

MELANOMA AND NEVI

The incidence of malignant melanoma is rising. In the United States, there is approximately a 4% increase per year in incidence and a 2% increase per year in mortality. There is also an increase in frequency in young people with 1 in 4 new cases arising in people under 40 yrs old. It's the second most common cancer among women 20-29 yrs old. Melanoma ranks second behind leukemia among adult cancers in lost productive years.

Besides the well-known environmental risk factor of UV exposure, melanoma risk is increased in the setting of two characteristic nevi.

Dysplastic Nevus

Dysplastic nevi can be a precursor to melanoma. In 1978, these lesions were first described. There have been many disagreements over the years concerning the nomenclature, reproducibility, and histologic criteria for dysplastic nevi. In 1992, the NIH had a consensus conference concerning melanoma and its precursors. They recommended replacing the term dysplastic nevus with "nevus with architectural disorder." Since there was so much disagreement, physicians at this conference tried to "formulate a reproducible schema in diagnosing and reporting these nevi." Unfortunately, problems still occur in clinical reproducibility of finding the lesions and in diagnosing atypical nevi.

Dysplastic nevi are usually large (>6 mm), irregularly shaped, frequently with uneven borders or ill-defined borders. They can vary in color from tan to dark brown to pink, or be variegated. Dysplastic nevi are sometimes surrounded by an erythematous macule called the shoulder phenomenon. The skin creases are frequently unaffected. If central nodules arise within a macular nevus, there is a higher possibility of malignancy. Histologically, when a melanoma arises in a dysplastic nevus, it's usually the superficial spreading subtype.

Features of malignant transformation of nevi include the development of contour asymmetry, variation in pigmentation, development of black foci or gray discoloration suggesting regression. All relatives of patients with the dysplastic nevus syndrome should be carefully

examined. Approximately 50% of them will have evidence of clinical involvement.

Individuals may develop large numbers of normal appearing nevi in early childhood. As the child grows, the nevi become more numerous and acquire atypical features, especially at puberty. The most common sites involve trunk, face or arms, but other sites such as buttocks, scalp, genitalia or breasts may be affected.

Currently, there are four clinical classes of dysplastic nevi:

- Hereditary where there is a family member with melanoma;
- Familial dysplastic nevi where a blood relative has dysplastic nevi but not melanoma;
- Those individuals with a personal history of both melanoma and dysplastic nevi;
- Sporadic dysplastic nevi where there is no family/personal history of melanoma or dysplastic nevi.

Congenital Nevi

Congenital nevi are common and found in 1.6% population. These lesions are present from birth and often multiple. Congenital nevi are flat and pale brown, reminiscent of a café-au-lait macule. The nevi can become heavily pigmented, hairy and thicker in nature. Congenital nevi can also have a warty appearance with discrete small nodular projections. These lesions are categorized by size:

- Small, measuring up to 1.5 cm in diameter;
- Medium, measuring from 1.5-20 cm;
- Large, measuring greater than 20cm.

The large ones may cover an entire extremity or trunk, and are some times called bathing-trunk type. Those occurring over the vertebral column can be associated with leptomeningeal melanocytosis, hydrocephalus; spina bifida or meningomyelocele. The giant congenital melanocytic nevi have at least a 6-7% lifetime risk of malignant transformation. Malignant change usually takes place before puberty, and can be present at birth.

Melanoma

Besides the melanoma risk associated with the nevi mentioned above, it is fairly well-recognized that melanoma risk is increased by UV exposure, both chronic life-long exposure and sporadic, intensive exposure such as occasional episodes of severe sunburn in childhood. Frequent use of tanning beds represents a significant risk factor today. It's interesting to note that superficial spreading melanoma is more closely related to episodic severe sunburn in childhood, rather than to chronic life long exposure

Scientists are discovering that family history with inherited mutations in CDKN2A and CDK4 genes confer a 60-90% lifetime risk for developing melanoma

The prognosis of melanoma is to some extent dependent on the location of the tumor. Those occurring on the BANS sites (upper Back, Arm, Neck, Scalp) behave less favorably than those on the extremities.

Skin lines that are usually seen in the benign melanocytic nevi are absent over the surface of melanomas. Melanomas of the nail bed often produce linear pigmentation of the nail matrix. These lesions will distort the nail plate resembling a fungal infection. Evaluation of the nail plate and underlying nail tissue bed is important since these tend to be more aggressive lesions.

Pathological staging of the primary tumor guides the prognosis and decisions regarding further surgeries. Superficial shave biopsies are suboptimal since deep margins cannot be fully assessed. Increasing thickness of the melanoma and ulceration are inversely correlated with survival. Lymph node status has emerged as the most important predictor of recurrence and survival.

Wide local excision is the preferred treatment for the primary melanoma. Several recent controlled studies have

determined what the appropriate resection margin should be based on the thickness of the tumor. For melanoma-in-situ, margins of 0.5-1cm around the lesion are recommended. For melanomas 1 mm or less, a 2 cm margin is recommended if anatomically possible, but 1 cm margin is acceptable. For tumors between 2-4 mm thick, a 2 cm margin is recommended. Tumors >4mm thick have a high risk of lymph node involvement and distant metastasis. Several national and international melanoma study groups recommend 2-3 cm margins for these large tumors.

Sentinel lymph node biopsy should be considered with large tumors. Metastatic deposits in lymph nodes occur in 1% of cases if the thickness of the tumor is < 0.8mm, if the tumor is > 4mm, there is a 36% chance of having positive lymph nodes. An excellent flow chart for management of melanomas is found in article NEJM 2004; 351:998-1012.

Melanoma Diagnosis and FNA

FNA is an excellent diagnostic procedure for diagnosing metastatic melanoma in lymph nodes. If a regional lymph node is present at the time of initial diagnosis of melanoma, FNA of the lymph node should be considered to look for metastatic disease. FNA would also be the first line procedure for diagnosing recurrent metastatic melanoma, either to regional or distant lymph nodes. Confirmation that the cells aspirated are indeed melanocytic in origin can be accomplished using immunohistochemical stains on the material obtained by FNA.

References

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COMPANY PROFILE

OUTPATIENT CYTOPATHOLOGY CENTER (OCC) is an independent pathology practice that specializes in performing and interpreting fine needle aspiration biopsy specimens. OCC is accredited by the College of American Pathologists. The practice was established in 1991 in Johnson City, Tennessee. Patients may be referred for aspiration biopsy of most palpable masses as well as for aspiration of non-palpable breast and thyroid masses that can be visualized by ultrasound. OCC is a participating provider with most insurance plans. Our referral area includes patients from Virginia, West Virginia, North Carolina, South Carolina and Georgia.

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