Erdheim–Chester disease (ECD) is a rare multiple system histiocytosis that is characterized pathologically by xanthogranulomatous infiltrates and radiologically by symmetrical sclerosis of long bones. The diagnosis is often confirmed by biopsy of bone or of orbital or retroperitoneal soft tissue. Intracranial involvement is rare. The authors report a case of ECD in which the diagnosis was made after biopsy of a hypothalamic mass. The mass had been discovered during a workup for panhypopituitarism in a 55-year-old man with urological and bone disease. Aside from diabetes insipidus, other features of pituitary insufficiency have seldom been reported and no patients have presented with a hypothalamic tumor. The endocrinological and neurological aspects of ECD are discussed, as is its differential diagnosis. Reported cases of the disorder associated with hypopituitarism or found during biopsy of central nervous system structures are also reviewed.

**KEY WORDS** • hypothalamus • pituitary • meninges • Erdheim–Chester disease • non–Langerhans cell histiocytosis • hypothalamic–pituitary insufficiency

### Case Report

**History.** This 55-year-old retired Chinese businessman presented in June 1999 with the complaint of months of lethargy, 1 year of episodic low-grade fevers, and 2 years of bone pain. He had experienced polyuria and polydipsia due to DI for 7 years and had responded well to desmopressin treatment. In 1994 a head CT scan had been performed and the results were reportedly normal. In 1995, the patient began to experience progressive renal impairment and hydronephrosis, leading to the necessity of intermittent ureteric stenting and, over the past year, peritoneal dialysis.

In 1998, the patient first noted bilateral hip and thigh pain in addition to decreased libido, impotence, lethargy, and weight loss. Hypopituitarism was confirmed by laboratory findings, including the following concentrations of hormones: thyroxine at 3.3 μg/dl (normal 4.5–12 μg/dl), TSH at 1.45 mIU/L (normal 0.4–4.7 mIU/L), FSH at 0.9 IU/L (normal 1–12 IU/L), LH less than 0.1 IU/L (normal 1–12 IU/L), and testosterone at 0.2 nmol/L (normal 8.4–28.7

### Abbreviations used in this paper:
- ACTH = adrenocorticotropic hormone
- CNS = central nervous system
- CT = computerized tomography
- DI = diabetes insipidus
- ECD = Erdheim–Chester disease
- FSH = follicle-stimulating hormone
- GH = growth hormone
- LC = Langerhans cell
- LH = luteinizing hormone
- MR = magnetic resonance
- TSH = thyroid-stimulating hormone

In this paper we report the case of a 55-year-old man with a 7-year history of DI, in whom panhypopituitarism and hyperprolactinemia developed as well as progressive retroperitoneal and bone disease. The diagnosis of ECD was made on biopsy of a hypothalamic mass. A retrospective review of bone radiographs and neuroimages confirmed the diagnosis.

**Case Report**

This 55-year-old retired Chinese businessman presented in June 1999 with the complaint of months of lethargy, 1 year of episodic low-grade fevers, and 2 years of bone pain. He had experienced polyuria and polydipsia due to DI for 7 years and had responded well to desmopressin treatment. In 1994 a head CT scan had been performed and the results were reportedly normal. In 1995, the patient began to experience progressive renal impairment and hydronephrosis, leading to the necessity of intermittent ureteric stenting and, over the past year, peritoneal dialysis. In 1998, the patient first noted bilateral hip and thigh pain in addition to decreased libido, impotence, lethargy, and weight loss. Hypopituitarism was confirmed by laboratory findings, including the following concentrations of hormones: thyroxine at 3.3 μg/dl (normal 4.5–12 μg/dl), TSH at 1.45 mIU/L (normal 0.4–4.7 mIU/L), FSH at 0.9 IU/L (normal 1–12 IU/L), LH less than 0.1 IU/L (normal 1–12 IU/L), and testosterone at 0.2 nmol/L (normal 8.4–28.7
nmol/L), serum hormone-binding globulin at 34 nmol/L (normal 17–57 nmol/L), and a free androgen index of 0.6 (normal 18–210). The patient’s serum prolactin level was increased to 41.1 μg/L (normal 1.6–18.8 μg/L). Correlating with the low-grade fever (38˚C) was a markedly elevated erythrocyte sedimentation rate of 137 mm/hour.

