LYMPHOMAS

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Reader

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Proud to be an INDIAN!
Jai Hind

- Lymphomas constitute a group of neoplasms of varying degrees of malignancy which are derived from the basic cells of lymphoid tissue, the lymphocytes & histiocytes in any of their developmental stages.
- Malignant lymphoma is a neoplastic proliferative process of the lymphopoietic portion of the reticuloendothelial system that involves cells of either the lymphocytic or histiocytic series in varying degrees of differentiation.

- Lymphomas are malignant neoplasms of component cells of lymphoid tissues.
- Broad division-

  A) Hodgkin's lymphoma

  b) Non-Hodgkin's lymphoma

- Hodgkin's lymphoma is primarily a disease of lymph nodes characterized by the presence of large binucleated cells called Reed-Sternberg cells and a lymphoid stroma composed of large numbers of nonneoplastic cells.
- HL is very rare in the oral cavity.

- Non-Hodgkin's lymphomas are a heterogeneous group of lymphoproliferative malignancies which can involve both lymph nodes and lymphoid organs as well as extranodal organs and tissues.
- The lymph nodes of the head and neck are commonly involved as well as the extranodal tissues of this area.
- Commonly seen in HIV-infected (AIDS) patients.

CLASSIFICATION

- Working Formulation

  Low-grade

a) small lymphocytic

b) follicular, predominantly small cleaved cell (FSC)

c) Follicular, mixed small cleaved and large cell

- Intermediate-grade

Follicular, predominantly large cell

Diffuse, small cleaved cell

Diffuse, mixed, small and large cell

Diffuse, large cell cleaved or noncleaved cell

- High-grade

Immunoblastic, large cell

Lymphoblastic, convoluted or nonconvoluted cell

Small noncleaved cell, Burkitt's or non-Burkitt's

Updated REAL/WHO Classification(2001)

1. B-cell neoplasms
   - A) Precursor B-cell neoplasms
   - B) Peripheral B-cell neoplasms
2. T-cell neoplasms
   - A) Precursor T-cell neoplasms
   - B) Peripheral T-cell neoplasms
3. Hodgkin's lymphoma

Etiology of NHL

- Strong genetic predisposition
- Immunodeficiency
- Chromosome translocations(t(8;14), t(8;22) and t(2;8) in Burkitt's lymphoma and t(11;14) in mantle cell lymphoma.
- Familial pattern- co-existence of multiple breast cancers, ovarian cancer, sarcomas, lymphomas.

- ***Environmental factors-*** pesticides and herbicides (e.g. organophosphates, chlorophenols), solvents and organic chemicals(e.g. benzene, carbon tetrachloride) and wood preservatives.

- Increased risk in pesticide applicators, workers in petroleum, rubber, plastics and synthetic industries.
- Patients who receive cancer chemotherapy and/or radiation therapy
- Viruses like Epstein- Barr virus in Burkitt's lymphoma, HTLV-1 in adult T-cell lymphoma.

- Connective-tissue disorders like Sjogren syndrome, rheumatoid arthritis, SLE(systemic lupus erythematosus).
- Immunodeficiency states. e.g. HIV infection, organ or bone marrow transplant recipients.

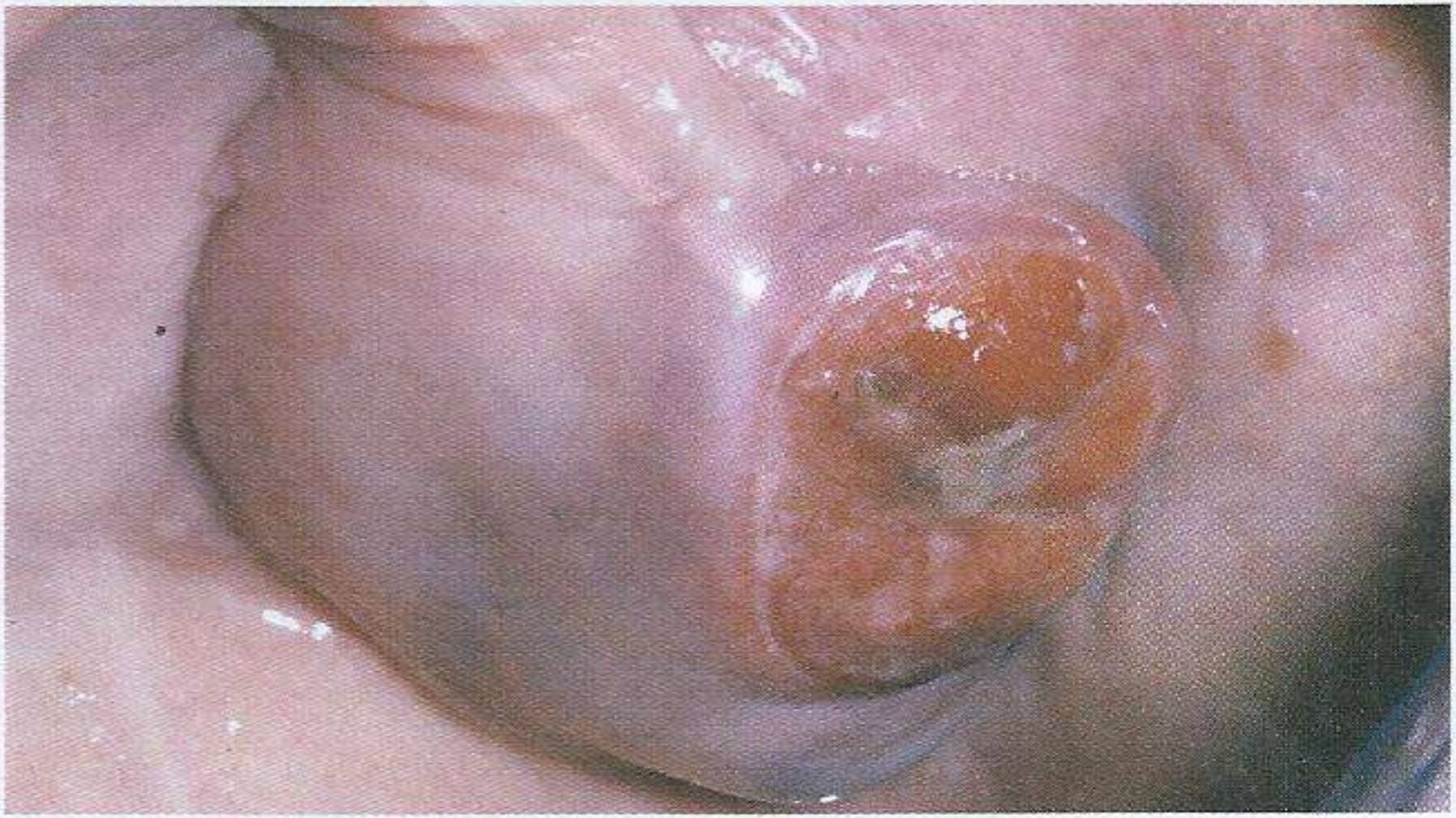


Fig. 13-28 **Non-Hodgkin's lymphoma.** Ulcerated mass of the left posterior maxilla.

ANN ARBOR STAGING SYSTEM

Stage I – Involvement of a single lymph node region or of a single extranodal organ or site.

