

AJNR

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AJNR Am J Neuroradiol 1995, 16 (4) 735-740
<http://www.ajnr.org/content/16/4/735>

This information is current as of October 4, 2024.

Neuroradiologic Aspects of Chester-Erdheim Disease

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Summary: In three cases of histologically proved Chester-Erdheim disease there was a large anterior epidural lesion from C-3 to L-2 in one patient; dural masses and orbital infiltration in a second patient; and dural, choroid plexus, retroorbital, and hypophyseal lesions in a third patient. Diabetes insipidus, exophthalmia, long bone lesions, and retroperitoneal infiltration were present.

Index terms: Granuloma; Histiocytosis

In 1930, Chester reported two cases of an uncommon form of lipogranulomatosis, with clinical and histologic features that were different from those seen in Hand-Schuller-Christian disease or primary lipidoses (1). The disease was characterized by proliferation of cholesterol-containing foamy histiocytes in the skeleton, especially in the long bones, but the viscera were also affected. The eponym *Chester-Erdheim disease* was subsequently coined by Jaffe (2). Chester-Erdheim disease has been reported in 40 cases (2-9), and special mention of neurologic involvement has been described in 8 cases (8). We report three women with Chester-Erdheim disease who had worked in the textile industries in the north of France.

Case 1

This 74-year-old woman was admitted for a gait disorder and sphincter incontinence. Her medical history included exophthalmia and polyuria-polydipsia for 10 years, painful knees, and fatigability and mild behavioral disorders for 1 year. Positive findings included paraplegia and ataxia, xanthomas on her eyelids, an erythrocyte sedimentation rate of 90 mm/h, and diabetes insipidus. Roentgenograms of the lower limbs revealed symmetric sclerosis of the bones predominating in distal metaphyses of the femurs and proximal metaphyses of the tibiae, sparing the

epiphyses. Myelography revealed an extradural block at the L-2/L-3 level. The block was complete from the cervical spine to D-12 and was incomplete at L-1/L-2 (Fig 1A). After myelogram computed tomography (CT) showed a large lesion occupying the anterior epidural space at the level of L-1 (Fig 1B). Contrast-enhanced brain CT revealed bilateral infiltration of retroorbital fat. Thoracic and abdominal CT showed a proliferative process encircling the aorta. Inhalation pneumopathy developed, and the patient died. Autopsy revealed a xanthogranulomatous process involving the anterior epidural space, the pituitary stalk, and the adventitia of the aorta, sparing the other large vessels, characterized by fibrosis with foamy histiocytes and giant multinucleated cells (Fig 1C). Surface markers of Langerhans cells (S-100 protein and OKT6) were studied. A few cells were S-100 positive. Birbeck granules, which are intracytoplasmic granules specifically seen in histiocytosis X, were not visible on electron micrographs.

Case 2

This 56-year-old woman was admitted for metabolic disorders and chronic weakness. Her medical history included 18 years of exophthalmia, eyelid xanthomas, and diabetes insipidus, requiring treatment by vasopressin. Painful knees and skin lesions on the anterior face of the trunk were noted for 5 years and left hemiparesis for 1 year. Neurologic features included mild spastic hemiparesis but also paraplegia with diffuse pyramidal signs, cognitive impairment, and seizures. Laboratory studies revealed increased erythrocyte sedimentation rate (100 mm/h), C reactive protein, and fibrinogen levels. Roentgenograms of the lower limbs showed symmetric sclerosis of the bones predominately in the metaphyses proximal to the knees, sparing the epiphyses. Thoracic CT with intravenous contrast administration showed mediastinal infiltration, with abnormal thickening of the aortic wall, particularly at the level of the aortic arch. Abdominal CT revealed diffuse perirenal lesions with subcutaneous and retroperitoneal fat infiltration. Bilateral infiltration of retroorbital fat was identified on CT (Fig 2A). Magnetic reso-

Received February 3, 1993; accepted after revision June 14.

