Langerhans Cell Histiocytosis

58

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Abstract

Langerhans cell histiocytosis comprises a set of conditions ranging from a localized form represented by a solitary lesion to a disseminated multiorgan involvement and having in common the microscopic findings of foci of proliferating Langerhans cells. Variants include eosinophilic granuloma (localized disease), Hand–Schuller–Christian disease (disseminated form), and Letterer–Siwe disease (disseminated and fatal form).

Definition

- A set of conditions ranging from a localized form represented by a solitary lesion to a disseminated multiorgan involvement and having in common the microscopic findings of foci of proliferating Langerhans cells.
- Variants:
  - Eosinophilic granuloma: localized disease
  - Hand–Schuller–Christian disease: disseminated form
  - Letterer–Siwe disease: disseminated and fatal form

Synonyms

- Histiocytosis X (older nomenclature)
- Langerhans cell granulomatosis
- Nonlipid reticuloendotheliosis (generic term)

Etiology

- Unknown.
- The neoplastic and immunologic natures for the condition have been separately suggested without confirmation so far.

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Epidemiology

- Corresponds to less than 1 % of bone lesions.
- Monostotic disease is more frequent than polyostotic disease.

Age

- Can affect any age group but is seen more frequently in children

Sex

- Males are more affected than females.

Sites of Involvement

- LCH is a multisystem disease that can affect any organ either in the isolated or in the disseminated forms.
- The bone is the site more commonly affected either in the solitary or in the multicentric form of the disease.
- Within the skeleton, the cranial vault is the preferred site, but the mandible, the rest of the axial skeleton, and the long bones of the extremities follow closely.
- Ribs are more frequently affected in adults.
- In this section we will focus as exclusively as possible in the bone involvement of the disease.

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Signs and Symptoms

- Pain and swelling over the area of the affected bone are usually present.
- Neurological symptoms may result from spine involvement.
- Mandibular lesions may cause loosening of teeth.
- Diabetes insipidus in 15–20 % of patients.
- Hepatosplenomegaly may occur.

Image Diagnosis

Radiographic and CT Features

- When the diagnosis of LCH is suspected, a complete skeletal survey must be done.
- Radiographs' most common picture is of one or more well-defined lytic lesions.
- In the cranial vault, lesions typically have a beveled or "hole-in-hole" appearance because of the difference in lesion diameter in the two bone tables. CT may better evidence this feature. Some lesions may show a central radiodense focus.
- Peripheral sclerosis may appear with healing.
- Vertebral involvement may produce a "vertebra plana," the total collapse of the vertebral body, with preservation of the intervertebral disks, but the lesion may also be expansile and lytic.
- Lesions of long bones usually are located intramedullary, in the metaphysis or diaphysis.
- Periosteal reaction, when present, is usually solid, but some long bone lesions may look so aggressive as to suggest a malignant tumor, with cortical destruction and periosteal reaction, especially in early lesions of small children.
- Fluid-fluid levels and transphyseal lesion have been described on rare occasions.
- The confluence of multiple lesions in chronic disease may produce a geographic aspect.
- The disease may involve the supporting structure of the teeth, producing the "floating-teeth" appearance.

MRI Features

- By MRI, lesions show a hypointense signal intensity in T1-weighted images and hyperintense signal intensity in T2-weighted images that reduces with healing. Gadolinium injection shows enhancement of the image.

Image Differential Diagnosis

Ewing Sarcoma

- In long bones, it may have a radiographically similar appearance.

Cystic Angiomatosis

- Presents multiple widespread skeletal and visceral lesions. Soft tissue lesions usually contain phleboliths

Multiple Myeloma

- Is rarely seen before the third decade. Presents "punched-out" lytic lesions mainly in the skull and axial skeleton. Diffuse osteopenia may be present. Blood biochemistry suggests the correct diagnosis.

Metastatic Carcinoma

- May present lytic lesions but is also a disease of older patients. History or investigation for a primary disease helps in the differential.

