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A REVIEW ARTICLE ON MELANOMA: DIAGNOSIS AND TREATMENT

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ABSTRACT

Melanoma is a serious form of skin cancer. Melanoma, also redundantly known as malignant melanoma. In approximately the 5th century BC, Hippocrates was the first to record a description of melanoma, which he described as melas, meaning dark, and oma, meaning tumor, in Greek. Is the type of skin cancer that develops from the pigment producing cells known as melanocytes. Melanoma begins when healthy melanocytes changes and grow out of control, forming a cancerous tumor. Melanoma can grow quickly. It can becomes life-threatening in as little as six weeks, and if untreated, it can spread to the parts of the body. In women they most commonly occur on the legs, while in men the most commonly occur on the back. Ultraviolet radiation is the main environmental factor that increase the risk of developing melanoma. It damage the DNA of your skin cells and they start to grow out of control. Exposure during childhood is a more risk factor than exposure in adulthood. Melanoma is relatively rare in people with darker skin. According to the American Cancer Society, in 2000 the lifetime risk of being diagnosed with melanoma will be approximately 1 in 75. Compare this with the lifetime risk in 1980, 1 in 250. So in this Malignant melanoma review article we will see new treatment/ therapy and self- helping techniques for patients.

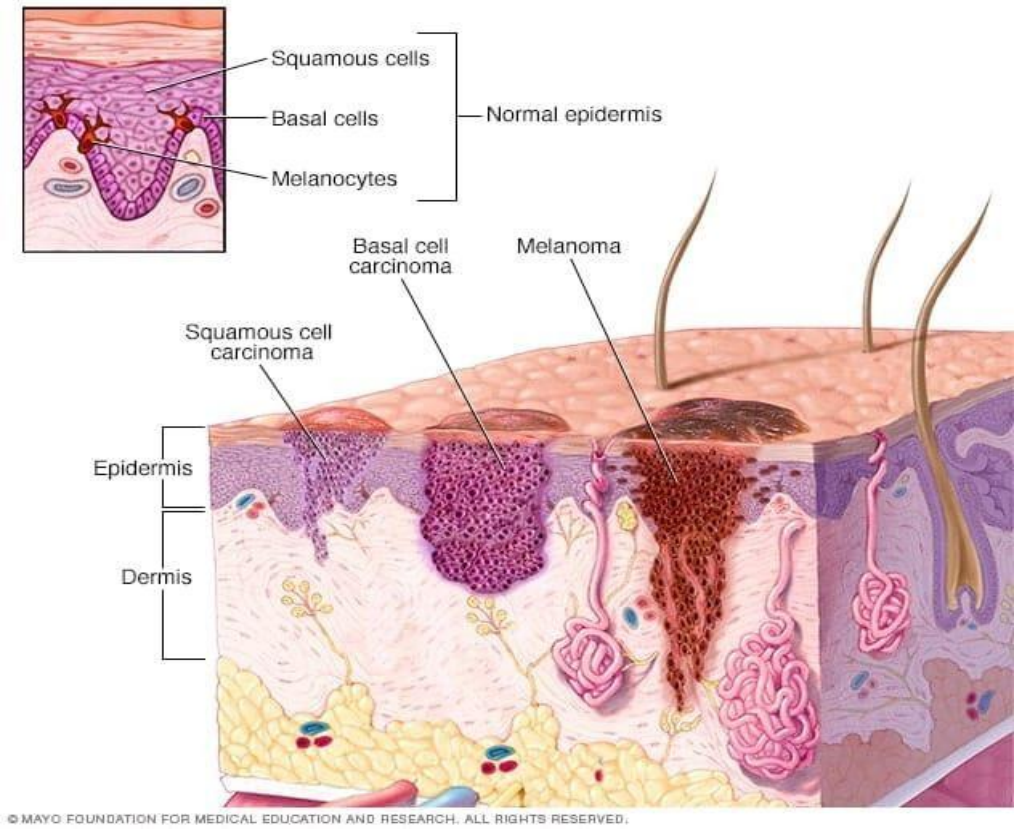
KEYWORDS: Malignant melanoma, Life-threatening, Cancerous tumor, Treatment.

