Squamous cell carcinoma

see Squamous cell lung cancer.

Squamous cell carcinoma (SCC) is a type of cancer that arises from squamous cells, which are thin, flat cells found in the outer layer of the skin (epidermis) and in the lining of various organs and cavities of the body, such as the respiratory and digestive tracts. SCC can occur in many parts of the body, including the skin, lungs, head and neck, esophagus, cervix, and more. The classification of squamous cell carcinoma is primarily based on histological features and the site of origin.

1. **Classification by Histological Differentiation:**

Squamous cell carcinomas are often classified based on their degree of differentiation, which refers to how much the cancer cells resemble normal squamous cells under a microscope. This classification helps in assessing the aggressiveness of the tumor.

- **Well-Differentiated SCC:**

1. Cells closely resemble normal squamous cells and tend to form keratin (a key structural protein in skin).
2. These tumors usually grow more slowly and are less likely to spread compared to poorly differentiated SCCs.
3. Histologically, these cancers show prominent keratinization and intercellular bridges.

- **Moderately Differentiated SCC:**

1. Intermediate in terms of cellular appearance and behavior.
2. These tumors show some keratinization but not as much as well-differentiated SCCs.
3. They may have a higher tendency to invade nearby tissues and metastasize than well-differentiated tumors.

- **Poorly Differentiated SCC:**

1. Cells appear very abnormal and bear little resemblance to normal squamous cells.
2. These tumors usually lack keratinization and can be highly aggressive with a higher propensity for rapid growth and metastasis.
3. Histologically, they show minimal differentiation with sparse or no keratinization, and the cell structure is often more chaotic and irregular.

- **Undifferentiated SCC:**

1. Extremely abnormal cells with no resemblance to normal squamous cells.
2. These tumors are typically very aggressive, with a high tendency for invasion and metastasis.
3. Histological features are similar to poorly differentiated SCCs but may show even less cellular differentiation.

2. **Classification by Keratinization:**

Keratinization refers to the production of keratin, a protein that gives skin its strength and resilience.

Based on keratinization, SCC can be further classified as:

- **Keratinizing SCC:**

1. Produces visible keratin pearls or whorls within the tumor.
2. More common in well-differentiated SCCs.
3. Typically has a more favorable prognosis than non-keratinizing types.

- **Non-Keratinizing SCC:**

1. Does not produce visible keratin and usually presents with less differentiated cells.
2. More likely to be poorly differentiated and aggressive.
3. Commonly found in areas like the oropharynx and cervix.

3. **Classification by Anatomical Site:**

Squamous cell carcinoma can develop in various anatomical sites, each with distinct biological behaviors and clinical implications. Some common sites include:

- **Cutaneous SCC (Skin):**

1. The most common type of SCC, typically arises due to prolonged sun exposure and is found on sun-exposed areas such as the face, ears, neck, and hands.
2. Generally has a good prognosis if detected early and treated properly.
3. Risk factors include UV radiation, immunosuppression, and chronic wounds or scars.

- **Head and Neck SCC:**

Head and neck squamous cell carcinoma

- **Lung SCC:**

1. One of the major histological types of non-small cell lung cancer (NSCLC).
2. Typically arises in the central bronchi and is strongly associated with smoking.
3. Symptoms may include cough, hemoptysis, and obstructive pneumonia.

- **Esophageal SCC:**

1. Commonly found in the upper and middle thirds of the esophagus.
2. Risk factors include smoking, heavy alcohol consumption, and dietary factors.
3. Symptoms include dysphagia (difficulty swallowing) and weight loss.

- **Cervical SCC:**

1. The most common histological subtype of cervical cancer.
2. Strongly associated with persistent infection with high-risk types of human papillomavirus (HPV).
3. Often detected through screening methods like Pap smears and HPV testing.

- **Anal SCC:**

1. Often associated with HPV infection, particularly in individuals with immunosuppression (e.g., HIV infection).
2. Symptoms may include rectal bleeding, pain, and changes in bowel habits.

4. **Classification by Growth Patterns and Molecular Features:**

Some squamous cell carcinomas are classified based on their growth patterns or molecular characteristics:

- **Basaloid SCC:**

1. A subtype that features a basaloid (basal cell-like) appearance under the microscope.
2. Often found in the head and neck region and may have a more aggressive clinical course.