Primary Lymphoma of the Bone

- Aggressive lytic lesions, with a permeative pattern

Osteomyelitis

- A serpiginous lytic pattern and sequestrum, when present, are more specific for infection. Has a regular surrounding enhancement due to inflammatory changes.

Pathology

Gross Features

- Lesions are rarely excised but usually only biopsied or curetted, at most.
- Tissue is soft or friable, with a gray to reddish to yellowish color.

Microscopic Features

- Dense or scattered foci of mononuclear histiocytes (Langerhans cells) are seen. Langerhans cells have light or eosinophilic cytoplasm and oval, sometimes indented, nuclei with nuclear grooves. Some cases may present high mitotic activity. Mitoses are always typical.
- Giant cells are usually present in variable number.
- Infiltration by eosinophils is a very common finding, sometimes in clusters or in large numbers, which may suggest the diagnosis.

- Foamy histiocytes may be seen.
- An inconspicuous spindle cell background infiltrated by other leukocytes and plasma cells, as well as areas of necrosis, complements the microscopic picture.

Pathology Differential Diagnosis

Giant Cell Tumor

- When there are abundant giant cells. Affects patients after closure of the growth cartilage

Osteomyelitis

- May present a difficult differential diagnosis. Immunohistochemistry techniques will make the diagnosis.

Lymphoma

- When there is a compact diffuse monomorphic proliferation of cells. Distinct immunohistochemistry profiles

Ancillary Techniques

Immunohistochemistry

- Langerhans cells are S-100 protein, CD1a, and langerin positive. CD45 is negative.

Ultrastructure

- Intracytoplasmic Birbeck granules are unique ultrastructural findings, characteristic of LCH.

Prognosis

- Patients with solitary or a few isolated bone lesions have an excellent prognosis with and, sometimes, without treatment. Vertebra plana may resolve and the height of the vertebra may be subsequently recovered.
- Patients with disseminated disease may have long survival, especially if they survive the first 3 years of treated disease.
- Signs of worse prognosis and possible death of the disease are:
  - Young age at diagnosis, less than 3 years of age
  - Involvement of more than three bones
  - Hematologic manifestations
  - Hepatosplenomegaly

Treatment

- Solitary or few isolated lesions may, occasionally, resolve spontaneously.
- Corticosteroids, administered by intralesional injection or systemically, have been used with good results.
- Radiotherapy is also reported to present good response.
- Disseminated disease requires systemic administration of corticosteroids and/or other chemotherapies.

Images

See Figs. 58.1, 58.2, 58.3, 58.4, 58.5, 58.6, 58.7, 58.8, 58.9, and 58.10 for illustrations of Langerhans cell histiocytosis.