Stage II- Involvement of two or more lymph node regions on the same side of the diaphragm, or localized involvement of an extranodal site or organ and one or more lymph node regions on the same side of the diaphragm.

- Stage III- Involvement of lymph node regions on both sides of the diaphragm, which may also be accompanied by localized involvement of an extranodal organ or site or spleen, or both.
- Stage IV- Diffuse or disseminated involvement of one or more distant extranodal organs with or without associated lymph node involvement.

Subclassification:

A. without systemic symptoms

B. Systemic symptoms: presence of fever, night sweats and/or unexplained loss of 10% or more of body weight during the 6-month period before diagnosis.

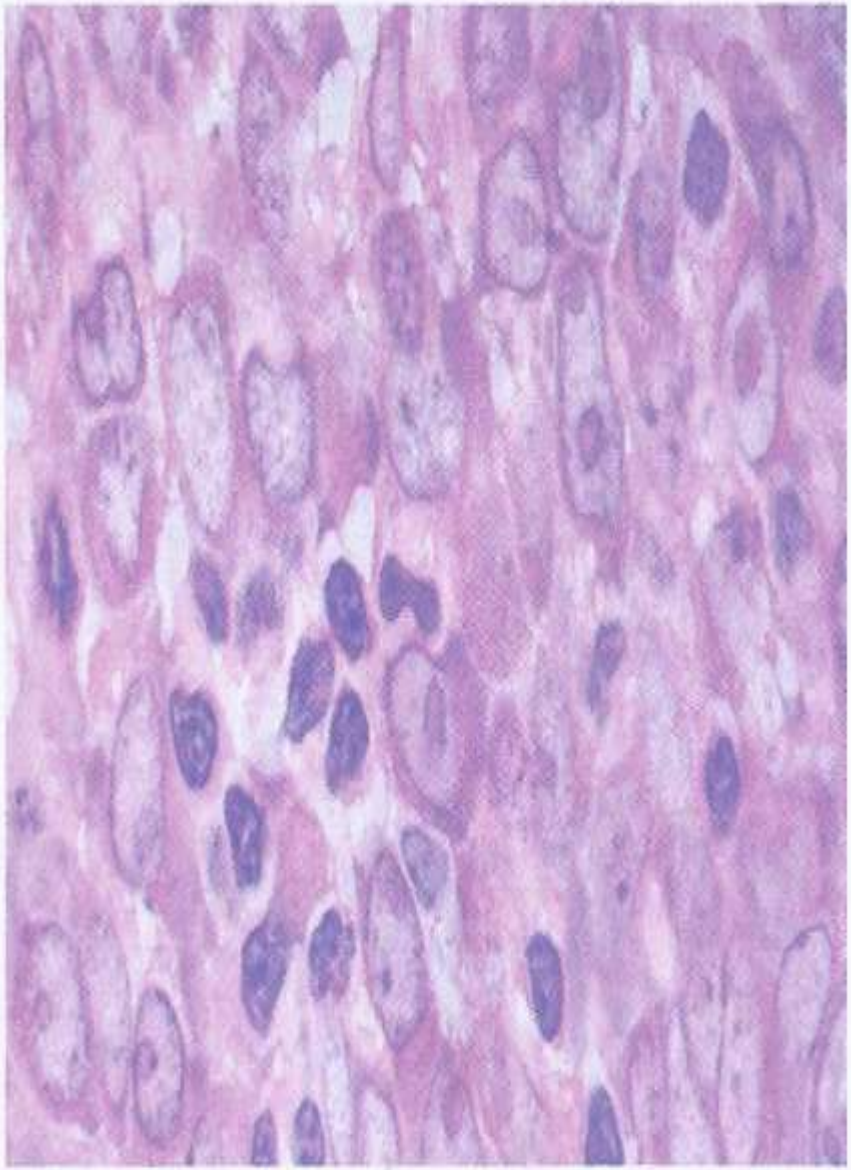
CLINICAL FEATURES

- Age older than 50 years.
- More common in male subjects.
- Lymphadenopathy
- Fevers, night sweats, weight loss and fatigue, pruritus.

Oral manifestations

- Swellings which may grow rapidly and then ulcerate.
- In some cases, these become large, fungating, necrotic, foul smelling masses.
- Soft, fluctuant swellings.
- Pain is a variable feature.
- Commonly seen in the hard palate.

HISTOLOGIC FEATURES



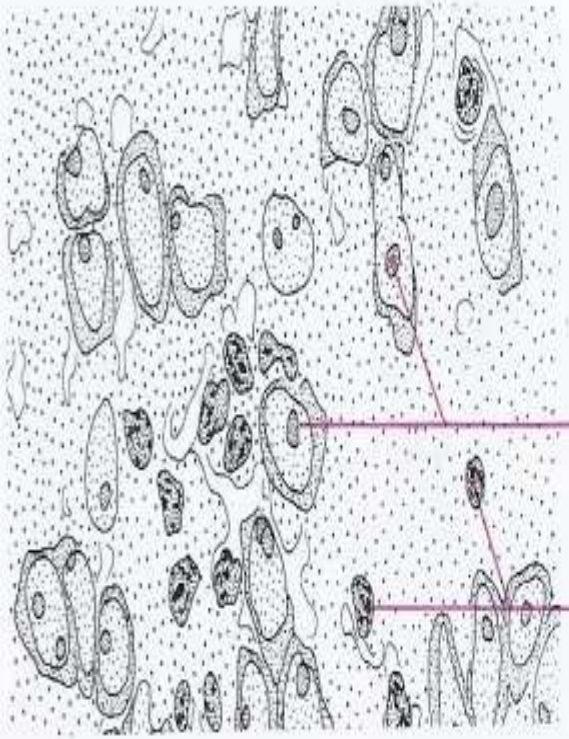


Fig. 18.33 Diffuse lymphoma, large non-cleaved cell type: the appearance comprises centroblasts and immunoblasts predominantly.

HISTOLOGIC FEATURES

- Nodular pattern- neoplastic cells tend to aggregate in such a way that large clusters of cells are seen.
- Diffuse pattern – monotonous distribution of cells with no evidence of nodular or germinal centre formation. Produce an entire effacement of lymph node architecture.

- Histologic pattern is very important as there is clinicopathologic and prognostic correlation between the two.
- Nodular pattern seen in adults and has a more favorable prognosis than the diffuse type.
- A diagnosis of nodular or diffuse lymphoma is highly reproducible among pathologists, and has definite clinical significance.

- Small cells with irregular or cleaved nuclear contours and scant cytoplasm referred to as centrocytes.
- Larger cells with open nuclear chromatin, several nucleoli and modest amounts of cytoplasm are referred to as centroblasts.
- In follicular type, small cleaved cells prominent.

- NODULAR- seen in adults more often than in children & is associated with a more favourable prognosis.
- Nodular lymphomas are of B-cell origin.
- Follicular (nodular) lymphoma – 22% of all NHLs.

HODGKIN'S LYMPHOMA

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- Thomas Hodgkin first described Hodgkin's disease in 1832.
- Almost 100% of HIV-associated HD cases are EBV-positive.
- Genetic predisposition.