The patient’s symptoms were relieved by medical treatment consisting of hormone replacement therapy (cortisone acetate 12.5 mg twice daily and thyroxine 0.1 mg once daily).

Examination. When the patient presented to us in 1999, he was thin with a sallow complexion and minimal body hair. Ophthalmological examination yielded normal findings, but bitemporal hemianopsia was noted during visual field testing. The patient’s neurological examination was unremarkable. His prostate was small, as were his testes (6 cm³ each).

Laboratory abnormalities included anemia with a hemoglobin level of 10 g/dl (normal 13–18 g/dl) and elevated serum levels of creatinine at 168 μmol/L (normal 88–132 μmol/L) and uric acid at 14.9 mg/dl (normal 4.3–8 mg/dl). Urea, sodium, potassium, and glucose levels were normal. Pituitary insufficiency was again documented, with concentrations of LH lower than 0.07 mIU/ml (normal 1.5–9.3 mIU/ml), FSH at 0.7 mIU/ml (normal 1.4–18.1 mIU/ml), ACTH lower than 10 mIU/L (normal 10–46 mIU/L), GH lower than 0.13 mIU/L (normal 0.16–13 mIU/L), TSH at 0.06 mIU/ml (normal 0.47–5.01 mIU/ml), thyroxine at 81 nmol/L (normal 57–141 nmol/L), and testosterone at 0.1 ng/ml (normal 2.7–10.7 ng/ml). Again the serum prolactin level was elevated to 39.2 ng/ml (normal 2.1–17.7 ng/ml).

Central DI was also confirmed by an elevated serum osmolality of 318 mmol/kg (normal 275–295 mmol/kg), and an overnight water deprivation test revealed persistent diuresis (200 ml/hour) at an osmolality of 140 mmol/kg in the face of a plasma osmolality of 310 mmol/kg.

Chest x-ray films appeared normal, aside from an old fracture of the right seventh rib. Although an intravenous urogram showed bilateral hydronephrosis with poor excretion from the left kidney, there was good clearance of contrast agent following intravenous administration of Lasix (40 mg). A CT scan of the abdomen revealed an extensive abnormality of the perirenal spaces and paraaortic regions, wherein the ureters were encased by ill-defined tissue of increased density. This was interpreted as retroperitoneal fibrosis. The cytological findings of a specimen obtained by fine-needle aspiration of the perirenal space were nondiagnostic. Radiographs revealed extensive sclerosis of both femoral necks without an associated periosteal or soft-tissue abnormality. Lytic lesions were also noted in the neck of the right femur. The heads of both femurs and the lumbar vertebrae were unremarkable. The possibility of a metabolic bone disease was raised when an isotopic bone scan showed increased uptake of tracer in the patient’s shoulders, hips, and knees bilaterally.

Magnetic resonance imaging of the head (Fig. 1) revealed a homogeneously enhancing suprasellar mass measuring approximately 18 mm, which displayed intermediate signal intensity on T₂-weighted images. The mass extended from the infundibulum to the hypothalamus, superiorly displacing the floor of the third ventricle. It also extended anterolaterally, resulting in enlargement and enhancement of the optic nerves and chiasm. The pituitary fossa appeared normal. The remainder of the brain was unremarkable. Leading diagnostic considerations included a granulomatous disease, such as sarcoidosis or tuberculosis, and tumor, particularly LC histiocytosis or lymphoma.

Operation. A right pterional craniotomy with complete resection of the suprasellar tumor was performed. Supplied by branches of the internal carotid artery, the tumor was well defined, soft, and yellow.

Postoperative Course. Displaying no deterioration of neurological function, the patient was discharged 1 week after surgery. Hormone replacement included cortisol acetate (25 mg every morning and 12.5 mg every night), thyrxine (0.1 mg daily), desmopressin (0.1 mg daily), and testosterone esters (250 mg delivered by injection monthly).

Because no reported treatment strategies, including steroid medications, chemotherapy, or radiotherapy, had resulted in more than temporary or minimum relief of symptoms, our patient chose not to undergo further treatment. At his most recent follow-up examination, performed 16 months following the craniotomy, he complained of progressive bone pain. Although an MR image of the head

Fig. 1. Preoperative contrast-enhanced MR images revealing a discrete, bosselated intra- and suprasellar tumor that is enhancing.
revealed no residual or recurrent mass in the hypothalamic region, new, diffuse enhancing infiltrates of the meninges developed (Fig. 2). Absence of the normally bright signal of the posterior pituitary was also noted. Fully 8 years after onset of DI, our patient is alive and receiving hormone replacement therapy.

