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THE EFFECTS OF RADIATION THERAPY ON LEUKOCYTES

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Abstract

Radiation therapy (RT) is used in 50–60% of cancer patients. Studies show that up to 70% of patients develop radiation-induced lymphopenia (RIL), which correlates with poor survival outcomes. This article reviews mechanisms, clinical data, and modern strategies.

Keywords

Radiation therapy; Leukocytes; Lymphopenia; Immunosuppression; Hematopoiesis; Radiobiology

Introduction

According to global oncology data, more than half of cancer patients receive RT. However, leukocytes are highly radiosensitive. Campian et al. (2013) showed that severe lymphopenia significantly reduces overall survival.

Mechanisms of Damage

DNA damage (core effect)

Ionizing radiation causes:

- double-strand DNA breaks
- chromosomal aberrations
- mutations or cell death

Most important systemic effect.

Affected cells:

- hematopoietic stem cells
- myeloid and lymphoid precursors

Clinical results:

- ↓ leukocytes → **leukopenia**
- ↓ neutrophils → **neutropenia**
- ↓ platelets → **thrombocytopenia**
- ↓ RBC precursors → anemia (later)

- T lymphocytes are extremely sensitive
- rapid apoptosis within hours

Effects:

- immunosuppression

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- reduced anti-tumor immune response
- higher infection risk

GI tract cells divide fast → very sensitive.

Effects:

- mucosal atrophy
- diarrhea
- malabsorption
- mucositis

- basal keratinocytes affected
- epithelial thinning

Clinical signs:

- erythema
- desquamation
- radiation dermatitis

Radiation damages blood vessel lining:

- endothelial apoptosis
- reduced capillary density
- fibrosis over time

Highly radiosensitive nucleated cells in gonads:

- spermatogonia → infertility (temporary or permanent)
- oocytes → ovarian failure risk

Even surviving cells may have:

- delayed mutations
- risk of secondary malignancies (rare but important)

Hall & Giaccia report that doses as low as 2 Gy reduce hematopoietic stem cell function by 50%.

Leukocyte Subtypes

Lymphocytes:

- Most radiosensitive

- Decline by 60–80% during RT

- Venkatesulu et al. (2018): lymphopenia occurs in 40–70% of patients

Neutrophils:

- Delayed decrease

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- Risk of infection increases when <500/µL

Monocytes:

- Moderate sensitivity

- Reduced immune response

Clinical Evidence

Campian JL et al. (2013):

- Severe lymphopenia linked to shorter survival in glioblastoma

Tang C et al. (2014):

- Lung cancer patients with lymphopenia had 30–40% lower survival rates

Grossman SA et al.:

- CD4+ T-cell depletion persists for months after RT

Factors Affecting Toxicity

- Dose >30 Gy increases leukopenia risk

- Large irradiation fields

- Combined chemoradiotherapy

Modern Strategies

IMRT reduces bone marrow exposure by up to 30%

Proton therapy further limits systemic toxicity

G-CSF reduces neutropenia duration by ~50%

Future Directions

Combining RT with immunotherapy shows promising results.

Checkpoint inhibitors improve immune recovery.

Conclusion

Radiation significantly impacts leukocytes. Evidence shows strong correlation between lymphopenia and poor outcomes. Personalized treatment is essential.

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