CLINICAL FEATURES

- Bimodal distribution, peaking in young adults (aged 15-34 years) & older individuals (>55 years).
- Males more affected than females.
- HD more common among whites.
- Clinical signs & symptoms are extremely variable.

- Painless enlargement of one or more cervical lymph nodes.
- Palpable painless lymphadenopathy occurs in the cervical area (60-80%).
- Lymph nodes are firm & rubbery in consistency.
- Unexplained weight loss, fever, night sweats present in about 40% of patients.

- Chest pain, cough and/or shortness of breath may be present due to a large mediastinal mass or lung involvement.

ORAL MANIFESTATIONS

- Primarily a disease of lymph nodes. Seldom occurs as a disease primarily in the oral cavity. Oral cavity could be involved secondarily, but this appears to be an exceedingly rare happening.

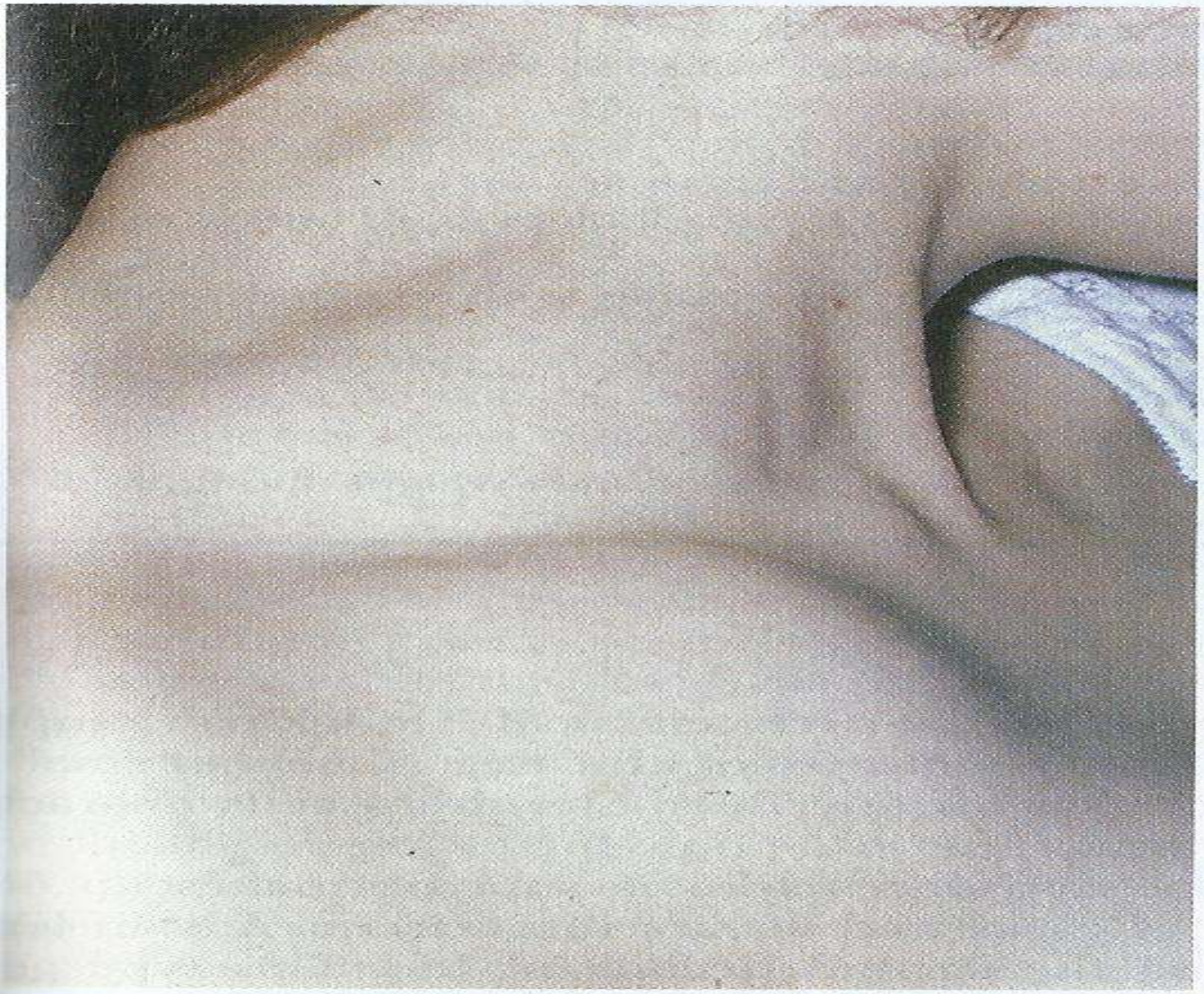


Fig. 13-24 Hodgkin's lymphoma. The prominent supraclavicular and cervical masses represent Hodgkin's lymphoma.

HISTOLOGIC FEATURES

1) Nodular Sclerosis (NS) HD-

- Comprises 60-80% of all cases.
- Nodular pattern.
- Broad bands of fibrosis divide the node into ‘ nodules’
- Capsule is thickened.

- The characteristic cell is the lacunar- type RS cell, which has a monolobated or multilobated nucleus with abundant & pale cytoplasm.
- NS frequently is observes in adolescents & young adults & usually involves the mediastinum & other supra-diaphragmatic sites.

2) mixed- cellularity HD-

- 15-30% cases.
- Diffuse infiltrate.
- RS cells of classic type seen.
- Commonly affects the abdominal lymph nodes & spleen.
- 1 or 2% of malignant cells are admixed within a reactive cell infiltrate composed of variable proportions of lymphocytes, histiocytes, eosinophils & plasma cells.

3) lymphocyte- depleted HD

- < 1% cases.
- Infiltrate is diffuse & often appears hypocellular.
- Large numbers of RS cells.
- Associated with older age & HIV positivity.

4) lymphocyte-rich classic HD-

- RS cells of the classic or lacunar type observed with a background infiltrate of lymphocytes.

5) nodular lymphocyte-predominant HD- constitutes 5%.

- Typical RS cells are not observed.
- A variant of RS cells, the lymphocytic & histiocytic cells (L&H) or popcorn cells (their nuclei resemble an exploded kernel of corn).

Reed-Sternberg cells

- Characteristic malignant cells of Hodgkin's lymphoma are large cells known as RS cells, ***20-50 micrometer in diameter, abundant, amphophilic, finely granular/homogeneous cytoplasm; two mirror-image nuclei(owl eyes) each with an eosinophilic nucleolus & a thick nuclear membrane (chromatin is distributed at the cell periphery).***
- ***Immunohistochemical marker- CD15 and CD30***

- In approximately 50% of cases, the Reed-Sternberg cells are infected by the Epstein-Barr virus.