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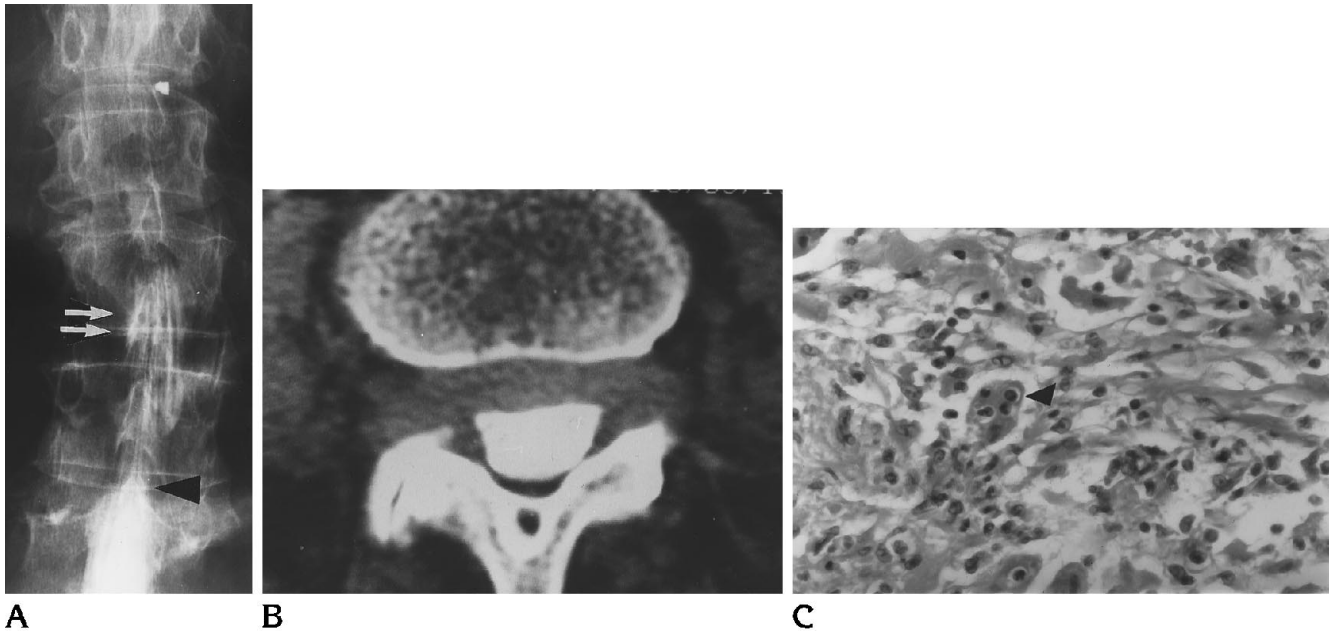


Fig 1. Case 1. A, Myelography reveals an extradural block at L-2/L-3 (*single arrow*). The block was incomplete in the midlumbar region (*double arrow*).

B, Postmyelogram CT of the spine shows a large lesion occupying the anterior epidural space. The level of the section is L-1.

C, A photomicrograph of the epidural specimen shows a fibrous tissue infiltrated with foamy histiocytes and multinucleated cells, with an erythrophagocytosis picture. A granulocyte phagocytosing red cells is pointed out with a black arrow (magnification, 250 \times).

nance (MR) (Fig 2B) showed extraaxial masses in the frontal region and along the falx in addition to infiltration of the sphenoid sinus. Bone, retroperitoneum, and skin biopsies showed proliferation of fibrocytes with foamy histiocytes and multinucleated cells. Cells were negative for OKT6 and S-100 protein. No Birbeck granules were seen. After corticoid treatment was started, paraparesis and cognitive disorders improved. Nine months after discharge, there was recurrence of her metabolic disorders, and 2 years later she died from a diffuse sepsis related to

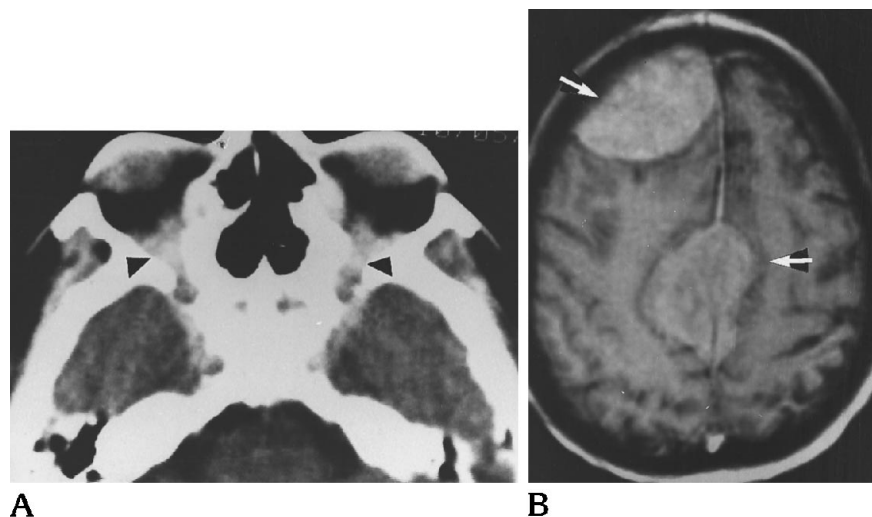
a fasciitis in the left leg and associated hepatic and renal failure.