INTRODUCTION

Skin cancer is an abnormal growth of skin cells. Skin cancer is also called as skin neoplasia. The three most common type are melanoma, Basal cell skin cancer, Squamous cell skin

cancer. Melanoma is a deadliest form of skin cancer. Identifying a potential skin cancer is not easy, and not all melanomas follow the rules. Melanomas come in many forms and may display none of the typical warning signs. It's also important to note that about 20 to 30 percent of melanomas develop in existing moles, while 70 to 80 percent arise on seemingly normal skin. A painless medical technique being used for early detection of melanoma is epiluminescence microscopy, or dermoscopy. Melanocytes are found between the outer layer of the skin (epidermis) and the next layer (dermis). They produce a pigment know as melanin, which gives skin it's color. There are two types of melanin: eumelanin and pheomelanin. When skin is exposed to ultraviolet (UV) radiation from the sun or tanning beds, it cause skin damage that triggers the melanocytes to produce more melanin, but only the eumelanin pigment attempts to protect the skin by causing the skin to darken or tan. Melanoma occurs when DNA damage from burning or tanning due to UV radiation triggers changes (mutation) in the melanocytes, resulting in uncontrolled cellular growth. Often the first sign of melanoma is a change in the shape, color, size or feel of an existing. Melanoma may also appear as a new mole. In more advanced melanoma, the texture of the mole may change. The skin on the surface may break down and look scrapped. If may becomes hard or lumpy.

The surface may ooze or bleed. Sometimes the melanoma is itchy, tender, or painful. Most people with melanoma need to have surgery. In some cases, melanomas may be treated by immunotherapy and targeted therapy, chemotherapy, and (less frequently) radiotherapy. Immunotherapy drugs may be used as a first-line treatment for melanoma and some other cancers, orthey may be used in combination with other treatments, such as chemotherapy and surgery. Melanoma rarely occurs before age 18 However, the risk of melanoma rises rapidly in young adulthood, making it one of the most common life - threatening form of cancer in people between the ages of 20 and 50. After age 50, the risk of melanoma rises more slowly with advancing age. Malignant is far more common now that it was 100 years ago. In the United States, more than 75,000 people are diagnosed withmelanoma each year slightly more men than women and nearly 10,000 die of it.



Signand Symptoms

Melanoma skin cancer often starts as an abnormal mole anywhere on the skin. A mole is a common non-cancerous growth. It is normally a small, round or oval spot that is usually brown, tan or black. It may be raised or flat. Most people have a fewmoles. A change in the colour, size or shape of a mole is usually the first sign of melanoma skin cancer. These changes can happen in a mole or spot that is already on your skin, or changes can appear as a new mole.

The ABCDE Rule of skin cancer is an easy-to-remember system for determining whether a mole or growth may be cancerous. They describe the physical condition and/or progression of any skin abnormality that would suggest thedevelopment of a malignancy.

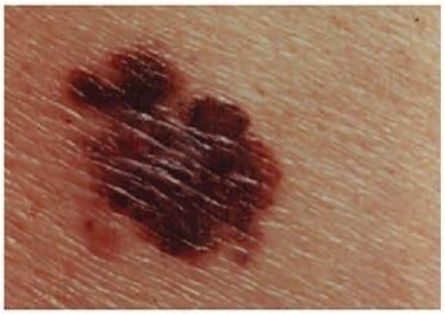
A is for Asymmetry: Most melanomas are asymmetrical. If you draw a line through the middle of the lesion, the two halves don't match, so it looks different from a round to oval and symmetrical common mole.

B is for Border: Melanoma borders tend to be uneven and may have scalloped or notched edges, while common molestend to have smoother, more even borders.

C is for Color: Multiple colors are a warning sign. While benign moles are usually a single shade of brown, a melanoma mayhave different shades of brown, tan or black. As it grows, the colors red, white or blue may also appear.

D is for Diameter or Dark: While it's ideal to detect a melanoma when it is small, it's a warning sign if a lesion is the size ofa pencil eraser (about 6 mm, or ¼ inch in diameter) or larger. Some experts say it is also important to look for any lesion, nomatter what size, that is darker than others.