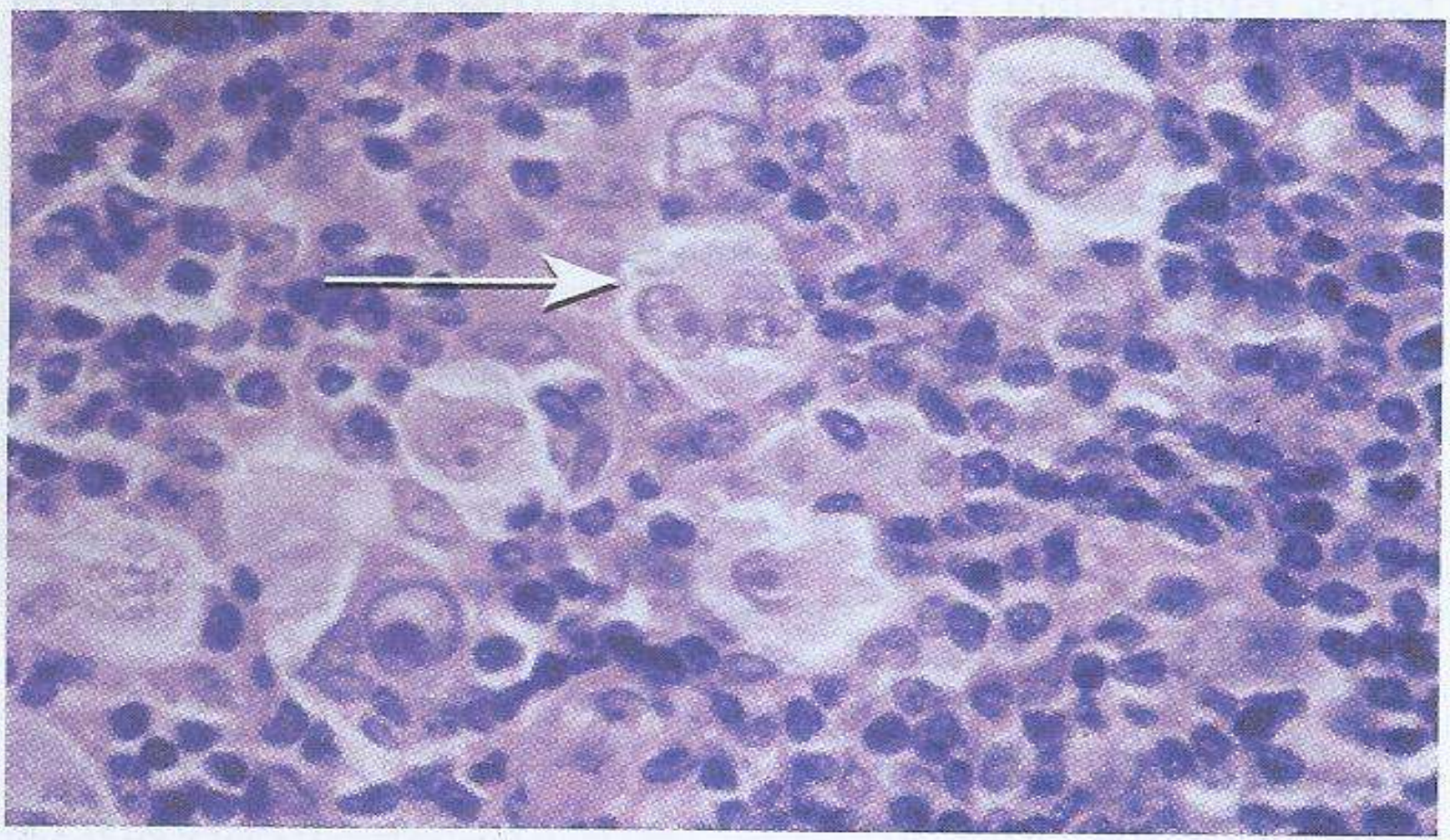
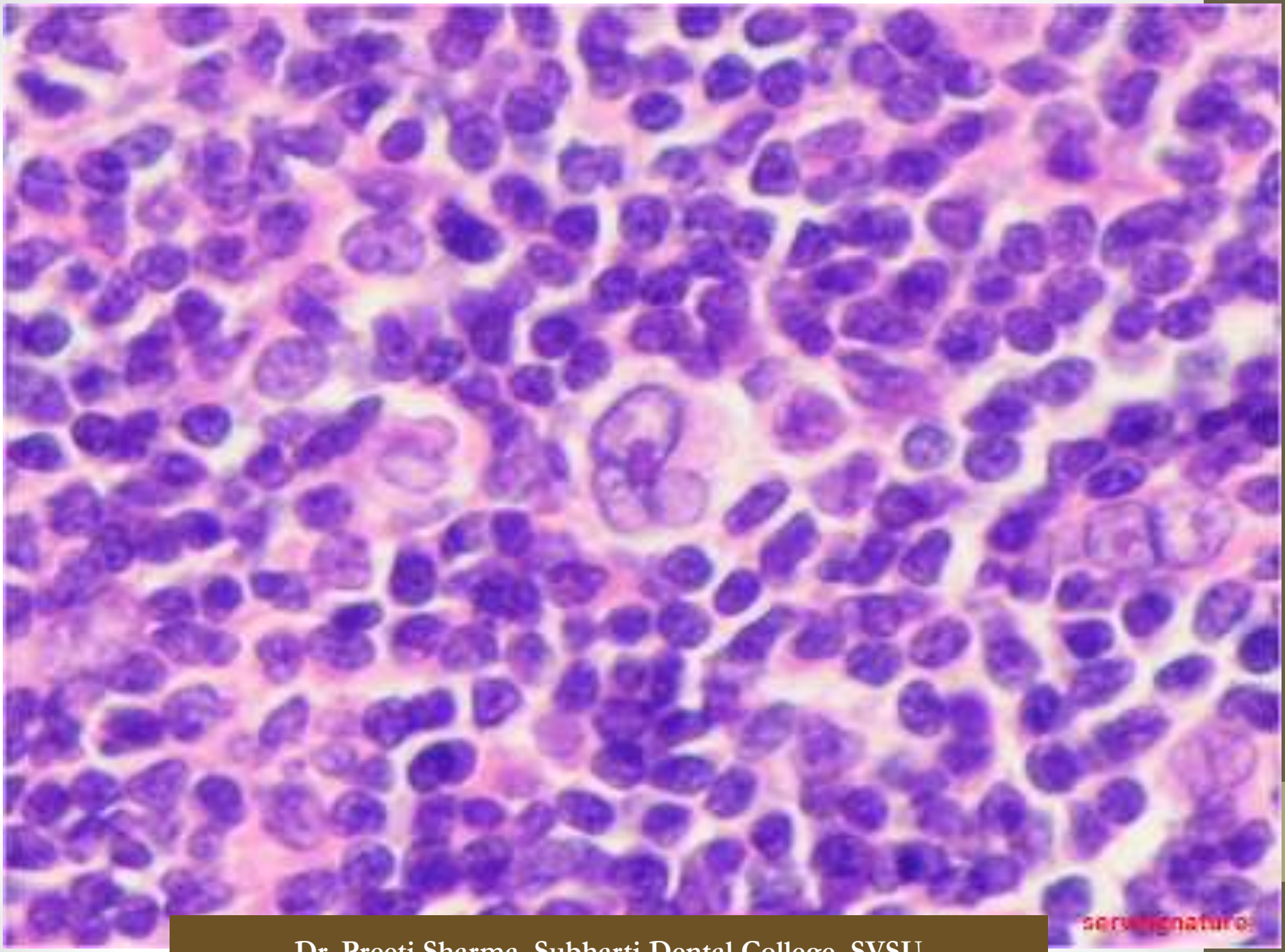


Fig. 13-25 Hodgkin's lymphoma. This high-power photomicrograph shows the characteristic Reed-Sternberg cell *(arrow)* of Hodgkin's lymphoma, identified by its "owl-eye" nucleus.