Case 3

This 50-year-old woman was admitted for acute respiratory failure, but dyspnea appeared 1 year earlier and was related to a diffuse infiltrative lung disease. She had a 10-year history of bilateral exophthalmia and eyelid xanthomas, and painful knees for 5 years. Although there

Fig 2. Case 2. A, Brain CT with contrast shows bilateral infiltration of retroorbital fat at the level of the two black arrows.

B, MR (0.5 T; spin-echo T1; 500/25/2 [repetition time/echo time/excitations]; matrix, 256; 224 voxels; field of view, 250 mm) reveals two enhancing extraaxial lesions, one involving the frontal dura, the other the falx.



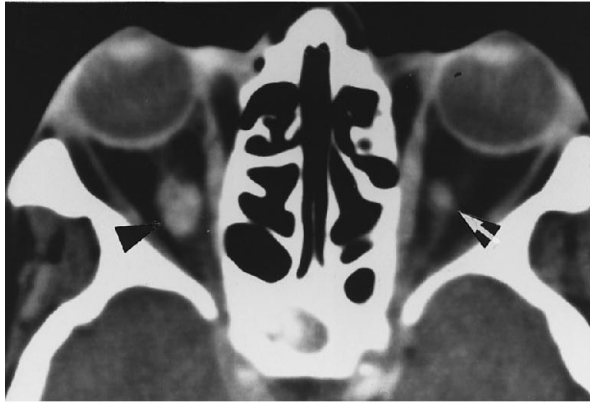
were no neurologic complaints, examination revealed mild paraparesis with diffuse pyramidal signs and a mild frontal lobe syndrome. Polyuropolydypsia that had persisted for more than 10 years improved spontaneously. Erythrocyte sedimentation rate was 65 mm/h; C reactive protein, 65 mg/L. A chest x-ray showed a diffuse reticular pattern in both lungs and thickening of the interlobular septa and interlobar fissures. Radiographic study demonstrated widespread osteosclerosis in the metaphyses of long tubular bones, without epiphyseal lesions. Lytic lesions were noted in both femoral diaphyses. Osteosclerosis was present at the T-9, L-1, and L-2 levels. Thoracic and abdominal CT with contrast showed abnormal thickening of the aortic wall from the aortic arch to the iliac bifurcation. CT, with intravenous contrast administration, confirmed the exophthalmia and revealed bilateral masses involving the optic sheath (Fig 3A). The optic sheath lesions and the sphenoid mass were seen on MR (Fig 3B). Brain CT and MR showed diffuse infiltration of the dura and the falx cerebri (Fig 3C). MR also revealed pituitary, sphenoid sinus, and choroid plexus infiltration with intense gadolinium uptake (Figs 3D and E). A second MR study performed 4 months later showed hyperintense lesions after gadolinium administration and an enlargement of the left intraventricular lesion involving both choroid plexi, larger on left side (Fig 3F). Transbronchial and bone biopsies showed fibrous tissue with foamy histiocytes. Cells were negative for OKT6 and S-100 protein. No Birbeck granules were seen. There was progressive memory impairment, mild ataxia, and worsening respiratory function. Brain MR revealed that all the lesions had enlarged. The most striking change was that of bilateral choroid plexi lesions, with extension into both temporal lobes (Fig 3G). Infiltration of the hemispheric dura increased, notably on the right side, and new lesions were present, involving the dura in the pontocerebellar angle and infiltrating the right cerebellar lobe (Fig 3H). Her respiratory failure worsened, and the patient needed progressively permanent oxygen therapy. Coma with decerebration occurred, caused by an enlargement of the right cerebellar lesion, in the pontocerebellar angle. She died after a 3-year follow-up. Postmortem examination confirmed all lesions and histologic appearance of Chester-Erdheim disease.