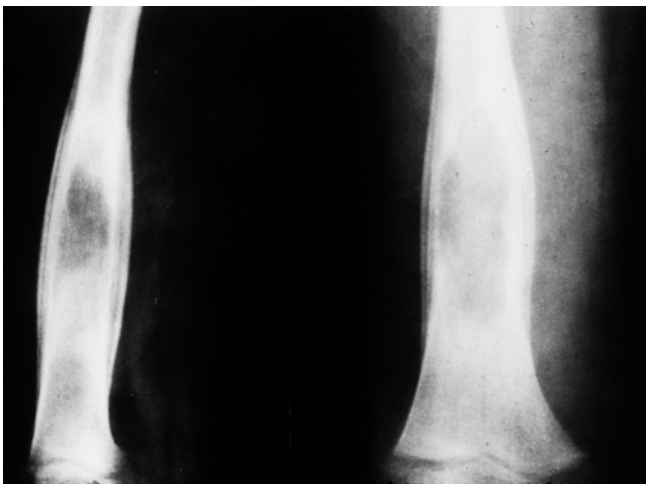
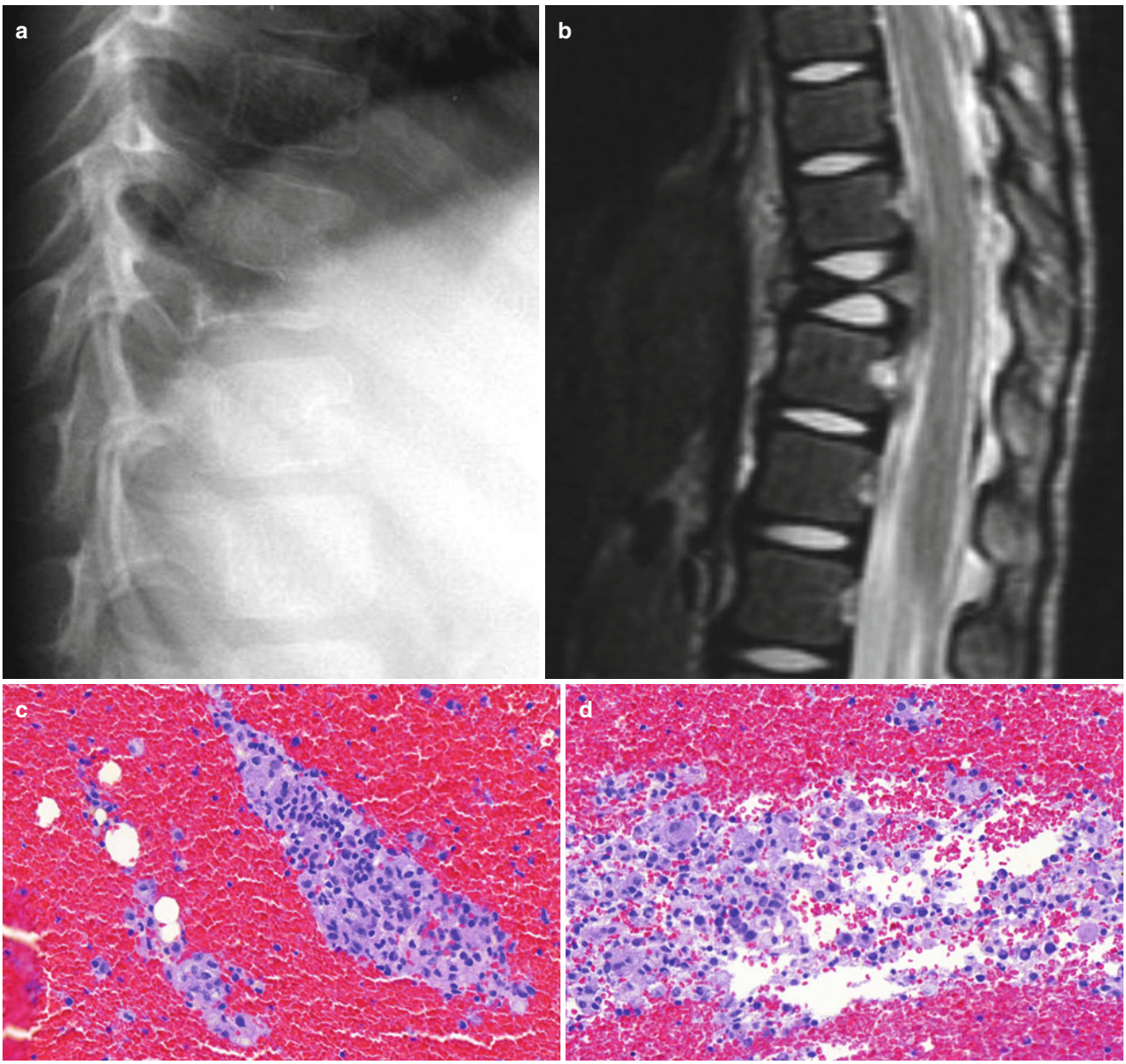


Fig. 58.1 Radiograph of a solitary Langerhans cell histiocytosis (eosinophilic granuloma) in the femoral diaphysis of a young child. Lytic lesion with extensive reactive sclerosis and lamellar periosteal reaction. Radiologic differential diagnosis with Ewing sarcoma and osteomyelitis