TREATMENT AND PROGNOSIS

- Radiation therapy and chemotherapy.
- Most important prognostic determinants are the histologic type and the clinical stage of the disease.
- Nodular lymphocyte predominant type has the most favorable prognosis, followed by nodular sclerosis, mixed cellularity.
- Lymphocyte depletion has the least favorable prognosis.

African Jaw lymphoma/Burkitt's lymphoma

- Peculiar to children of central Africa.
- Reported by Burkitt.
- Also occurs sporadically throughout the world.
- High-grade B-cell neoplasm with 2 major forms- African(endemic) and sporadic(non-endemic).
- Is one of the fastest growing malignancies in humans, with a very high growth fraction.

Clinical features

- African form most often involves the maxilla or mandible.
- Involvement of abdominal organs, such as the kidneys, ovaries or retroperitoneal structures is less common.
- Sporadic form involves abdominal organs, pelvic organs and facial bones.

Etiology

- EBV – African form
- African form- patients present with swelling of the affected jaw or other facial bones, loosening of the teeth, and swelling of the lymph nodes, which are non tender and rapidly growing, in the neck or below the jaw.
- Abdominal presentation is less common.

- Major signs of Burkitt's lymphoma include a soft tissue mass associated with the involvement of the jaw or other facial bones, enlarged cervical lymph nodes, abdominal masses.

Histological features

- Monoclonal proliferation of B lymphocytes characterized by small noncleaved cells that are uniform in appearance & that produce a diffuse pattern of tissue involvement.
- Burkitt cells are homogeneous in size & shape, have round to oval nuclei and slightly coarse chromatin, with multiple nucleoli, & with intensely basophilic vacuolated cytoplasm.
- Frequent mitotic figures.

- Characteristic 'starry sky appearance' imparted by scattered macrophages with an abundant clear cytoplasm, often containing phagocytic cellular debris.

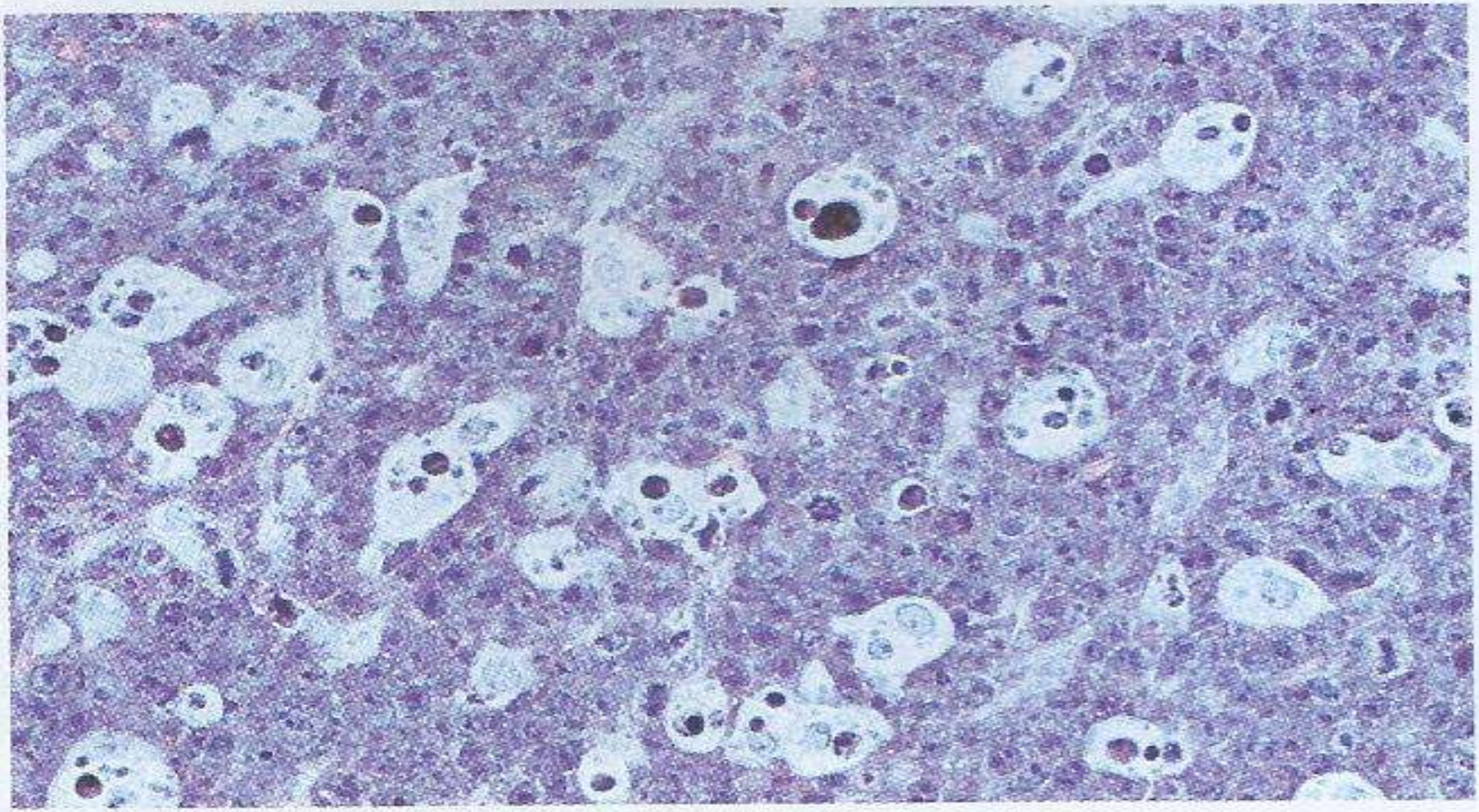


Fig. 13-38 Burkitt's lymphoma. This high-power photomicrograph demonstrates the undifferentiated, small, dark lesional cells with numerous histiocytes.