Discussion

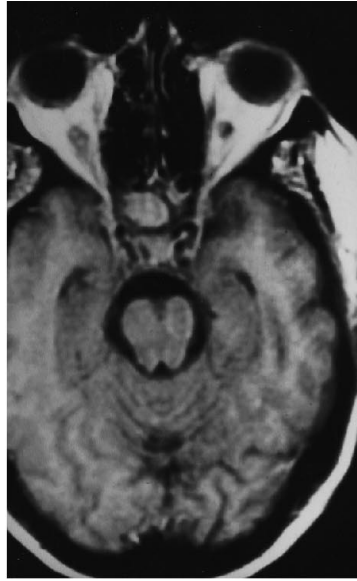
Chester-Erdheim disease is a rare lipogranulomatosis. Forty cases have been reported since the description in 1930. Neurologic involvement was demonstrated in 8 cases. Chester-Erdheim disease is characterized by lipid granulomata in the long tubular bones, which give typical radiologic features, namely symmetric sclerosis of the metaphyses of long bones, sparing the epiphyses. Lipid granuloma may also involve other mesenchymal tissues,

especially retroperitoneal space, lung, skin, and orbit. There is a wide range of clinical features and prognosis, depending on the location of the lesions. Some patients are admitted only for painful legs, whereas other patients die from extensive visceral lesions. In our three cases, the diagnosis of Chester-Erdheim disease was made on the basis of associated signs: (a) osteosclerotic lesions of long bones; (b) diffuse visceral involvement; and (c) pathologic findings.

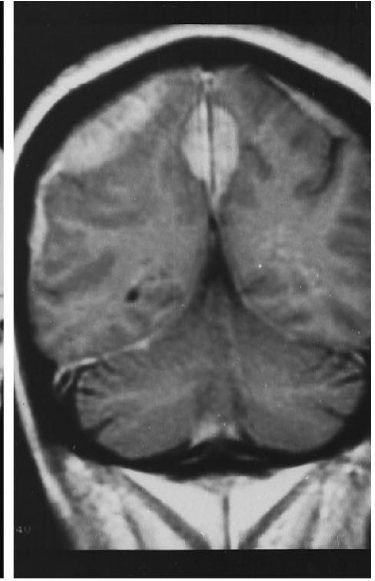
In our three patients, as in previous reports, the occurrence of exophthalmia, diabetes insipidus, and bone lesions was very confusing, because it mimicked Hand-Schuller-Christian disease (5, 9). In our view, some of the features of Chester-Erdheim disease seem to be quite different from those of Hand-Schuller-Christian disease, thus permitting the differentiation of these two entities. Skeletal lesions, the most specific features of Chester-Erdheim disease, are different from those in Hand-Schuller-Christian disease, which are lytic lesions involving usually the skull (10). However, skeletal involvement in Chester-Erdheim disease also may affect the skull, vertebrae, or ribs as in our third case and in previous reports (5, 11-14). Moreover, the age when the diagnosis is made is different (13). A review of literature shows a mean age of 52.8 years (SD, 15.9) in Chester-Erdheim disease, with a range of 7 to 78 years (12, 15), whereas Hand-Schuller-Christian disease occurs in young children. Furthermore, retroperitoneal involvement seems to be a characteristic feature of Chester-Erdheim disease (5, 9, 11, 16). Involvement of aortic adventitia was previously reported by Chester (1) and reiterated by Hallervorden (17). Fibrous encasement of the aorta was described by Mergancova et al (18), but this also was reported in a case of xanthogranulomatous pyelonephritis (19). This could suggest an infectious process in both diseases. Finally pathologic findings are different; in Chester-Erdheim disease, there is fibrous tissue containing lipid-laden histiocytes (3), cells that do not express S-100 protein or OKT6 antigens (5), and absence of Birbeck granules, also called X cells, on electron micrographs, although light microscopic images may be confusing (3). Although Chester-Erdheim disease may be a late-healing phase of Langerhans cell histiocytosis (20), distinguishing between them is useful, because prognosis and therapy may