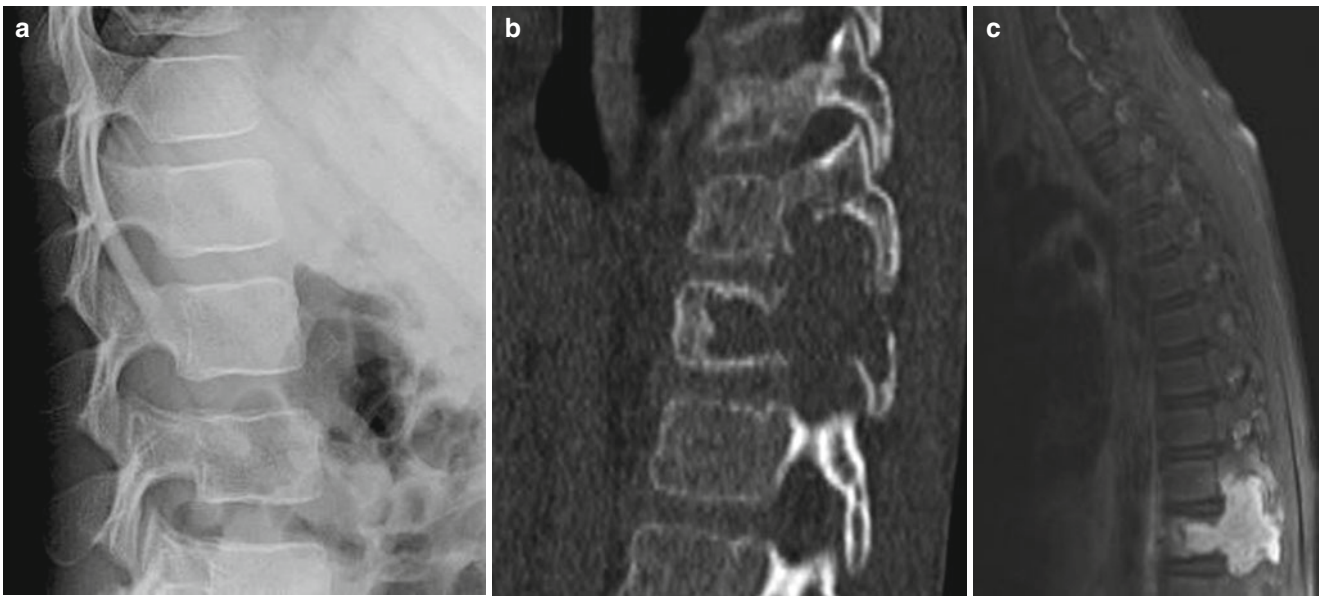


Fig. 58.3 (**a**) Radiograph of LCH affecting the lumbar spine. Lytic lesion in the body and pedicles of a vertebra can be seen. Vertebra shape is maintained. (**b**) MPR CT of the same case as previous figure. Although vertebral height is maintained, a lytic lesion extends to its posterior elements. (**c**) Same case as previous figure. MRI demonstrates better the extension of the lesion

Fig. 58.2 (**a**) Radiograph of the spine of another young child showing a *vertebra plana*, flattening of the vertebral body, common occurrence in LCH of the vertebra. (**b**) MRI of same case of previous figure, better demonstrating the flattened vertebra. (**c**) Needle biopsy of the lesion in previous figure retrieved some hemorrhagic material. Processing of the blood clots disclosed small fragments sufficient for the diagnosis of LCH (**d**)