Pathological Findings. Macroscopically, the tumor consisted of a soft, tannish yellow, 1.7-cm lobulated tissue fragment. Histologically, it was composed of sheets of foamy histiocytes with abundant lipidization and small, round nuclei lacking grooves or atypia. Scattered multinuclear Touton-type giant cells were also noted, as were aggregates of mature lymphocytes and rare eosinophils (Fig. 3). Fibrosis and gliosis were focally noted.

Immunostains confirmed the histiocytic nature of the mono- and multinuclear cells, which stained strongly and diffusely for CD68 (Fig. 4). Both S-100 protein (polyclonal, dilution 1:800; Dako Corp, Carpinteria, CA) and CD1a (monoclonal, dilution 1:5; Immunotech/Coulter, Westbrook, ME), markers of LCs, were negative. The cells also proved to be negative for CD30 (monoclonal, dilution 1:150), CD20 (monoclonal, dilution 1:60), ALK-1 (monoclonal, dilution 1:20), myeloperoxidase (polyclonal, dilution 1:5000), and glial fibrillary acidic protein (polyclonal, dilution 1:800; all antibodies purchased from Dako Corp.). Neurofilament protein staining highlighted the expansive rather than infiltrative nature of the lesion: the axons were displaced to the periphery of the lesion. No organisms were noted on methenamine-silver stains for fungi or on acid-fast and auramine–rhodamine stains for tubercle bacilli.

Ultrastructural examination confirmed the presence of mono- and multinuclear cells with features of histiocytes (Fig. 5). The cytoplasm contained a small quantity of lysosomes as well as lipid droplets. Intermediate filaments were occasionally seen dispersed in whorls. No characteristic inclusions were noted to suggest a specific storage disease. Birbeck granules were lacking.

Given the pathological features of the brain biopsy, the patient’s clinical history, and the radiographic features of the long-bone lesions, a firm diagnosis of ECD was established. Nevertheless, other xanthogranulomatous processes were considered in the differential diagnosis. Although usually diseases of children, these included juvenile xanthogranuloma, multiple system reticuloendothelialosis, and hemophagocytic lymphohistiocytosis. Rosai–Dorfman disease was also considered, but was excluded because of the lack of emperipolysis and S-100 protein immunostaining. In light of the patient’s clinical history, strong consideration was given to LC histiocytosis; however, this was excluded because of the lack of the histological, immunocytochemical, and ultrastructural findings.

Discussion

The two earliest cases of ECD were described by Chester in 1930 as “lipoid granulomatosis.” Since then, a number of reports have been published. Although most have been case reports or very small series, a literature review of 59 patients was recently published by Veyssier-Belot, et al.24 To date, the literature contains more than 60 cases of this sporadically occurring, systemic form of non-LC histiocytosis. The median age of patients with ECD is in the sixth decade and there is a slight male preponderance. By definition, bone involvement is always present; whether asymptomatic or causing pain, it is the cardinal feature of ECD. Radiographically, characteristics of the disease include symmetrical sclerosis of long bones with diaphyseal or metaphyseal involvement and epiphyseal sparing. Additional lytic lesions are present in 30% of the cases. Bone scans reveal increased radionuclide uptake, particularly at the ends of long bones. Our patient suffered from bone pain, accompanied by typical radiographic and scintigraphic findings. In addition to bone disease, involvement of the retroperitoneal space and renal dysfunction, with or without hydronephrosis, has been observed in more than 25% of patients. All were features in the present case. Infiltration of orbital and retroorbital soft tissue with resulting exophthalmus is also a frequent presentation. Involvement of the lungs and heart, although less common and not a feature of our case, is a major contributor to mortality in these patients.

Diabetes insipidus attributed to infiltration of the pituitary–hypothalamic axis follows bone pain in frequency. Although it often precedes arrival at the diagnosis of ECD by a decade or longer, neuroimaging rarely detects abnor-
malities. When present, findings range from thickening of the pituitary stalk to a rare tumorlike mass, as was seen in our patient. Absence of the normal high signal of the posterior pituitary on T1-weighted MR images has been reported in a few cases. This is not specific to ECD, however, because it also occurs in DI from other causes, including LC histiocytosis.

