Immunology in Head and Neck Cancer

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Tumor Immunology

- recognize and react against tumors
- prevent initial appearance or limit growth
- recognition not as effective
- histology shows mononuclear infiltrate
- patients with impaired immunocompetence
- complex role
Malignant Transformation

- result of errors in genetic programming
- chemical, physical, or viral carcinogens
- multistep process
  - **initiation** : alterations in cellular DNA
  - **promotion** : altered presentation of genetic information
  - **progression** : abnormal phenotypes cloned
Risk Factors for Head and Neck Cancer

- Tobacco: carcinogens initiate and promote
- Alcohol: additional promoter
- Viruses: Ebstein-Barr and HSV
- Nutritional status
- Ionizing radiation: injures cellular DNA
- Interference with immunity
Immunosuppression

- etiology is multifactorial
- alcoholism: abnormalities in B and T cells
- malnutrition: impairs B and T cell response
- viruses: effect immunity
- aging: cellular immunity wanes
- tobacco: decrease cytotoxicity and reactivity
Immune Recognition of Tumors

- immunosurveillance
- tumor-specific antigens
- tumor-associated antigens
- monoclonal antibody technology
- major histocompatibility complex
- still inadequate immune response to tumor
Immunologic Escape

- tumor kinetics
- antigenic modulation
- antigen masking
- blocking factors
- tolerance
- genetic factors
- tumor products
- growth factors
Immune Response to Tumor

- Cellular immune system
- Humoral immune system
Cell-mediated Immunity

- helper, suppressor, and cytotoxic lymphocytes
- activation produces lymphokines
- patients have altered immune function
- peripheral total lymphocytes
- Wanebo et al - decrease in total B and T cells and decreased stimulation
Regional Immune Reactivity

- draining lymph node morphology
- Berlinger et al - evaluated 84 patients
- active immunological response - greater five year survival
- depleted or unstimulated response - no patients alive at five years
- relationship between regional immunoreactivity and survival
Humoral Immunity

- augments cellular response
- immunoglobulins
  - serum glycoproteins produced by B cells
  - specificity in binding to substrate
  - two heavy and two light chains
  - heavy chain type determines class
  - variable region is antigen binding site
Response to Cancer

- **Immunoglobulins**: IgG and IgA primarily
  - **IgG**: functions by fixing complement and via ADCC
  - **IgA**: confers protective effect to tumor
- **Immune complexes**: elevated in patients
- **Cytokines**: interleukin, interferon, growth factor, and colony-stimulating factor
Interferon

- three subclasses
  - type I: interferon alpha and beta
  - type II: interferon gamma
- mediate a large range of biologic responses
- interferon gamma
  - direct cytotoxic effects
  - combined with chemotherapy
  - enhances antitumor effects of other cytokines
Interleukins

- Interleukin 1
  - immunologic, inflammatory, and reparative
  - induces production of interleukin 2
- Interleukin 2
  - produced by activated T lymphocytes
  - stimulates T, B, and NK cell proliferation
- Interleukin 4
- Tumor growth factor beta
Potential for Therapy

- **Active immunotherapy**
  - administer agents that activate immune reaction
  - goal is to stimulate areas responsible for antitumor immunity

- **Passive immunotherapy**
  - administer externally stimulated immunologic components
  - initially obtained from patient
Active Immunotherapy

- Tumor Vaccines: development limited
- Biological Response Modifiers
  - BCG
  - interferon
  - interleukin 2
Passive Immunotherapy

- Monoclonal Antibodies
- Cytotoxic Reagents
  - radioisotopes
  - toxins
  - chemotherapeutic drugs
  - cytokines
Conclusion

• immunosuppression more frequent
• patients have leukocytes with antitumor reactivity
• attempts at immunotherapy are not effective
• study may lead to improvement in diagnosis and to determining prognosis