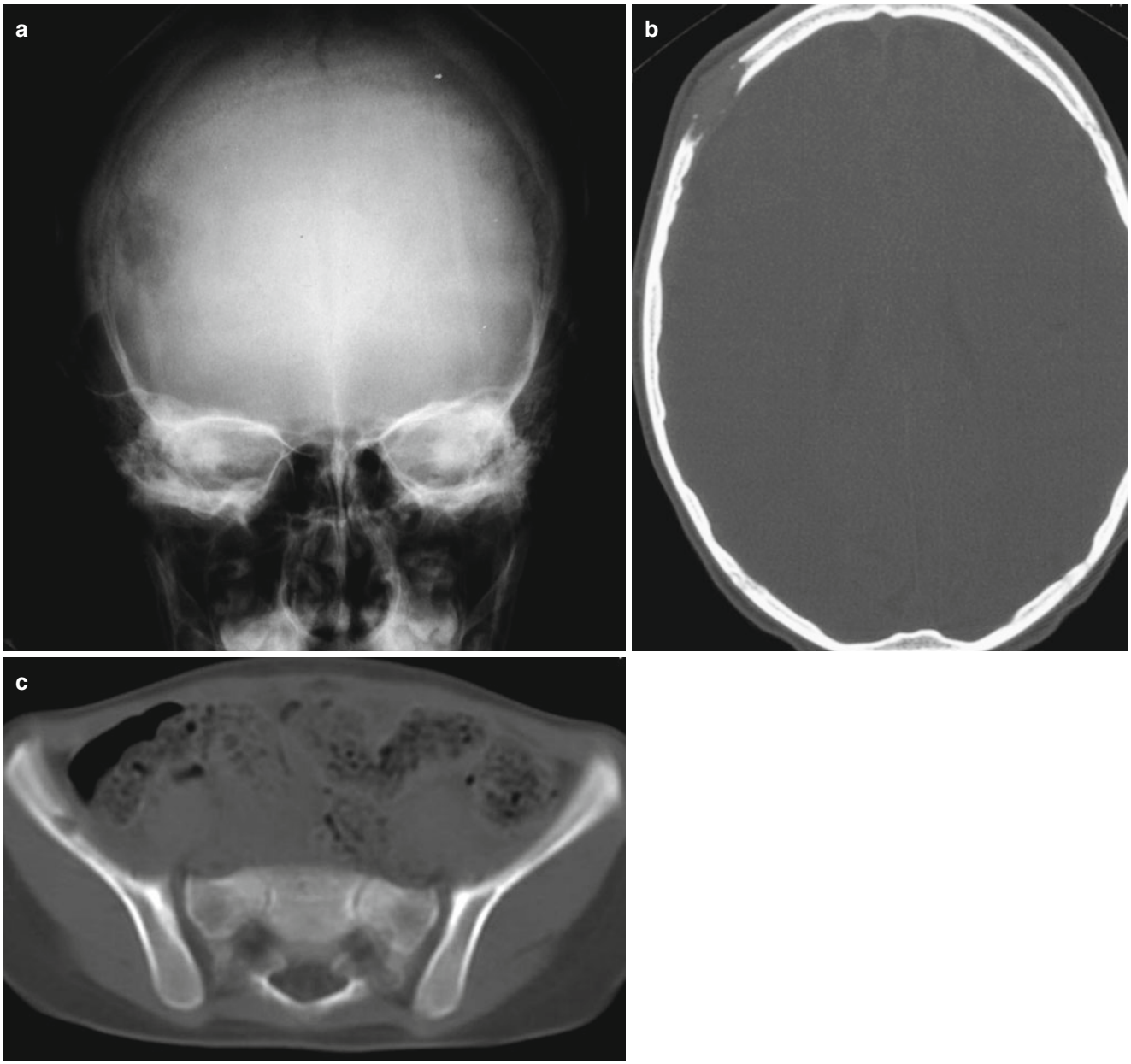


Fig. 58.4 (**a**) Radiograph of a skull lytic geographic lesion of LCH. (**b**) CT scan of the same case of (**a**). Characteristic beveled destruction of the two cranial cortices, responsible for the "hole-in-hole" aspect of radiographs. (**c**) CT scan of the pelvis of the same patient of (**a**). Secondary focus of LCH