Although DI is common in patients with ECD, anterior pituitary dysfunction has seldom been documented. Table 1 provides a summary of four previously reported cases,9,14,21,23 our case constitutes the fifth reported case. In three of these patients, including ours, low serum gonadotropin levels were detected and in two instances decreased libido and impotence were noted. A fourth patient presented with decreased libido; a low serum testosterone level was documented, but LH and FSH levels were reportedly normal.

Growth hormone levels were decreased in four patients, including ours. In a 7-year-old boy, the only child with ECD reported on in the literature,9 the disease was symptomatic and led to short stature (Table 1).

Our patient is the first in whom panhypopituitarism was documented, in addition to low serum levels of TSH, thyroxine, and ACTH. Hypothyroidism may have contributed to our patient’s lethargy, because this symptom improved in response to hormone replacement therapy.

Interestingly, in the case we describe and in two previously published cases,9,23 hyperprolactinemia was documented. This is likely due to a stalk section effect, that is, the mechanical disruption of the hypothalamic dopaminergic pathway that normally inhibits secretion of prolactin.

In all reported cases featuring anterior pituitary dysfunction, the presence of posterior pituitary dysfunction, that is, DI, had preceded it for years. Furthermore, DI has always occurred in the setting of multiple organ involvement. The actual incidence of anterior pituitary dysfunction may be higher than reported, because there is no doubt that there have been asymptomatic cases in which measurement of hormone levels was never undertaken.

In the four reported cases of ECD wherein CT and/or MR imaging of the hypothalamic–pituitary region was performed,9,14,22,23 results varied from the absence of detectable changes in three patients9,14,23 to thickening of the pituitary stalk in one.22 Orbital and meningeal involvement were detected in two different cases.4,7 Histological confirmation of hypothalamic involvement has not been previously reported. Involvement was assumed on the basis of laboratory and imaging findings, and the diagnosis was made on the basis of biopsies of extraneural disease. None of the previously published cases of ECD, in which there was dysfunction of both the anterior and posterior pituitary, was associated with a detectable mass. It is only in our patient that MR imaging detected a homogeneously enhancing suprasellar mass.

Because in our case the disease was not clinically suspected and a retroperitoneal fine-needle aspiration failed to
obtain diagnostic tissue, histological examination of the hypothalamic mass became a necessity. Before craniotomy and in light of the retroperitoneal and bone disease, the differential diagnosis included tumor (LC histiocytosis, lymphoma, or metastases) and granulomatous disease (tuberculosis or sarcoidosis). Resection of the tumor revealed it to be a xanthogranulomatous lesion. Cytologically, the features of the histiocytes were dissimilar from those of LCs. Their foamy cytoplasm, round nuclei with smooth contours, small nucleoli, and lack of nuclear grooves were distinguishing features, as was the lack of eosinophils and Birbeck granules viewed ultrastructurally. Rosai–Dorfman disease also entered into the differential diagnosis; however, lack of emperipolesis, a distinctive histological feature, as well as lack of immunoreactivity for S-100 protein did not support this diagnosis. Last, no specific ultrastructural features indicative of a storage disease were noted.

Although neurological involvement has been apparent in several reported cases of ECD, histological confirmation of the diagnosis has rarely relied on brain biopsy. Central nervous system involvement usually has been suspected on the basis of neurological symptoms in the setting of histologically and/or radiologically proven ECD. Cerebellar symptoms have followed DI in frequency. Focal neurological deficits indicative of cerebral or spinal lesions have only rarely been encountered. Computerized tomography and/or MR images have been used to confirm the clinical diagnosis. Regarding the lesion, most have been diffuse and meningeal based, although some have been more localized and caused mass effects. Intraparenchymal involvement is very uncommon and is evident on MR images as multifocal, diffuse, or infiltrative lesions mimicking granulomas, infarcts, or demyelinating disease. On CT scans, typical lesions have appeared hypodense and displayed contrast enhancement. On MR images, they have appeared isosensitive; enhancement has persisted for prolonged periods in some instances and up to 23 days in one case. Laboratory tests usually have provided nonspecific findings. The presence of histiocytes in cerebrospinal fluid was noted in one case.