A



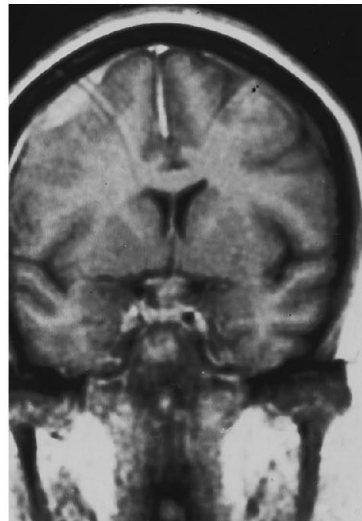
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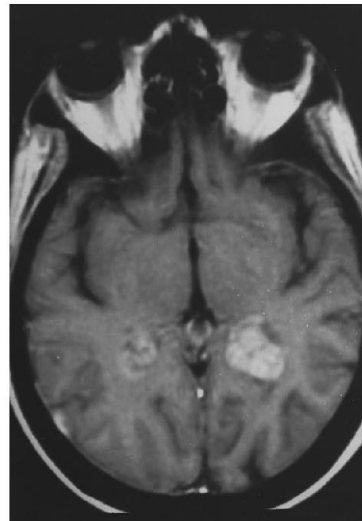
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F



G



H

Fig 3. Case 3. A, CT of the orbits shows bilateral exophthalmous and lesions of both optic sheaths (*bilateral arrows*).

B, MR shows the lesions involve the optic sheaths.

C, MR, with gadolinium administration, reveals diffuse enhancing lesions involving the dura and falx.

D, MR, without gadolinium administration, shows a mass below the chiasm, surrounding the infundibulum of the pituitary gland. The gland itself seems to be spared.

E, MR shows gadolinium uptake of the sphenoid sinus and pituitary stalk. Enhancing dura mass along the convexity on the right is seen.

F, MR, with gadolinium administration, shows a hyperintense lesion involving both choroid plexi, predominately on left, and dural enhancement on the right.

G, MR, with gadolinium administration, reveals that lesions involving both choroid plexi had progressively enlarged (*single arrow*) and that the sphenoid enhancing lesion had spread to the pons (*double arrow*).

H, MR shows gadolinium enhancement involving the dura anterior to the cerebellum on the right with infiltration of the adjacent cerebellum (*double arrow*). An enhancing lesion appeared in the sphenoid sinus (*single arrow*).

infiltration of the adjacent cerebellum (*double arrow*). An enhancing lesion appeared in the sphenoid sinus (*single arrow*).

be different (17, 21–23). Differential diagnosis also includes malignant histiocytosis or primitive brain lymphoma and sinus histiocytosis with massive lymphadenopathy associated with epidural lesions (24).

Neurologic involvement is variable in Chester-Erdheim disease and, in fact, the patient may be asymptomatic. Neurologic deficits, reported in eight cases up to now, included ataxia (8, 14, 23, 25). The more usual features are dural granulomas involving brain stem and cerebellum (8). The involvement of sacral dura was described in one case (26). Reported intracranial lesions have included falcine and dural masses (1, 8, 14, 23, 25, 26). Asymptomatic choroid plexus involvement has been described in one case (8) and also was found in our case 3. Exophthalmia appeared with orbital involvement, usually bilaterally (7, 27). In our cases, diabetes insipidus was associated with hypophyseal lesions and cognitive impairment with a frontal lobe syndrome. Poehling et al (28) described a woman with altered mental status, but the results of brain CT were not reported.

In our cases, the dural lesions remained circumscribed, compressing but not infiltrating the brain or the spine, whereas in Hand-Schuller-Christian disease and other granulomatous process or lymphoma, infiltrative intracerebral tumors often have been described (29, 30). This may be the most striking feature that distinguished Chester-Erdheim disease from other histiocytic lesions.

The outcome in all three cases suggest that the course of Chester-Erdheim disease includes two stages: the first stage is asymptomatic and could last for 5 to 15 years, and the second stage is symptomatic and its prognosis poor.

Acknowledgments

We are grateful to Professor J. Rémy (Department of Radiology) and to Professor F. Basset for valuable comments. We thank Dr D. Caparros and Dr H. LeMonies de Sagazan (CH. Roubaix), and Dr G. SotoAres (Department of Neuroradiology, Lille) for their clinical help. We are grateful to Dr Ruberg for her assistance in translation and to Drs Parent and Gosselin who performed the pathology study. We thank M. Leroy, E. D'Haese, and J. Saulnier for their helpful contribution to the production of the figures.

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