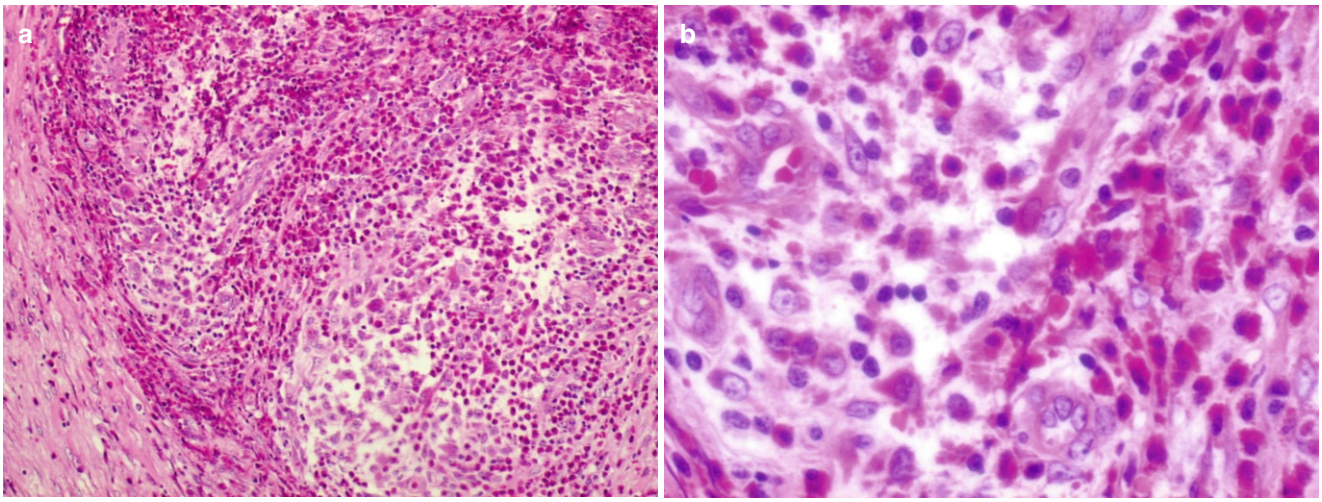


Fig. 58.5 (**a**) Histologic low-power view of an LCH lesion. Dense proliferation of histiocytes with abundant eosinophils, surrounded by fibrous tissue, can be seen even in this magnification. (**b**) Higher magnification of previous histologic field depicting histiocyte and eosinophil proliferation