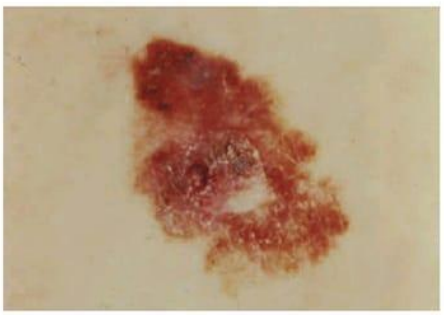
E is for Evolving: Any change in size, shape, color or elevation of a spot on your skin, or any new symptom in it, such asbleeding, itching or crusting, may be a warning sign of melanoma.



Asymmetrical (irregular shape)

Border (irregular or jagged border)

Color (more than one color identified or uneven coloring)



Diameter (>6 mm or roughly the size of a pencil eraser)

Evolving (change that occurs over weeks or months)

CAUSES

UV Rays

Exposure of ultraviolet radiation from sun frequently , especially in those with low level of skin pigment due to radiation exposure a DNA damage to skin cells and form a malignant tumor,[2],[10] UV light doesn't causes all melanomas, especially those part of body which don't receive exposure to sunlight. This indicates may be other factor contribute to risk of melanoma.

Fair Skin

Having less pigment (melanin) in your skin means you have less protection from damaging UV radiation. If you have blond or red hair, light-colored eyes, and freckle or sunburn easily, you're more likely to develop melanoma than is someone with a darker complexion. But melanoma can develop in people with darker complexions, including Hispanic people and black people.

A family history of melanoma

If a close relative — such as a parent, child or sibling — has had melanoma, you have a greater chance of developing amelanoma, too.

Weak Immune System

A weakened immune system caused by AIDS, immunosuppressive drugs, or certain cancers.

Types of melanoma

Melanoma skin cancer can grow into and destroy nearby tissue. It can also spread (metastasize) to other parts of the body. Melanoma skin cancer is also called cutaneous melanoma and malignant melanoma of the skin.

There are 4 main types of melanoma skin cancer

Superficial spreading melanoma

It is the most common type of melanoma, accounting for around 70 percent of all cases. It starts growing along the top layer of the skin. Overtime it penetrates deeper into the skin.

Nodular melanoma

Nodular melanoma is the second most common type of melanoma skincancer. It makes up about 15% to 20% of all melanoma skin cancers.

Nodular melanoma are aggressive and usually develop more rapidly than superficial melanoma.

Lentigo maligna melanoma

Lentigo maligna is a subtype of melanoma in situ that is characterized by an atypical proliferation of melanocytes within the basal epidermis; lentigo maligna that invades the dermis is termed lentigo maligna melanoma.[1] Lentigo maligna melanoma is most often found on sun- exposed skin in the head and neck of middle-aged and elderly person andis slightly more common in women. It makes up about 15% to 20% of all melanoma skin cancer.

