of the body. Many clinical syndromes are associated with basal cell carcinoma, including xeroderma pigmentosum, Gorlin syndrome, (neviod basal cell carcinoma syndrome), and syndromes associated with melanin deficiency such as Rasmussen, Rombo, and albinism. 60% of cases are nodulo-ulcerative or "rodent ulcers. It is named after its resemblance to the rat bite. These lesions begin as small, reddish, translucent nodules with telangiectasias, which ulcerate as they grow, leaving behind the classic "rolled borders." In advanced cases, the lesions can lead to destruction of underlying tissue, including bone. The appearance of basal cell carcinoma on imaging depends on the size. Small lesions are soft-tissue masses in the skin usually with deep extension into the subcutaneous tissues. Larger lesions appear as deeply infiltrating soft-tissue masses.

Benign skin lesions

In cancer patients, the differentiation of cutaneous metastases from benign lesions is of utmost importance for proper staging. Some points may help in differentiation between metastatic lesions and benign lesions such as epidermoid cysts, lipomas and granulomas:

- The internal composition of the lesion:-
  - Fluid, fat, and calcium content of the lesion suggest a benign etiology, such as in epidermoid cysts, lipomas and granulomas.
  - Metastatic nodules are usually solid lesions.

Yet some benign lesions are also solid as neurofibroma.

- Number and Size :
  - Multiplicity of lesions or change in size and number over time may suggest malignancy.

- Location of lesions
  - Epidermoid cysts are usually just below the epidermis.
  - Metastases may be distant from the epidermis.
Subcutaneous vessels may simulate a nodule on a single axial image, but they can be identified on contiguous images, and are usually smaller and more sharply defined than metastatic lesions.

Functional imaging modalities such as PET-CT and diffusion MRI may be helpful in differentiating benign from malignant lesions.

**Epidermoid cyst is one of the most common incidentally encountered lesions.** The term sebaceous cyst is a misnomer and should be avoided because these cysts are not of sebaceous origin. Its radiological picture varies depending on its contents. When it has high proteinaceous content, it has attenuation similar to muscle on CT and can be misdiagnosed as a solid nodule. By US, the cysts appear as a circumscribed circular or oval hypoechoic masses, often in association with a hair follicle.

**Another benign skin condition commonly encountered in oncology patients is diffuse thickening of the skin.** It is found in inflammatory conditions, post irradiation or, rarely, with tumor infiltration. Skin thickening can also be caused by trauma, in which case subcutaneous hemorrhage can also be seen. Clinical assessment is usually helpful. Serial imaging can be used in equivocal cases.

- Inflammatory processes (e.g., cellulitis) either resolve or progress into abscess.
- Hematomas tend to show evolution and resolution.
- Radiation changes are relatively stable or improve with time.
- Tumors may progress to variable degrees, depending on their histology and aggressiveness.

**Images for this section:**
**Fig 1:** 1-year-old boy with nodule at the back of the neck (arrow). Left partially calcified mass is noted, pathologically proven as neuroblastoma (circle).
Fig. 2: 1-month-old boy with orbital lesion and skin nodules at the right axilla and right groin biopsy showed metastatic malignant extra renal rhabdoid tumor.
Fig. 3: 55-year-old woman with left breast infiltrating ductal carcinoma, right ductal carcinoma in situ, presented with subcutaneous back and subgaleal nodules, proven pathologically as **metastatic breast cancer**.
Fig. 4. 65-year-old man with small red bumps on his legs with growth of lesions over 6 months. Biopsy showed NK-cell lymphoma with blastoid features (mycosis fungoides).
Fig. 5: 87-year-old man who presented with a large occipital mass that was pathologically shown to represent as disseminated lymphoma.
Fig. 14: 59 years male with subcutaneous mass at the medial aspect of orbit with no bone destruction, pathologically proven cellular fibrous histiocytoma
Fig 15: 5–years-old boy presented with avidly enhanced mass at the upper lip **Hemangioma**

Fig. 15
Fig. 16: 10-year-old boy with stigmata of neurofibromatosis type 1 with multiple subcutaneous nodules.
Fig. 17: 45-year-old man/woman with multiple palpable nodules. Biopsy showed **multiple lipomas**
Fig 18: 2 y female with ALL ,, presented with diffuse swollen face and scalp regressed on anti-inflammatory therapy, **cellulitis**
Fig. 13: 90-year-old man presenting with a new right cheek nodule. Biopsy showed **nodular basal cell carcinoma**.
Fig. 12. 14- year- female with xeroderma pigmentosa presented with scalp nodule, enlarged right parotid lymph node (arrow) and left cheek basal cell carcinoma (circle).
**Fig. 11:** 62-year-old man with left cheek **Squamous cell carcinoma** presented with paresthesias in the distribution of the left cranial nerve V2. MRI showed perineural spread along infra-orbital nerve.
Fig. 10: 46-year-old man with left foot melanoma, metastatic to the skin and subcutaneous fat. The patient presented with a right calf mass, which was shown to represent a melanoma metastasis.
Fig. 9: 48 years old male presented with swelling at the lateral aspect of the left orbit. Pathologically proven **malignant cutaneous melanoma**.
Fig. 8: 64-year-old man with right back lesion, shown to represent **myeloid sarcoma**.
Fig. 7: 16-year-old female with AML who presented with right occipto-pareital swelling. Biopsy showed **chloroma**.
**Fig. 19:** 66-year-old man with follicular lymphoma, enlarged lymph nodes and splenomegaly. $^{18}$F-FDG PET shows multiple FDG-avid subcutaneous nodules. CT and radiography show calcifications, consistent with **injection granulomas**.
**Fig. 6**: 53-year-old woman who presented with swelling of the right thigh. Biopsy showed **follicular Lymphoma**.
Conclusion

Skin should be included in the check list during interpretation of the radiological images. The skin may be a mirror of internal pathology especially in the tumor patients. Detection of skin lesion and its characterization, differentiation between the benign and malignant lesions are of utmost importance for the proper staging, thus appropriate therapeutic plan and better prognosis of these patients.

References


Personal Information