Although only performed in occasional cases, autopsies have provided a complete picture of CNS involvement in patients with ECD, including those who were neurologically asymptomatic. Meningeal lesions, in particular, exhibit the typical xanthogranulomatous infiltrates observed in other organs. Involvement of various arteries, such as the vertebral and basilar, has also been documented. Intraparenchymal lesions are typically infiltrative and feature a perivascular distribution. Occasionally histiocytes have been few and lacked the distinctive cytological characteristics of foam cells. Nonetheless, CD68 staining is a regular feature. Scant S-100 protein staining of histiocytes has been noted, but CD1a stains have been negative and ultrastructural studies have shown Birbeck granules to be lacking. In one report the associated reactive gliosis was prominent and simulated infiltrative glioma. Rosenthal fibers may also be seen.

Because ECD is a multiple system process, establishment of a tissue-based diagnosis seldom depends on examination of CNS tissue. As a result, neurosurgical reports of

Fig. 5. Electron micrograph demonstrating that both mono- and multinuclear histiocytes are filled with lysosomes. There are few intermediate filaments (arrows) and no Birbeck granules. Original magnification × 25,000.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Patient Age (yrs)</th>
<th>Sex</th>
<th>Neuroendocrinological Symptoms</th>
<th>MR/CT Imaging Findings in Brain, Hypothalamus, &amp; Pituitary</th>
<th>Laboratory Findings</th>
<th>Other Symptoms/Signs</th>
<th>Treatment/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller, et al., 1986</td>
<td>44, M</td>
<td>for 10 yrs followed by impotence</td>
<td>central DI</td>
<td>brain scan initially normal; several yrs later, head CT scan normal, but sector scan of orbits revealed massive infiltrates surrounding length of both optic nerves from posterior surface of the globe to orbital apices</td>
<td>normal levels of T&lt;sub&gt;4&lt;/sub&gt;, cortisol, GH, &amp; PRL, but decreased levels of LH, FSH, &amp; testosterone; biopsies on bone &amp; skin</td>
<td>intermittent fever; bone pain, weight loss, &amp; rash</td>
<td>vinblastine &amp; prednisone given, but no improvement; hemibody radiation therapy w/ subjective improvement</td>
</tr>
<tr>
<td>Tien, et al., 1990</td>
<td>30, M</td>
<td>central DI followed by decreased libido</td>
<td>CT &amp; MR imaging revealed no brain or pituitary abnormalities; skeletal radiographic survey &amp; scans demonstrated multifocal skull &amp; long-bone lesions</td>
<td>normal imaging followed by enlargement of pituitary stalk (7 mm); partially empty sella; pituitary stalk thickness subsequently decreased to 4 mm; absence of normal high signal intensity on T&lt;sub&gt;1&lt;/sub&gt;-weighted images of posterior lobe</td>
<td>normal serum levels of PRL, T&lt;sub&gt;4&lt;/sub&gt;, FSH, LH, cortisol, &amp; TSH; decreased levels of GH &amp; testosterone; biopsy of bone</td>
<td>characteristic bone changes on radiographs</td>
<td>medical treatment of DI, asymptomatic at 2.5 yrs</td>
</tr>
<tr>
<td>Globerman, et al., 1991</td>
<td>7, M</td>
<td>central DI; short stature (2.7 SDs below mean); skeletal age 4.5 yrs</td>
<td>CT &amp; MR imaging revealed no brain or pituitary abnormalities; skeletal radiographic survey &amp; scans demonstrated multifocal skull &amp; long-bone lesions</td>
<td>inadequate peak GH responses to insulin-induced hypoglycemia &amp; to clonidine; 2 random somatomedin levels below baseline; hyperprolactinemia, hyperresponsive to TRH; normal responses of TSH to TRH &amp; of cortisol to hypoglycemia &amp; metapyrone test</td>
<td>lesions in neck, mediastinum, &amp; retroperitoneum; biopsy revealed bone, neck mass, &amp; mediastinum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tritos, et al., 1998</td>
<td>58, F</td>
<td>central DI, cerebellar dysfunction</td>
<td>MR imaging revealed cerebellar atrophy; diffuse leptomeningeal enhancement; no focal parenchymal or mass lesions, but normal bright signal of posterior pituitary lacking</td>
<td>normal levels of TSH, free T&lt;sub&gt;4&lt;/sub&gt;, total T&lt;sub&gt;4&lt;/sub&gt;, &amp; cortisol; decreased levels of LH, FSH, &amp; IGF-1; increased levels of PRL, serum sodium, &amp; osmolality</td>
<td></td>
<td>bilateral eyelid xanthomas; retroperitoneal mass; low hemoglobin &amp; platelet count</td>
<td>died of aspiration pneumonia</td>
</tr>
</tbody>
</table>