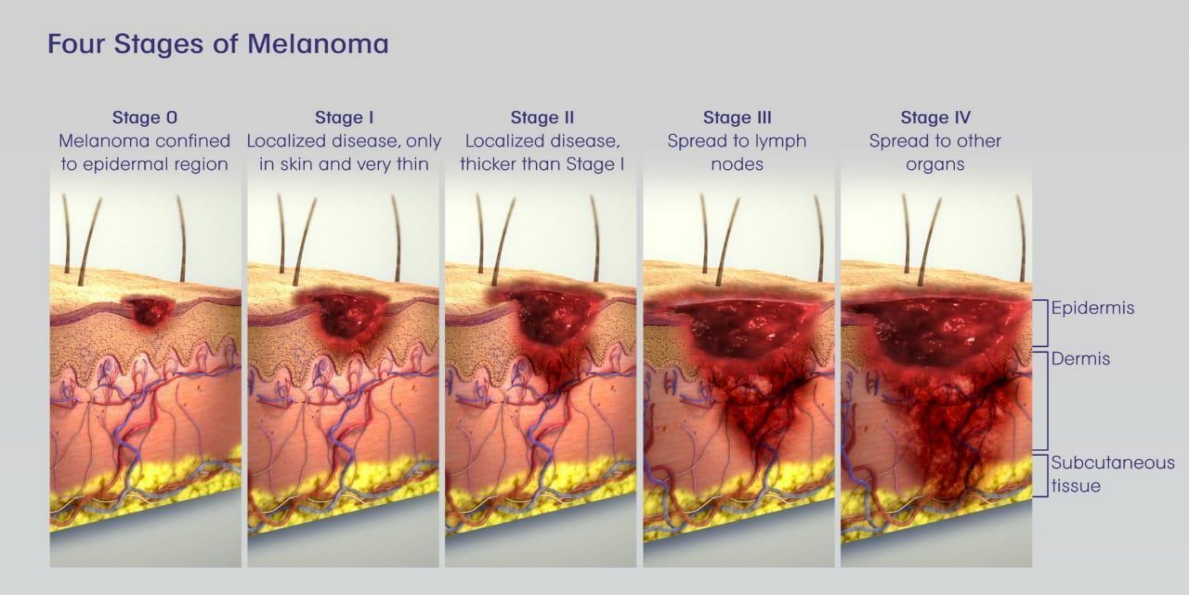
Acral lentiginous melanoma

Acral lentiginous melanoma (ALM) is a form of skin cancer that appears on the palms of the hands, the soles of the feet, or under the nails. Acral lentiginous melanoma is the most common subtype in people with darker skins and is rare in people with lighter skin types. Acral lentiginous melanoma are aggressive and large, with an average diameter of 3 cm.

STAGES OF MELANOMA

These are the stages of melanoma

- **Stage 0:** The melanoma involves only the top layerof skin. It is called melanoma in situ.
- **Stage I**: The tumor is no more than 1 millimeterthick (about the width of the tip of a sharpenedpencil.) The surface may appear brokendown. Or, the tumor is between 1 and 2 millimeter thick, andthe surface is not broken down.
- **Stage II:** The tumor is between 1 and 2 millimeterthick, and the surface appears broken down. Or, thethickness of the tumor is more than 2 millimeter, and the surface may appear broken down.
- **Stage III:** The melanoma cells have spread to atleast one nearby lymph node. Or, the melanomacells have spread from the original tumor totissuesnearby.
- **Stage IV:** Cancer cells have spread to the lung orother organs, skin areas, or lymph nodes far awayfrom the original growth. Melanoma commonlyspreads to other parts of the skin, tissue under theskin, lymph nodes, and lungs. It can also spread tothe liver, brain, bones, andother organs.



Diagnosisof melanoma

Diagnosis is the process of finding out the cause of health problems. A melanoma diagnosis usually begins with a visual examination. If you have a change on your skin, your doctor mustfind out whether or not the problem is from cancer. You may need to see a dermatologist, a doctor who hasspecial training in the diagnosis and treatment of skin problems. Your doctor will check the skin all over your bodyto see ifother unusual growths are present. If your doctor suspects that a spot on the skin iscancer, you may need a biopsy. For a biopsy, yourdoctor may remove all or part of the skin that does notlook normal. The sample goes to a lab A pathologistchecks the sample under a microscope. Often, the pathologist can easily tell whether these cellsrepresent melanoma or a non-cancerous mole. Many of the same tests used to diagnose cancer are used to find out the stage (how far the cancer has spread).

The following tests are usually used to rule out or diagnose melanoma skin cancer

Skin exam

A skin exam is often part of a physical exam Your doctor will check the entire surfaceof your skin and look for any abnormal moles or spots.

Skin Biopsy

During a skin biopsy, the doctor removes tissues or cells from the skin so they can be tested in a lab. A report from the pathologist will confirm whether or not cancer cells are found in the sample. The type of biopsy used often depends on whatthe growth looks like and its size.

There are four common types of skin biopsies

- **Shave biopsy:** The doctor uses a thin, sharp blade toshave off the abnormal growth.
- **Punch biopsy:** The doctor uses a sharp, hollow toolto remove a circle of tissue from the abnormal area.
- **Incisional biopsy:** The doctor uses a scalpel toremove part of the growth.
- **Excisional biopsy:** The doctor uses a scalpel toremove the entire growth and some tissue around it. This type of biopsy iS most commonly used forgrowths that appear to be melanoma.