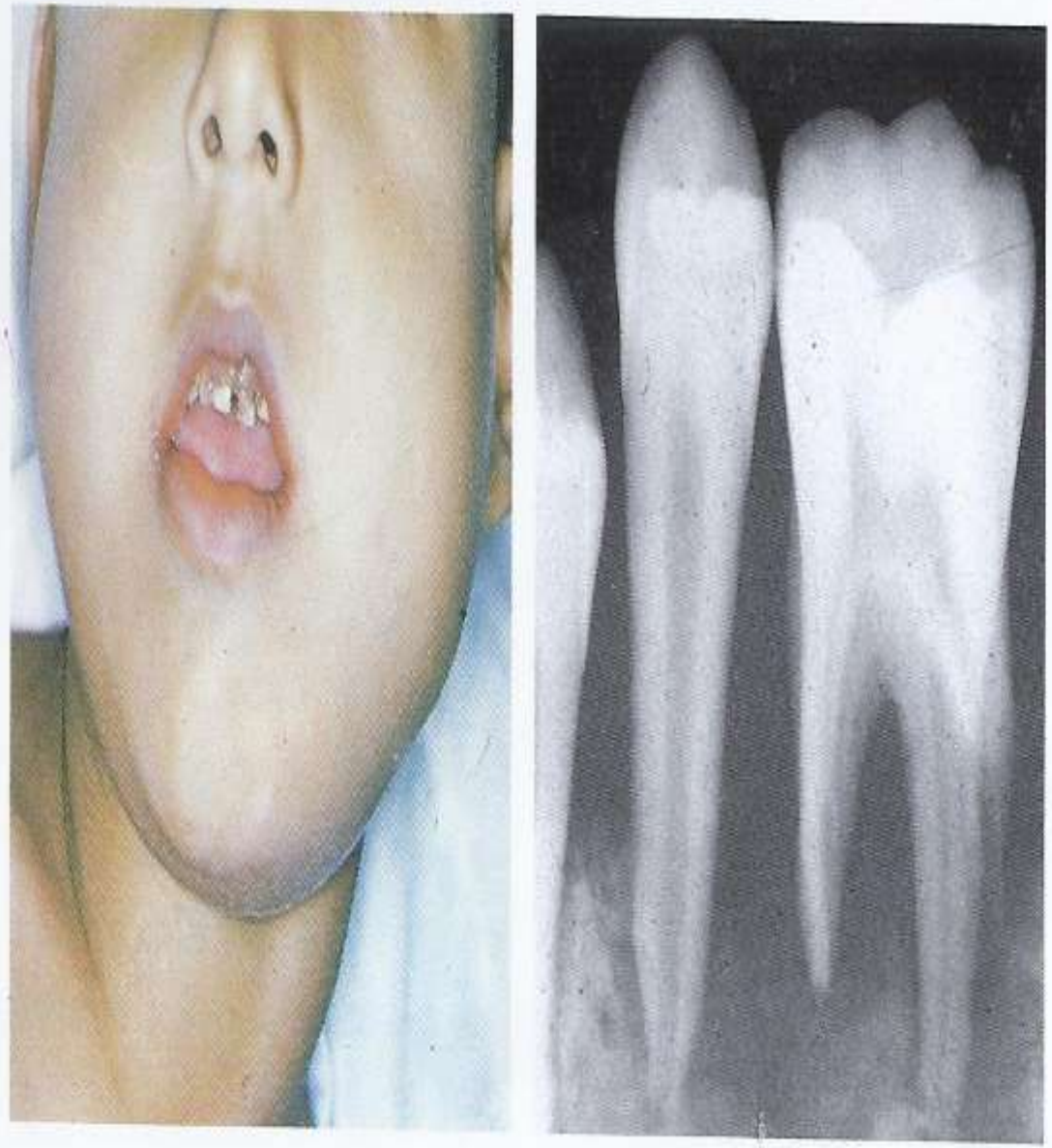


Fig. 18.37 Burkitt's lymphoma: (left) typical appearance resulting from mandibular and parotid involvement; (right) radiograph of the mandible shows characteristic bone destruction and root resorption.

MULTIPLE MYELOMA

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Multiple myeloma

- Most common primary neoplasm of the skeletal system.
- Malignancy of plasma cells.
- Plasma cells are a subset of B-cells, which are the producers of humoral immunity factors termed antibodies.
- If malignant transformation occurs in a single plasma cell, its clones produce only a single type of immunoglobulin.

- Electrophoresis demonstrates a monoclonal peak corresponding to this particular immunoglobulin

Pathogenesis

- MM – prototype of monoclonal malignancies, of plasma cells; may result from a mutation of terminally differentiated B cells .
- Radiation exposure(radiologists and radium-dial workers), occupational exposure(in agricultural, chemical, metallurgical,rubber plant, paper workers
- Chemical exposure to benzene, formaldehyde, hair dyes, paint sprays and asbestos.

Clinical features

- Older people aged 60-65 years; men;frequently among blacks.
- Diffuse disease of the bone marrow.
- 90% have osseous involvement.
- Sites are axial skeleton & include the vertebral column, ribs, skull, pelvis, and femur bone.
- Underlying pathology is expansion of a single line of plasma cells that replace normal bone marrow and produce monoclonal immunoglobulins.

- Bone pain
- Lytic bone lesions, anemia, azotemia, hypercalcemia and recurrent infections.

Oral manifestations

- Mandible more frequently than maxilla.
- Ramus, angle and molar region of the mandible which correspond to the most active hematopoietic areas.