* IGF-1 = insulin-like growth factor–1; PRL = prolactin; SD = standard deviation; TRH = thyrotropin-releasing hormone; T<sub>4</sub> = thyroxine.

Radiological and neurosurgical awareness of ECD may initiate a systemic review, including long-bone imaging studies. Some clinical features of the disease overlap with those of LC histiocytosis, but others are distinct. Although both diseases share a frequent occurrence of DI, bone pain, and exophthalmus, these are more often seen in cases of LC histiocytosis. On the other hand, cerebellar and cerebral involvement is more common in cases of ECD. And although LC histiocytosis is primarily a disease of children and young adults, only one pediatric case of ECD has been reported. Both conditions feature involvement of bone, but the osseous lesions of LC histiocytosis are typically lytic and more often involve flat bones, including the skull. When lytic lesions do occur in patients with ECD, the lesions are invariably accompanied by symmetrical sclerosis of long bones.

When ECD is suspected, histological confirmation is necessary. Tissue samples may be obtained more easily from bone or other organs than by CNS biopsy. Nevertheless, in our patient as well as in one with a spinal epidural mass and another with obstructive hydrocephalus requiring shunt placement, a neurosurgical approach is occasionally needed to reduce mass effects and provide symptomatic relief. In most reported cases, however, brain involvement has been sufficiently generalized and removal of the tumor has not been feasible. Furthermore, although debulking can provide temporary relief, the lesion may rapidly regrow to its original size. Postoperatively, patients may report symptomatic improvement, including abatement of fever and weight loss, as well as better control of the DI. Nonetheless, no therapies, including a regimen of steroid medication, chemotherapy, or radiotherapy, have resulted in more than temporary relief of symptoms or abatement of disease.

Although the initial course of ECD may be asymptomatic or slowly progressive over a period of years, rapid deterioration occurs at some point in most cases. The eventual, high mortality rate is attributed to lung or pericardial involvement and, occasionally, to renal failure.

In summary, we have reported a case of ECD in a patient presenting with hypothalamic–infundibular involvement and panhypopituitarism. It is the first reported case in the neurosurgical literature in which the diagnosis was first established by CNS biopsy. Although ECD is currently considered a distinct, progressive form of non-LC histiocytosis, there are reports of mixed or simultaneous occurrence of both diseases and of overlapping imaging and pathological findings. The possibility that these two diseases represent a disease spectrum is still under debate.
### TABLE 2