Blood test

Blood tests measure certain cells or substances in the blood. They often provide helpful information about your general health, how some organs are working, other medical conditions and how you might respond to treatment. Lactate dehydrogenase (LDH) is a tumour marker used to help stage advanced melanoma skin cancer and estimate a prognosis. Higher levels of LDH may mean that the melanoma skin cancer has spread to other parts of the body, such as the liver. It can also mean that the cancer will be harder to treat. Other tests of blood cell counts and blood chemistry levels may be done in a person who has advanced melanoma to see how the bone marrow (the soft spongy area of the bone where new blood cells are made), liver, and kidneys are responding during treatment.

Imaging Test

Melanoma is more likely than other skin cancers to metastasize, or spread to distant bones or distant organs. Several medicalimaging procedures, including CT scan, MRI, PET scan or X-ray, may be used to detect cancer cells or tumors throughout the body.

Chest x-ray

This test might be done to help determine if melanoma has spread to the lungs.

CT scan (computed tomography)

This is a powerful X-ray that makes detailed pictures inside your body's soft tissues. You lie on a table, and it rotates around you taking several pictures. If the melanoma has spread, it can show the size of a tumor. Sometimes doctors order a "contrast medium" or special dye to provide more detail on the image. Before a contrast scan, you'll get the dye injected into your veinor as a Magnetic resonance imaging (MRI) uses radio waves and strong magnets instead of X-rays to take images of tissue in different parts of the body and can show if the cancer has

spread.

MRI (magnetic resonance imaging): It uses powerful magnets and radio waves to make pictures of organs and structuresinside your body. For melanoma, an MRI can detect the tumor and measure its size.

Positron emission tomography (PET) or PET-CT scan

A PET scan is usually combined with a CT scan (see above), called a PET-CT scan. A PET scan is a way to create pictures of organs and tissues inside the body. A small amount of a radioactive sugar substance is injected into the patient's body. This sugar substance is taken up by cells that use the most energy. Because cancer tends to use energy actively, it absorbs more ofthe radioactive substance. A scanner then detects this substance to produce images of the inside of the body.

Treatment

Treatment for skin cancer depends on the type and stage of the disease, the sizeand place of the tumor, and your general health and medical history. In mostcases, the goal of treatment is to remove or destroy the cancer completely. Most skin cancer can be cured if if found and treated early. You may have a teamof specialists to help plan. Your treatment. Specialists who treat skin cancer include dermatologists and surgeons. Some people may also need a plastic surgeon. People with advanced skin cancer may be referred to a medical oncologist or radiation oncologist. Surgery is the usual treatment for people withskincancer. In some cases, the doctor may suggest chemotherapy, radiation therapy. People with melanoma may also have biological therapy.

Surgery

Surgery is the preferred treatment for small and/or early-stage melanomas. This is because it can often remove theenti Surgery: Surgery is the preferred treatment for small and/or early-stage melanomas. This is because it can oftenremove the entire cancerous area completely with little to no damage to other parts of the body.

The following are the most common types of surgery used to treat melanoma

Wide Excision

If an excisional biopsy cannot remove an entire tumor, then doctors may recommend wide excision surgery. This is a minor procedure in which the doctor will cut out the tumor before

it can grow and spread any further. This can often be done in adoctor's office as an outpatient procedure.

The step-by-step process of a wide excision will likely resemble the following:

Preparation: The area that will be removed is cleaned and disinfected. Anesthesia: A local anesthesia is injected into thearea so that it is completely numb.

Excision: The mole or tumor is removed, along with a thin margin of skin around it.

Analysis: A small sample of the surrounding skin is analysed under a microscope to look for cancerous cells. If some arefound, a wider excision may be made or another type of treatment (such as radiation therapy) may be recommended.

Closure: Once the tumor has been completely removed, the wound is stitched back together. The risks for this type ofprocedure are minimal, but may include bleeding, swelling, infection, or nerve damage.

Lymph node dissection

If the initial biopsy reveals that the melanoma has spread beyond the skin to surrounding lymph nodes, then it may be necessary to remove the lymph nodes in that region. This helps eliminate the most likely paths for the cancer to spread, preventing it from traveling to other organs. While a lymph node dissection is a more major procedure than a wide excision, its specifics will vary depending on the number and location of lymph nodes that need to be removed.

The following is the general step-by-step process of a lymph node dissection

Preparation

The patient undergoes a final physical exam so staff can start preparing them for surgery. Anesthesia: Just before surgery, an anesthesiologist will give the patient general anesthesia. This will put them into a deep sleep for the entirety of the operation.