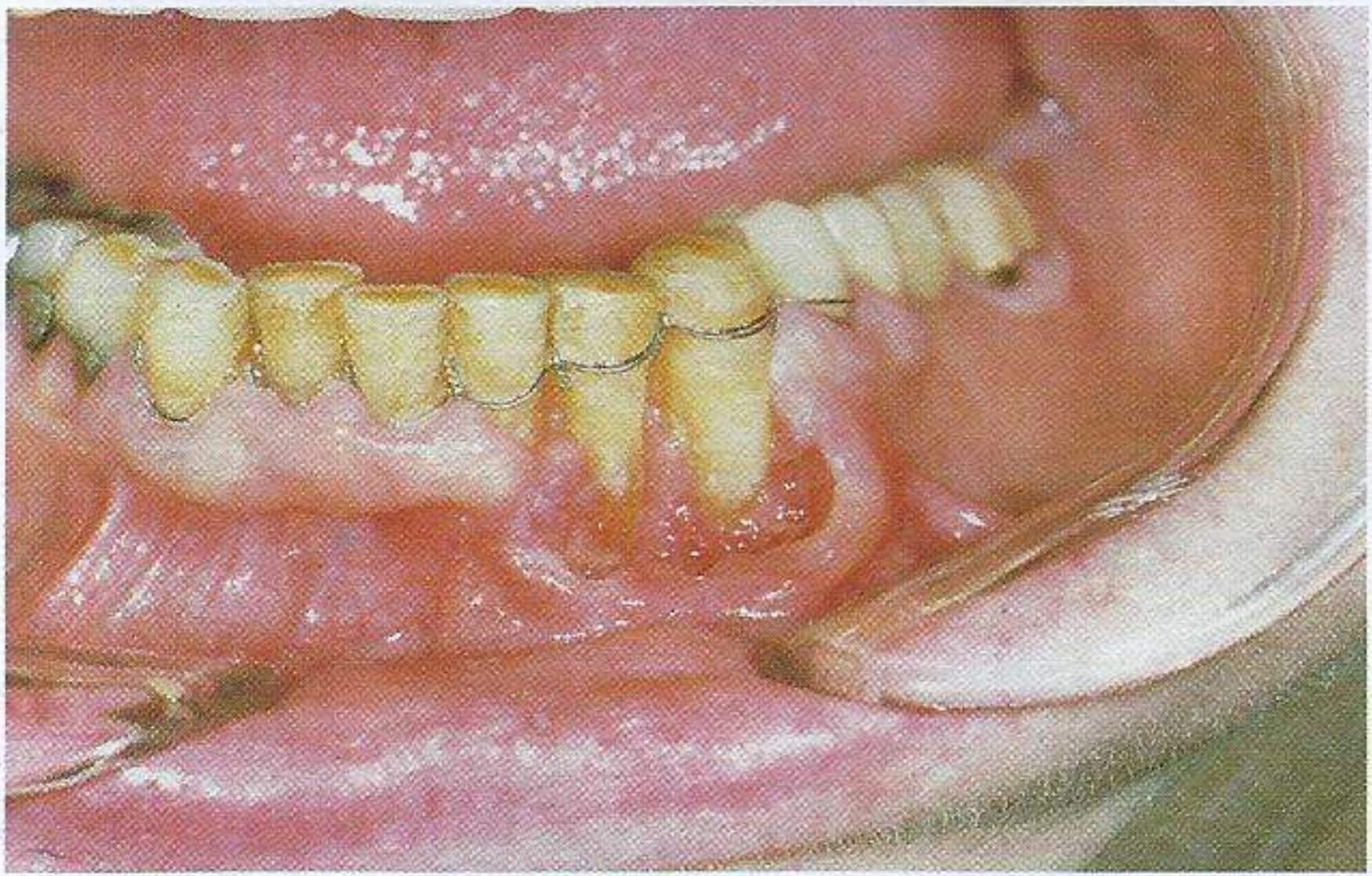

FIGURE 9-22 Multiple myeloma presenting orally as an ulcerated gingival mass.

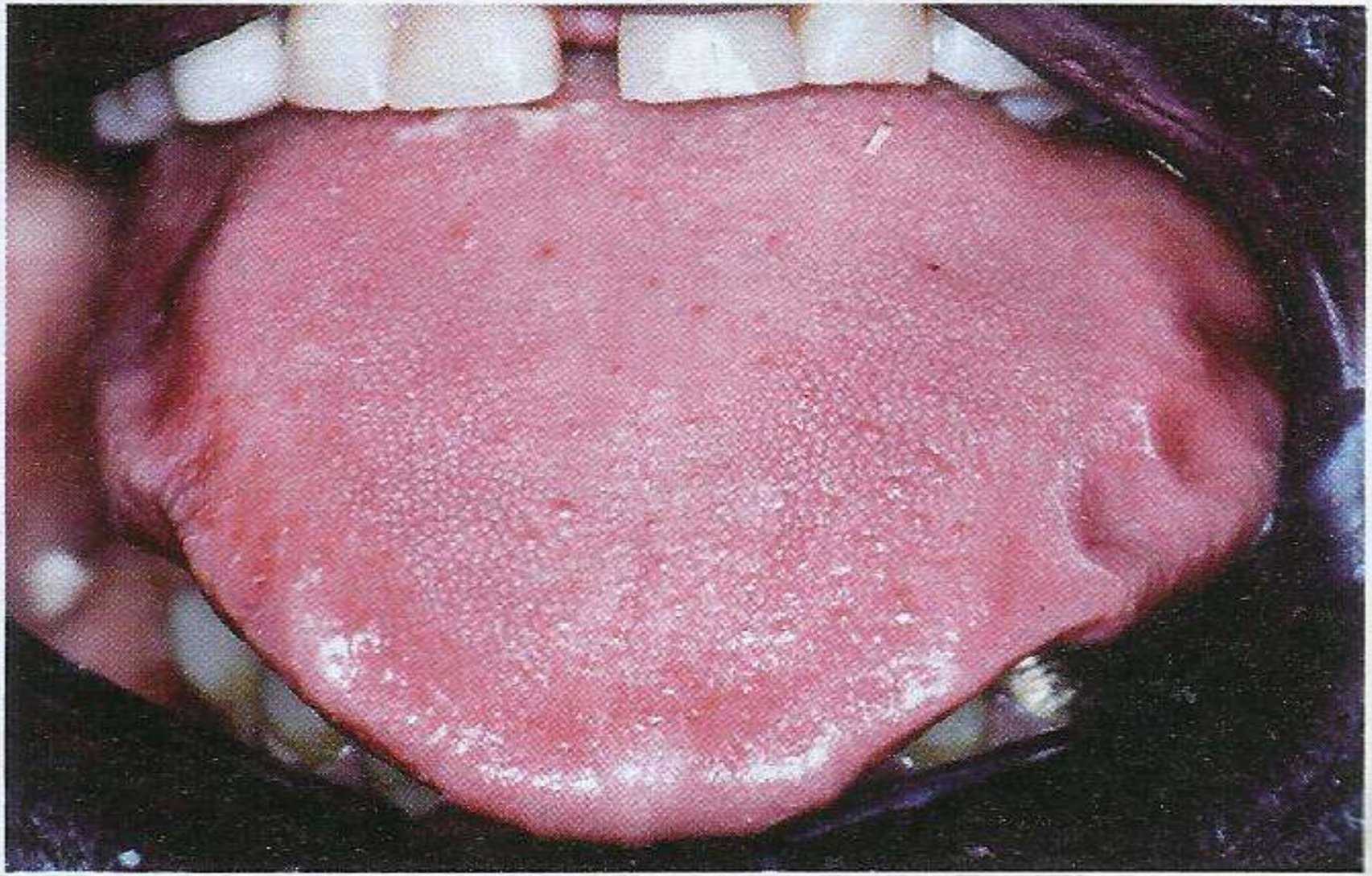

FIGURE 9-23 **Amyloidosis** of the tongue resulting in macroglossia. Note lateral indentations related to tongue pressure against teeth.

- Pain, swelling, expansion of the jaw, numbness and mobility of teeth.
- Amyloidosis of the tongue.

Radiographic features

- Numerous sharply punched- out areas in a variety of bones like vertebrae, ribs, skull, jaws, and ends of long bones. These are sites of active hematopoiesis.

