

Melanoma

Melanoma is a malignant tumor originating from melanocytes, the cells responsible for producing melanin, which gives the skin its color and facilitates tanning. It is one of the most aggressive forms of skin cancer, with the potential for early metastasis to other parts of the body, making it more dangerous than common non-melanoma skin cancers, such as basal cell carcinoma or squamous cell carcinoma. The global incidence of melanoma is increasing at a rate of approximately 5% annually, with an estimated 96,480 new cases and 7,000 related deaths in the United States in 2019. Melanoma is the 5th most common cancer in men and the 6th most common in women, with its highest incidence in individuals aged 25 to 29, where it is the most frequently diagnosed cancer.

Etiology and Pathophysiology

Melanoma arises from mutations in melanocytes, which are located in the basal layer of the epidermis. These mutations are often triggered by ultraviolet (UV) radiation, although genetic factors and other environmental exposures can also contribute to disease development. Unlike basal cell carcinoma and squamous cell carcinoma, melanoma has a higher propensity to metastasize, either through local extension via lymphatic channels or hematogenously via the bloodstream to distant organs. The primary sites of metastasis include the lungs, liver, and brain. The risk of recurrence decreases over time, but late relapses are still possible, especially in patients with advanced disease.

Clinical Presentation

Melanoma can present as a new pigmented lesion or a change in an existing mole. The key characteristics of a suspicious melanoma include changes in the size, shape, color, or texture of a mole, as well as signs of bleeding, oozing, or itching. Melanomas may appear as dark brown or black lesions, though some may be flesh-colored or pink. In adults, melanoma most commonly occurs on the trunk and head/neck areas in men, and on the limbs in women. While it is rare, melanoma can also develop in children. Early diagnosis is crucial, as melanomas that are detected in their early stages, when confined to the epidermis, are more treatable and less likely to metastasize.

Diagnosis and Staging

The diagnosis of melanoma is typically confirmed through a skin biopsy, where a sample of the suspicious lesion is excised and analyzed histologically. If melanoma is diagnosed, the depth of tumor invasion is measured using the Breslow thickness, which correlates with prognosis. Tumors

that extend deeper than 4 millimeters are associated with a significantly higher risk of metastasis. Staging of melanoma is essential for determining prognosis and guiding treatment. The staging is based on the extent of local invasion, lymph node involvement, and the presence of distant metastasis. Sentinel lymph node biopsy is often performed to evaluate regional lymph node involvement, as it is a key predictor of melanoma spread.

Treatment Options

Surgical resection remains the primary treatment for all stages of melanoma. The goal is to completely excise the tumor with clear margins to minimize the risk of recurrence. For melanomas that have not spread beyond the skin, complete surgical removal is curative. If melanoma is detected at a more advanced stage, a secondary procedure, called re-excision, is often performed to ensure that all malignant tissue is removed. For deeper tumors, a skin graft may be necessary to close the wound.

In cases of regional lymph node involvement or metastatic melanoma, additional treatments may be required, such as radiation therapy and chemotherapy. Radiation therapy is used to target residual cancer cells, particularly in areas where lymph nodes have been removed. Chemotherapy, which involves the use of cytotoxic drugs to kill cancer cells, has not shown significant effectiveness in treating melanoma. However, it may be used in combination with other treatments for advanced melanoma.

Recent Advances in Melanoma Treatment

In recent years, the treatment landscape for melanoma has changed dramatically, with the development of immunotherapy and targeted therapies that have significantly improved patient outcomes.

- **Immunotherapy:** Immunotherapy works by stimulating the body's immune system to recognize and attack melanoma cells. It can be administered systemically or locally. Systemic immunotherapy, such as immune checkpoint inhibitors (e.g., pembrolizumab and nivolumab), has revolutionized the treatment of advanced melanoma. These drugs block inhibitory signals that prevent immune cells from attacking the tumor, thereby enhancing immune response. Another approach involves the use of cytokines, such as interleukin-2, to boost the immune response.
- **Targeted Therapy:** Targeted therapies focus on inhibiting specific molecular pathways that contribute to melanoma cell growth. These therapies are particularly effective in patients with mutations in the BRAF gene, which is found in approximately 50% of melanoma cases. BRAF inhibitors, such as vemurafenib and dabrafenib, target the mutated BRAF protein, leading to inhibition of melanoma cell proliferation. When combined with MEK inhibitors like trametinib, these therapies can significantly improve progression-free survival in patients with metastatic melanoma.

Prognosis

The prognosis of melanoma depends on several factors, including the stage of the disease at diagnosis, the tumor's thickness and ulceration, and whether there is regional or distant metastasis. The five-year survival rate for patients with localized melanoma is high, exceeding 90%. However, once the disease spreads to distant organs, the survival rate drops significantly, making early detection and treatment crucial. Advances in immunotherapy and targeted therapies have greatly improved the prognosis for patients with metastatic melanoma, with some achieving long-term remission.

Conclusion

Melanoma is a potentially fatal form of skin cancer that can be effectively treated if detected early. Advances in surgical techniques, immunotherapy, and targeted therapies have significantly improved outcomes, even in advanced stages of the disease. Early detection through regular skin checks and timely treatment remain the most important factors in improving survival rates for melanoma patients.

References

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