Incision: The surgeon will begin by making an incision in order to access the infected lymph nodes. The size and location ofthis incision will depend on the lymph nodes that need to be removed.

Removal: The regional lymph nodes are removed and sent off for analysis. The surgeon will also insert a small tube into theincision to help drain fluid from the area and speed up recovery.

Closure: When all bleeding is controlled, the surgeon sews the incision closed. After this procedure, each lymph node that was removed is analysed for cancerous cells. This information helps doctors determine the stage of the cancer and decide if further treatment will be necessary. Risks of lymph node dissection include infection, nerve damage, and swelling from the build up of fluid (lymphedema).

Chemotherapy

Chemotherapy for melanoma skin cancerChemotherapy uses anticancer (cytotoxic) drugs to destroycancer cells. It is sometimes used to treat melanoma skin cancer.

Chemotherapy is given for different reasons. You may have chemotherapy to

1. Stop or control the growth and spread of cancer cells.
2. Shrink a tumourrelieve pain or control the symptoms of advanced melanoma skin cancer (calledpalliative chemotherapy)
3. Chemotherapy may be given as a systemic therapy or a regional therapy.

Systemic Chemotherapy

Systemic chemotherapy is when the drugs travel through the blood to reach and destroy cancer cells all over the body, including those that may have broken away from the primary tumour on the skin. It is mainly used to help shrink and control the growth of metastatic melanoma skin cancer.

Regional chemotherapy

In regional chemotherapy, the drug is given directly to a specific area of the body. It is rarely given, but may be used for locally recurrent melanoma skin cancer that is only in one arm or leg. It can be done when there are many large tumoursthat can't be removed with surgery.

The following are chemotherapy drugs that may be used alone or in combination to treat melanoma skin cancer: dacarbazine (DTIC) – this is the most common drug used temozolamide (Temodal) carboplatin (Paraplatin, Paraplatin AQ) paclitaxel (Taxol)cisplatin (Platinol AQ)vinblastin (velbel).

Most of these chemotherapy drugs are given through a needle into a vein (intravenously),

except temozolomide, which is given by mouth (orally). Dacarbazine (DTIC; available as a generic drug) is the only FDA-approved chemotherapy for melanoma. Temozolomide (Temodar) it is used for the treatment of stage IV melanoma. Both DTIC and temozolomide have been shown to shrink melanoma for about 12% to 15% of patients. However, no clinical trials have tested whether these drugs help people with melanoma live longer after treatment. Both drugs have a limited number of side effects. Other chemotherapies used to treat melanoma include a generic drug called cisplatin, fotemustine (Muphoran, which is only approved in Europe) lomustine (Gleostine), the taxanes (a group of drugs that includes docetaxel [Taxotere] and paclitaxel [Taxol]), and another generic drug called vinblastine. Combinations of chemotherapy drugs may be used, such as paclitaxel plus carboplatin or cisplatin combined with vinblastine and dacarbazine. Some chemotherapy combinations may have a higher chance of causing melanoma to shrink, but they also cause more side effects. How oftenlong chemotherapy is given depends on the type of drug used, the dose and if other treatments are used.

Radiation Therapy

Radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. The radiation beam produced by this machine can be pointed in different directions and blocked using special techniques to help decrease side effects. The radiation oncologist will recommend a specific radiation therapy regimen, or schedule, with a total number of treatments and dose of radiation. Sometimes, radiation therapy is recommended after surgery to prevent the cancer from coming back, called a recurrence. Radiation therapy given in this manner is called adjuvant radiation therapy. Research has shown that although this may reduce the risk of the melanoma coming back in the area that received radiation, it does not increase how long a person lives. People who receive adjuvant radiation therapy experience side effects based on which area of the body was treated. If melanoma that has spread and causes symptoms, such as bone pain or headaches, then radiation therapy may help relieve those symptoms. This is called palliative radiation therapy. For some people, palliative radiation therapy is given to an entire organ with several small doses of radiation, such as to the entire brain using whole-brain radiation therapy. Other times, 1 or just a few high doses of radiation therapy are given using a linear accelerator (or "linac," for short), Gamma Knife, CyberKnife, or TomoTherapy units. This is called stereotactic radiosurgery, stereotactic ablative radiation therapy, or stereotactic body

radiation therapy. It usually works best for just 1 or a few tumors in the brain or elsewhere in the body. Radiation therapymay be used when cancer has extensive spread to the lymph nodes or skin and cannot be removed by surgery.