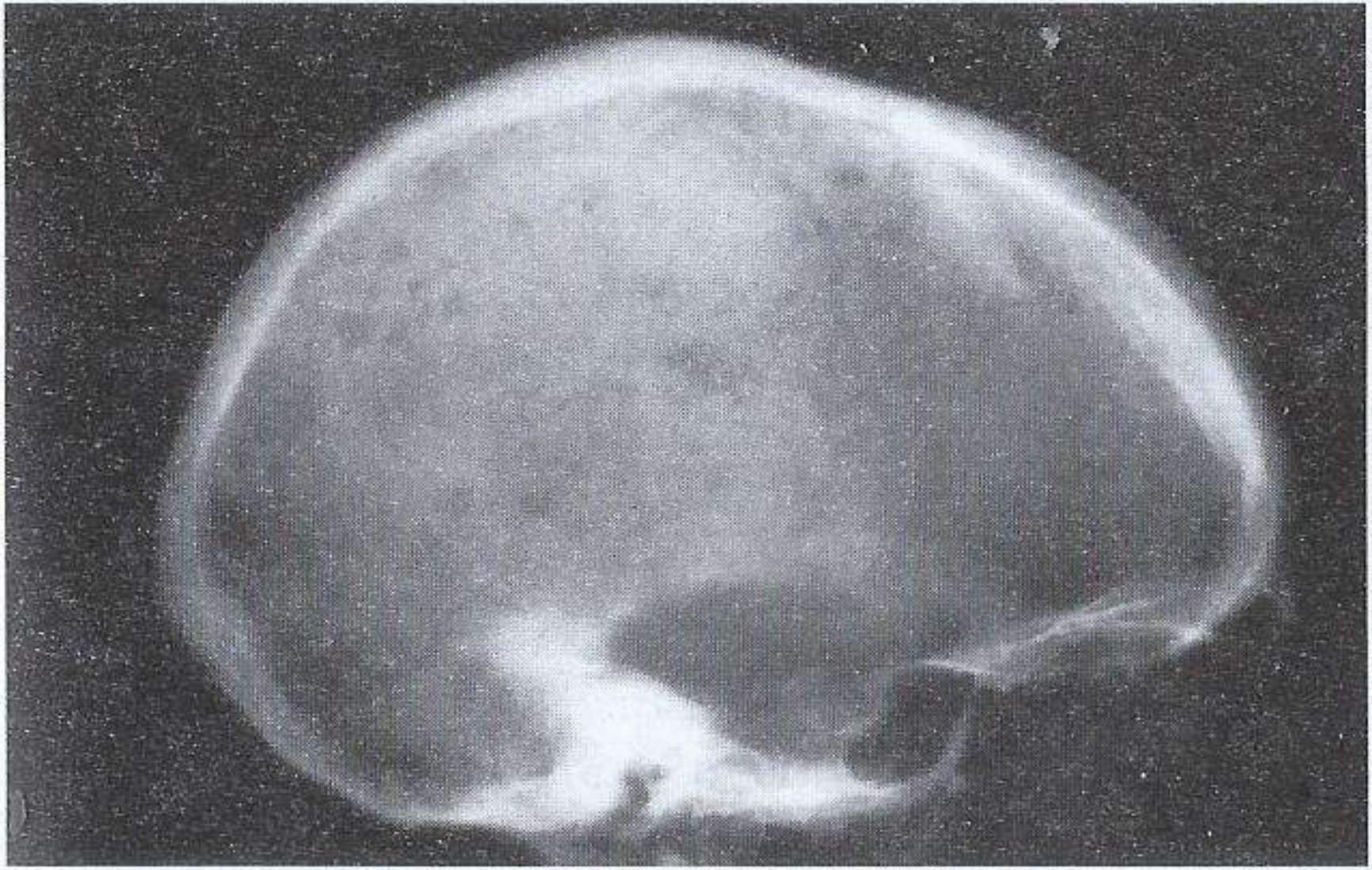

FIGURE 9-18 Multiple myeloma showing multiple punched-out lesions of the skull.

Laboratory findings

- Hyperglobulinimea resulting in the reversal of the serum albumin-globulin ratio and an increase in total serum protein level of 8-16gm%.
- In addition, Bence Jones protein in the urine is noted, which is an unusual protein which coagulates when the urine is heated to 40-60 degree C and then disappears when the urine is boiled. It reappears as urine is cooled.

- Occasionally, Bence Jones protein also found in leukemia & polycythemia.
- Elevated ESR and increased levels of alkaline phosphatase.

Histologic features

- Sheets of closely packed cells resembling plasma cells.
- Round or ovoid cells with eccentrically placed nuclei exhibiting chromatin clumping in a ‘cartwheel’ or ‘checkerboard’ pattern.
- Inflammatory plasma cell lesions characterized by polyclonal staining, whereas monoclonal staining is indicative of neoplasia.

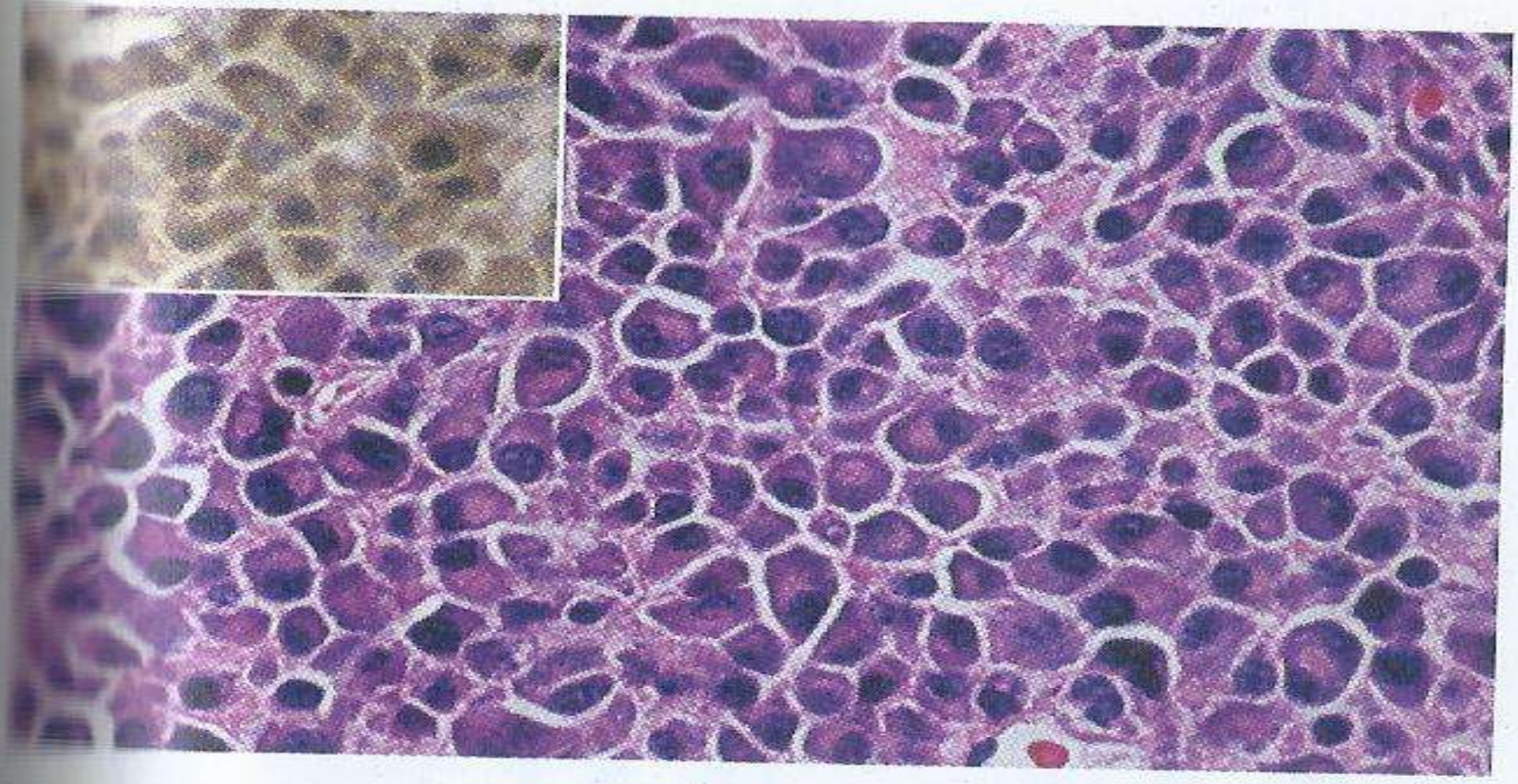

Fig. 13-42 Multiple myeloma. This high-power photomicrograph reveals sheets of malignant plasma cells with eccentric nuclei and stippled nuclear chromatin. Immunohistochemical studies (*inset*) show a uniform reaction of the lesional cells for antibodies directed against kappa light chains, indicating a monoclonal neoplastic proliferation.

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