**Literature review of cases of ECD in which neurosurgical biopsy was performed**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Patient Age (yrs), Sex</th>
<th>Neurological/Endocrinological Symptoms</th>
<th>MR/CT Imaging Findings in Brain, Hypothalamus, &amp; Pituitary</th>
<th>Operative Findings</th>
<th>Other Symptoms/Signs</th>
<th>Treatment/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tien, et al., 1989</td>
<td>54, M</td>
<td>orbital masses resulting in visual loss &amp; diplopia; gait disturbance &amp; lack of coordination</td>
<td>CT scan revealed multiple enhancing intracranial masses; multiple low attenuation, but intensely enhancing, parasagittal masses</td>
<td>craniotomy included subtotal resection of a 4-cm parasagittal, gray-yellow, &amp; friable falcine mass; no involvement of sagittal sinus</td>
<td>characteristic signs on bone radiological studies noted after brain biopsy</td>
<td>no changes in neurological status</td>
</tr>
<tr>
<td>Miyachi, et al., 1990</td>
<td>42, M</td>
<td>orbital exophthalmus; visual disturbance followed by vomiting &amp; altered neurological status, but no focal deficits</td>
<td>orbital lesions followed by development of a large CT–non-enhancing, low-density tentorial mass extending to rt posterior fossa w/ resultant obstructive hydrocephalus; low signal intensity of mass on T1- &amp; T2-weighted MR images; angiogram revealed avascular tentorial mass</td>
<td>orbital exenteration; subsequent craniotomy disclosed firm, xanthomatous mass, demarcated from brain w/ no leptomeningeal attachment; Torkildsen shunt placed</td>
<td>retroperitoneal mass</td>
<td>recovered postop, but died of pleural effusion w/in 3 mos; autopsy showed regrowth of dural tumor</td>
</tr>
<tr>
<td>Sandrock, et al., 1990</td>
<td>54, M</td>
<td>2 yrs of bilateral proptosis &amp; orbital pain; recent loss of balance, lack of coordination, &amp; headaches</td>
<td>CT scan revealed bilateral orbital masses that increased in size after 2-yr interval; MR imaging revealed 3 intracerebral masses; IVP showed hydro-nephrosis; MR imaging revealed renal medullary infiltrates, ureretal obstruction; echocardiogram demonstrated pericardial mass &amp; effusion; bone scan abnormalities</td>
<td>biopsy revealed exclusion of an orbital &amp; 1 of 3 CNS brainstem, cerebellum, &amp; cerebral masses</td>
<td>perhaps familial angioneurotic edema</td>
<td>radiotherapy to orbits (35 Gy), but no objective improvement; stable on regimen of prednisone; new white matter infarctate, but no neurological symptoms during follow-up exams</td>
</tr>
<tr>
<td>Smith, et al., 1993</td>
<td>58, M</td>
<td>initial lack of hand coordination, impaired tandem gait, diminished dysarthria, dysphagia, &amp; hemisensory deficit</td>
<td>MR images revealed multifocal hyperintensity in midbrain, cerebellar peduncles, &amp; lt occipital region on T2-weighted images &amp; confluent enhancement in abnormal areas on T1-weighted images</td>
<td>stereotactic biopsy of frontal lobe enhancing lesion</td>
<td>no other symptoms; CSF held increased levels of protein &amp; albumin; no oligoclonal bands; histiocytes present characteristic signs on bone radiological studies; periorbital swelling &amp; proprioception</td>
<td>prednisone &amp; azathioprine ineffective; WBRT led to improvement of symptoms in 6 wks &amp; decrease in lesion size in 6 mos recurrent dural mass at 8–18 mos; patient alive 4 yrs after 2nd decompressive laminectomy</td>
</tr>
<tr>
<td>Babu, et al., 1997</td>
<td>22, M</td>
<td>stiffness of gait followed by paraparesis &amp; reduced T6 sensory level</td>
<td>MR image revealed enhancing spinal epidural mass at T5–11; 6 mos later periorbital swelling developed; CT scan revealed bilateral intracranial infiltrative mass</td>
<td>decompressive laminectomy of T5–12; thick, white, rubbery masses densely adherent to dura mater; 2nd biopsy of orbital tissue</td>
<td>characteristic signs on bone radiological studies; periorbital swelling &amp; proprioception</td>
<td>questionable transient postop improvement in speech &amp; gait w/ oral prednisone treatment</td>
</tr>
<tr>
<td>Wright, et al., 1999</td>
<td>42, F</td>
<td>central DI; progressive gait disturbance; mild ataxic dysarthria; headache</td>
<td>MR images initially normal; 2 yrs later, patchy, enhancing pontine lesions, w/ abnormalities extending to medulla &amp; cerebellar peduncles seen on T2-weighted images</td>
<td>It suboccipital craniotomy showed fullness of brainstem above CN VII–VIII &amp; inferior to CN V; fibrous 1.5– to 2-cm mass indenting brainstem below CN V; mass removed</td>
<td>It knee pain; characteristic signs on bone radiological studies; slight exophthalmus &amp; chemosis</td>
<td>questionable transient postop improvement in speech &amp; gait w/ oral prednisone treatment</td>
</tr>
</tbody>
</table>

* CN = cranial nerve; CSF = cerebrospinal fluid; IVP = intravenous pyelogram; WBRT = whole-brain radiation therapy.

The cause of ECD is unknown. No causative infectious agents or familial or genetic predisposition has been reported. Whether ECD is a metabolic disease or a neoplastic clonal disorder similar to LC histiocytosis has yet to be determined.

### References

Multiple system Erdheim–Chester disease


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