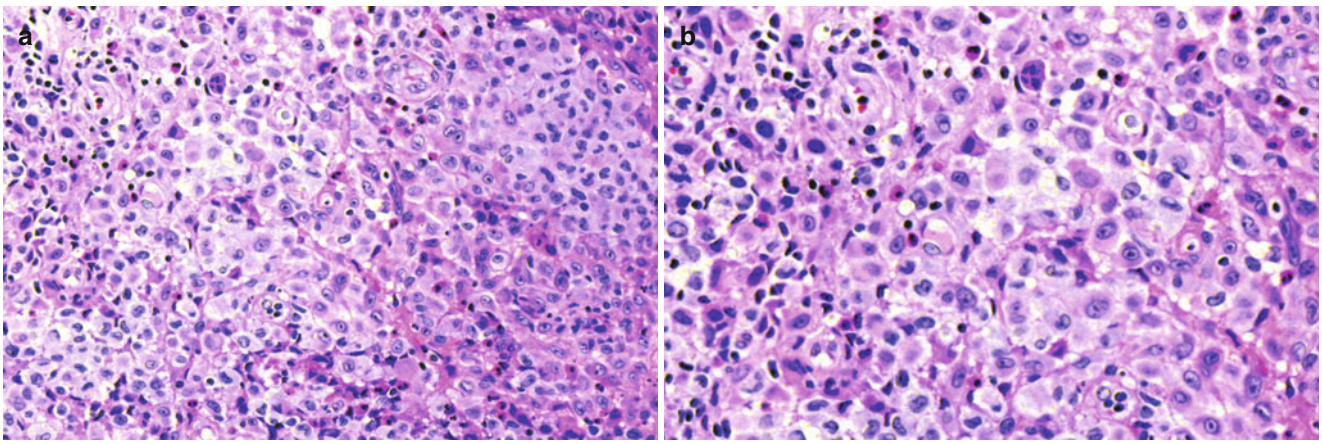


Fig. 58.6 (**a**) Histologic low-power view of another LCH lesion, in this case with dense, almost exclusive histiocyte proliferation. (**b**) Higher magnification of same case of previous figure. Indented nuclei of the histiocytes can be seen. Eosinophils and other inflammatory cells can also be identified among the histiocytes

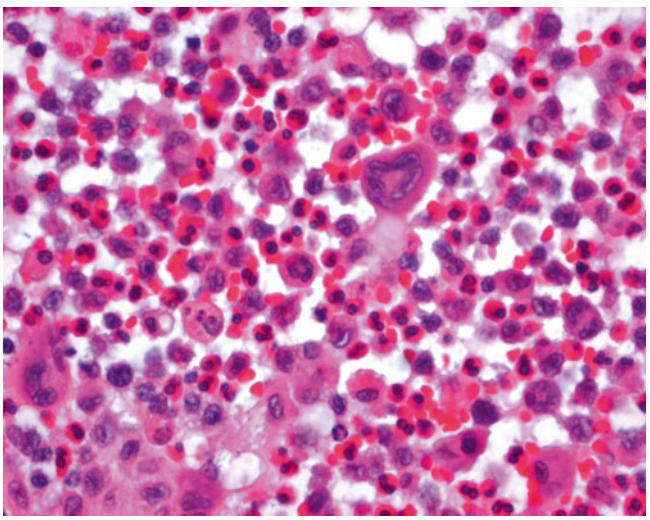


Fig. 58.7 Eosinophils may be abundant in some cases. Multinucleated giant cells are also frequently seen

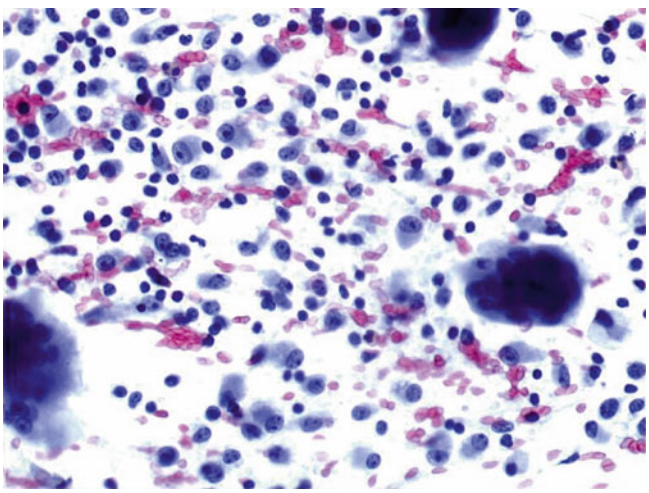


Fig. 58.8 Print cytology performed during needle biopsy procedure. Histiocytes, multinucleated giant cells, and occasional eosinophils seen in this case suggested the diagnosis