- **Verrucous Carcinoma:**

1. A well-differentiated variant of SCC that grows in a slow, exophytic (outward-growing) manner.
2. Typically found in the oral cavity, larynx, and anogenital region.
3. Less likely to metastasize but can be locally invasive.

- **Papillary SCC:**

1. Characterized by papillary (finger-like) projections of squamous epithelium.
2. Can occur in various locations, including the head and neck and respiratory tract.

- **HPV-Associated SCC:**

1. SCCs associated with human papillomavirus infection, particularly types 16 and 18.
2. Commonly found in the oropharynx, cervix, and anus.
3. Typically have distinct molecular features, such as overexpression of p16 protein, and tend to respond differently to treatment compared to HPV-negative SCCs.

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The classification of squamous cell carcinoma into various categories helps in determining the prognosis, appropriate treatment strategies, and potential outcomes for patients. It is based on factors like histological differentiation, keratinization, anatomical site, growth patterns, and molecular features. Understanding these classifications allows healthcare providers to better tailor treatments and predict the behavior of the cancer.

Treatment

Squamous Cell Carcinoma Treatment

The treatment of squamous cell carcinoma (SCC) depends on various factors, including the type, location, stage, and grade of the cancer, as well as the overall health of the patient. Here’s an overview of common treatment options:

1. Surgical Treatment

- **Excision:**

For early-stage SCCs, surgical excision is often the primary treatment. The tumor is removed along with a margin of surrounding healthy tissue to ensure complete removal and reduce the risk of recurrence.

- **Mohs Micrographic Surgery:**

A specialized technique used primarily for skin SCCs, particularly on the face, ears, and other cosmetically sensitive areas. Involves removing the cancerous tissue layer by layer and examining each layer microscopically until no cancerous cells are detected.

- **Laser Surgery:**

Uses a focused beam of light to remove or destroy cancerous tissue. Often used for superficial SCCs or to treat SCCs in areas where traditional surgery might be challenging.

- **Cryotherapy:**

Involves freezing the tumor with liquid nitrogen to destroy cancer cells. Typically used for superficial SCCs or precancerous lesions.

- **Electrodesiccation and Curettage (ED&C):**

Involves scraping off cancerous tissue with a curette and using electrical currents to destroy remaining cancer cells. Suitable for superficial skin SCCs.

2. Radiation Therapy

- **External Beam Radiation Therapy (EBRT):**

Uses high-energy rays to target and destroy cancer cells. It is often used for SCCs that cannot be surgically removed or in patients who are not surgical candidates.

- **Brachytherapy:**

Involves placing a radioactive source directly inside or near the tumor. May be used for localized SCCs in specific sites, such as the cervix or prostate.

3. Chemotherapy

- **Topical Chemotherapy:**

Involves applying chemotherapy drugs directly to the skin or mucous membranes. It is used for superficial SCCs or actinic keratosis.

- **Systemic Chemotherapy:**

Involves administering chemotherapy drugs orally or intravenously to treat more advanced or metastatic SCCs. Commonly used when SCC has spread beyond the primary site.

4. Targeted Therapy

- **Small Molecule Inhibitors:**

Drugs that target specific molecules involved in cancer cell growth and survival. For SCCs, these might include agents targeting growth factor receptors or signaling pathways.

- **Monoclonal Antibodies:**

Laboratory-made molecules that can bind to specific cancer cell proteins or immune system proteins to help the immune system target and destroy cancer cells.

5. Immunotherapy

- **Checkpoint Inhibitors:**

Drugs that help the immune system recognize and attack cancer cells by blocking proteins that inhibit immune responses. Commonly used for advanced SCCs, particularly those with high PD-L1 expression or associated with HPV.

- **Cancer Vaccines:**

Although still under research, vaccines designed to stimulate the immune system to recognize and fight cancer cells might be used in the future.

6. Hormonal Therapy

- **Hormonal Treatment:**

Less common for SCCs but may be used if SCC has hormone receptors, though this is more typical in other types of cancers like breast cancer.

7. Palliative Care

- **Symptom Management:**

Focuses on relieving symptoms and improving quality of life for patients with advanced or terminal SCC. Includes pain management, nutritional support, and psychological support.