Immunotherapy

Immunotherapy for melanoma skin cancerSome people with melanoma skin cancer have immunotherapy. Immunotherapyhelps to strengthen or restore the immune system's ability to fight cancer. Immunotherapy is sometimes called biological therapy or targeted therapy depending on how it works.

You may have immunotherapy to

1. Lower the risk that the cancer will come back (recur). 2. Stop or control the growth and spread of cancer cells. 3. Shrink metastatic melanoma skin cancer.

Immunotherapy drugs used for melanoma skin cancer. The following types of immunotherapy drugs are used to treatmelanoma skin cancer.

Cytokines

Cytokines are proteins made by certain cells of the immune system. They can also be made in a lab and given as a drug.Cytokines act as chemical messengers so the immune system cells communicate with each other and help control the immune response. Interferons and interleukins are types of cytokines.

Interferon alfa-2b (Intron A)

It is a type of cytokine that may be used for early stage or locally advanced melanoma skin cancer. It is mainly used after surgery to lower the risk of the cancer coming back. High doses of the drug are given by injection several days each week for1 year. Usually the injections are given into a vein (intravenous) for the first 4 weeks. Then the injections are given into the tissue under the skin (subcutaneous) for the rest of the year.

Interleukin-2 (aldesleukin, Proleukin)

It is also a type of cytokine that may be used to help shrink and control the growth of metastatic melanoma skin cancer. Many doses of the drug are injected 2 or 3 times per day for 1 to 2 weeks. Interleukin-2 may also be used to treat locally recurrent melanoma skin cancer when there are many tumours on the skin that can't be removed with surgery. The drug isinjected directly into a tumour (called intralesional treatment).

Immune checkpoint inhibitors

The immune system normally stops itself from attacking normal cells in the body by using specific proteins called checkpoints, which are made by some immune system cells. Melanoma skin cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. Immune checkpoint inhibitors are drugs that work by blocking the checkpoint proteins so immune system cells (called T cells) can attack and kill the cancer cells. Immune checkpoint inhibitorsare monoclonal antibodies, which are substances that find and attach to a specific antigen on a cancer cell. Sometimes they are given along with chemotherapy.

Ipilimumab (Yervoy): It is an immune checkpoint inhibitor that targets the CTLA-4 checkpoint protein. It is used to help shrink and control the growth of metastatic or unresectable melanoma skin cancer. It is given through a needle into a vein (intravenous infusion) once every 3 weeks for a total of 4 doses.

Nivolumab (Opdivo): It is an immune checkpoint inhibitor that also targets the PD-1 checkpoint protein. It may be used after surgery that completely removes stage 3 or stage 4 melanoma to lower the risk of the cancer coming back (recurring). Nivolumab is also used to help shrink and control the growth of metastatic or unresectable melanoma skin cancer. It can be given alone when there is a change (mutation) in the BRAF gene or given in combination with ipilimumab. It is given through a needle into a vein (intravenous infusion) once every 2 or 3 weeks until the disease progresses or the side effects outweigh the benefits of having the treatment.

Pembrolizumab (Keytruda): It is an immune checkpoint inhibitor that targets the PD-1 checkpoint protein. It may be usedafter surgery that completely removes stage 3 melanoma to lower the risk of cancer coming back (recurring).

Pembroluzumab is also used to help shrink and control the growth of metastatic or unresectable melanoma skin cancer. It is given through a needle into a vein (intravenous infusion) once every 3 weeks until the disease progresses or the side effects outweigh the benefits of having the treatment.

CONCLUSION

According to our findings, melanoma accounts for only about 1% of skin cancers. Unusual

moles, sores, lumps, blemishes, markings are the sing of melanoma. Males tend to have the highest incidence of melanoma on the head and neck than females. Improving the melanoma patients lifestyle is relevant to the regular body checkup andhow to protect your skin from sun burns. Melanoma is usually curable when detected and treated early .Our data show the more options of treatment and diagnosis for melanoma skin cancer.

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