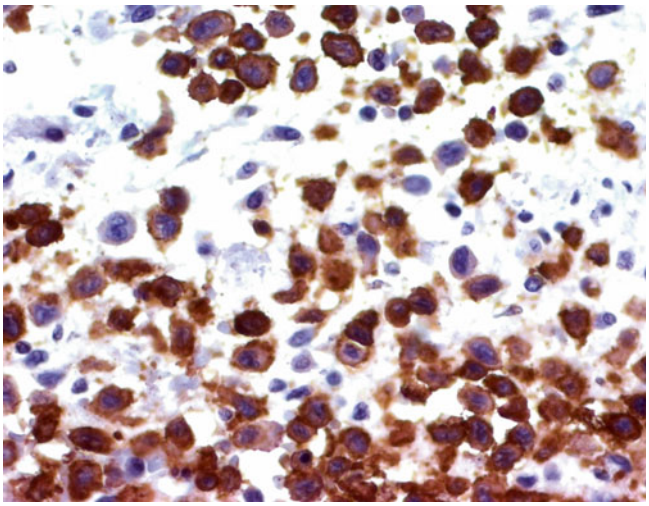


Fig. 58.9 Immunohistochemistry: CD1a positivity in Langerhans cells

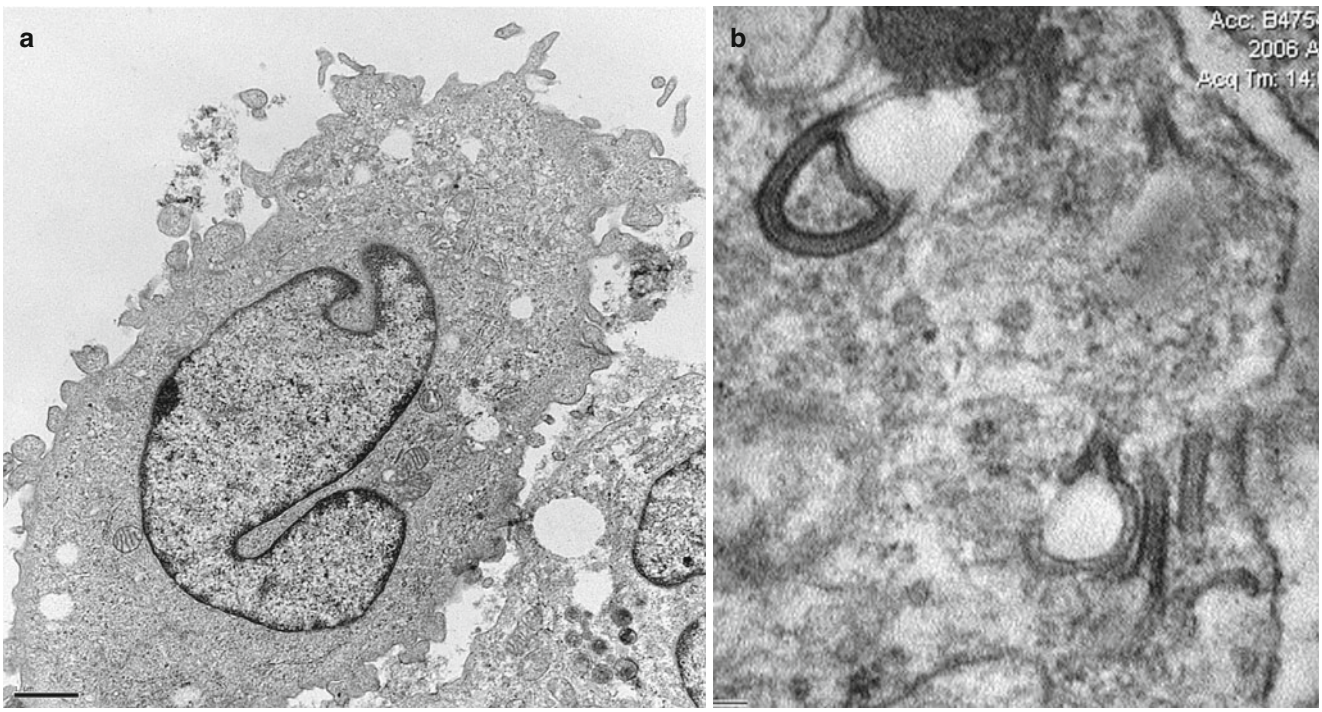


Fig. 58.10 (**a**) Transmission electron microscopy showing the typical folded nuclei of Langerhans cells. (**b**) Transmission electron microscopy identified the pathognomic presence of Birbeck granules

Recommended Reading

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