8. Multimodal Treatment

- **Combination Therapy:**

Often, a combination of treatments is used to achieve the best outcomes. For instance, surgery may be followed by radiation or chemotherapy to ensure complete eradication of cancer and address any remaining cells or metastases.

Treatment Planning

- **Individualized Approach:**

Treatment plans are tailored to each patient based on the specifics of their SCC, overall health, and preferences. A multidisciplinary team, including oncologists, surgeons, radiologists, and pathologists, collaborates to develop the most effective treatment strategy.

- **Follow-Up Care:**

Regular follow-up is essential to monitor for recurrence, manage side effects, and address any new symptoms.

Summary

The management of squamous cell carcinoma involves a range of treatment modalities tailored to the tumor's characteristics and the patient's condition. Early-stage SCCs may be treated effectively with surgery or localized therapies, while advanced or metastatic SCCs often require a combination of surgery, radiation, chemotherapy, and targeted or immunotherapies. The treatment approach is personalized and managed by a team of specialists to optimize outcomes and quality of life.

Prognosis

Squamous cell carcinoma of the skin is usually not life-threatening, though it can be aggressive. Untreated, squamous cell carcinoma of the skin can grow large or spread to other parts of your body, causing serious complications.

Squamous cell carcinoma is the most common type of sinonasal malignancy. Despite improvements in surgical resection and adjuvant therapy, which are considered the standard of care, the outcome for patients with locoregionally advanced disease remains poor. The objective of this study was to investigate the role of induction chemotherapy in patients with locoregionally advanced sinonasal squamous cell carcinoma and to determine the oncologic outcomes in those patients.

Methods: The study included 123 consecutive patients with previously untreated, locoregionally advanced (stage III and IV) sinonasal squamous cell carcinoma who were treated with curative intent at The University of Texas MD Anderson Cancer Center between 1988 and 2017 with induction chemotherapy followed by definitive local therapy. Patient demographics, tumor staging, treatment details, and oncologic outcomes were reviewed. The outcomes of this study included response to induction chemotherapy, recurrence, organ preservation, and survival.

Results: The median follow-up was 32.6 months (range, 12.4-240 months). Of the 123 patients, 110 (89%) had T4 disease, and 13 (11%) had T3 disease. Lymph node metastases at the time of presentation was observed in 36 patients (29.3%). The overall stage was stage IV in 111 patients (90.2%) and stage III in 12 patients (9.8%). The chemotherapy regimen consisted of the combination of a platinum and taxanes in most cases (109 patients; 88.6%), either as a doublet (41 patients) or in

combination with a third agent, such as 5-fluorouracil (34 patients), ifosfamide (26 patients), or cetuximab (8 patients). After induction chemotherapy, 71 patients (57.8%) achieved at least a partial response, and 6 patients had a complete response. Subsequent treatment after induction chemotherapy was either: 1) definitive chemoradiation or radiation followed by surgical salvage for any residual disease, or 2) surgery followed by adjuvant radiation or chemoradiation. Overall, 54 patients (49.5%) underwent surgical resection. The 2-year overall and disease-free survival rates for the whole cohort were 61.4% and 67.9%, respectively. The rate of orbital preservation was 81.5%. The recurrence rate was 26.8% (33 patients), and distant metastases occurred in 8 patients (6.5%). Patients who had at least a partial response or stable disease had significantly better overall and disease-free survival than those who had progressive disease (P = .028 and P = .021, respectively).

Conclusions: The current results indicate that a high proportion of patients with sinonasal squamous cell carcinoma achieved a favorable response to induction chemotherapy. The data suggest that response to induction chemotherapy is associated with an improved outcome and a good chance of organ preservation. The oncologic outcomes in this cohort with locally advanced (mostly T4) disease are better than those historically reported in the literature. Further study of induction chemotherapy in patients with advanced sinonasal squamous carcinoma is warranted [1)].

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Abdelmeguid AS, Teeramatwanich W, Roberts DB, Amit M, Ferraroto R, Glisson BS, Kupferman ME, Su SY, Phan J, Garden AS, Raza SM, DeMonte F, Hanna EY. Neoadjuvant chemotherapy for locoregionally advanced squamous cell carcinoma of the paranasal sinuses. Cancer. 2021 Feb 10. doi: 10.1002/cncr.33452. Epub ahead of print. PMID: 33567468.