Journal of Clinical Neuroscience 17 (2010) 1489–1492

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review

Surgical treatment of intracranial Erdheim-Chester disease

Alex Alfieri [a,*], Roberto Gazzeri [b], Marcelo Galarza [b], Massimiliano Neroni [b]

[a] Department of Neurological Surgery, Martin-Luther University Halle-Wittenberg, Ernst-Grube Straβe 40, Halle, Germany
[b] Department of Neurosurgery, San Giovanni Addolorata Hospital, Rome, Italy

ARTICLE INFO

Article history:
Received 12 February 2010
Accepted 28 March 2010

Keywords:
Erdheim-Chester disease
Histiocytosis
Intracranial Erdheim-Chester disease
Intracranial tumor

ABSTRACT

We review the clinical presentation, radiological and histological characteristics, and the natural history, of intracranial Erdheim-Chester disease (ECD). ECD is a rare form of non-Langerhans histiocytosis that affects multiple organs. It is clinically characterized by leg pain, exophthalmos and diabetes insipidus (DI). Central nervous system involvement is rare, with only 27 patients reported in the international literature. DI and cerebellar signs represent the most common neurological symptoms. Its treatment is controversial. Intracranial surgical procedures for ECD have been reported in 11 patients with a complete surgical resection performed in six, and an intracerebral biopsy performed in five patients. In seven patients the cranial procedures represented the initial diagnostic method. Surgical resection and radiation therapy have been used in the further management of these cerebral lesions.

1. Erdheim-Chester disease

Histiocytoses are a large, heterogeneous group of xanthogranulomatous diseases resulting from proliferation and accumulation of reactive or neoplastic histiocytes. Three classes of histiocytoses have been defined: (i) class I, Langerhans cell disease; (ii) class II, non-Langerhans cell histiocytic disease without features of malignancy; and (iii) class III, malignant histiocytic disorders.[1,2] In this context, Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytosis that involves multiple organ systems. Typical systemic features include osteosclerotic lesions in the metaphysis of long tubular bones, exophthalmos, pulmonary and retroperitoneal fibrosis.[1–6] Central nervous system involvement is rare, with diabetes insipidus (DI) and cerebellar signs representing the most common neurological symptoms.[7–11] Occasionally, intracerebral and dural tumour-like lesions have been reported.[12–15] It was first described by Jacob Erdheim and William Chester in 1930.[16] However, the term ECD was first coined by Jaffe[17] in 1972 and until 1980, a total of 47 patients with ECD had been reported in the medical literature, with 80 patients reported up to 2004.[18] The median age of all reported patients is 56 years (range: 7–78 years), with a slight male preponderance (2.7/1).[19–21] The clinical manifestations of ECD vary from asymptomatic or minimally symptomatic benign bone lesions to a severe and often fatal multi-systemic disease.[22,23] Non-specific symptoms such as weight-loss, fever, weakness, pruritus and cutaneous rush are frequently reported, but the most frequent systemic manifestations are bone lesions secondary to histiocytic infiltrations of long bones. Typically, the diagnosis relies on clinical features in addition to appropriate biopsy findings. Characteristic plain film radiographic findings consist of bilateral and symmetric sclerotic, or in 30% of patients, lytic lesions, predominantly in the lower limbs.[4,22,24] Bone CT scans demonstrate typical bilateral and symmetric sclerotic bone lesions along the diaphysis and metaphysis of the femur, tibia, and humerus. Scattered lytic areas may be also present. Skeletal involvement may also affect the skull, spine, and ribs. Abnormal areas may also be detected by increased tracer uptake in radionuclide bone scans. MRI of the bony skeleton reveals diffuse infiltration of the marrow with patchy metaphyseal T2-weighted hyperintense signal using a fat suppression technique and decreased signal on T1-weighted and T2-weighted sequences.[25,26] Dermatological manifestations include xanthelasma, periorbital xanthomata and pruritic rash. In 25% of patients there is involvement of the retroperitoneal space with renal dysfunction, hydronephrosis and retroperitoneal fibrosis secondary to a xanthogranulomatous infiltration (Fig. 1). Involvement of the aortic adventitia with fibrous encasement of the major vessels has also been reported.[16] Lung involvement is fairly uncommon but, when present, contributes to morbidity and mortality. Lung involvement usually shows a diffuse interstitial infiltrate with an upper lung predominance, and scattered reticular or centrilobular opacities with pleural thickening and effusion. Typically, the clinical course is characterized by a progressive course with dyspnea and respiratory failure.[24]

2. Central nervous system involvement

The central nervous system (CNS) involvement is variable in ECD. Sometimes neurological symptoms are secondary to a diffuse hypothalamic and orbital involvement of the disease. In these

* Corresponding author. Tel.: +39 345 557 1407; fax: +39 345 557 1412.
E-mail address: alex.alfieri@medizin.uni-halle.de (A. Alfieri).

0967-5868/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2010.03.062

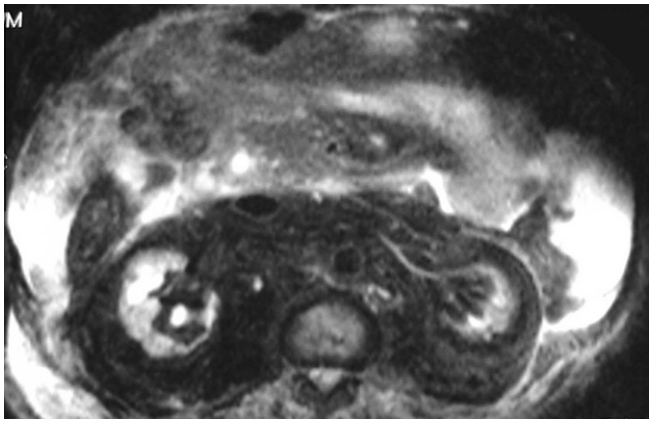

Fig. 1. Axial T2-weighted abdominal MRI showing retroperitoneal fibrosis involving the perirenal and para-aortic regions with right hydronephrosis, enlarged renal calices and left kidney atrophy.

instances a neurogenic DI can be related to a hypothalamic lesion detectable on MRI not associated with other causes. Orbital involvement has been reported in 23 patients, with infiltration of the retro-orbital tissues, which may lead typically to painless bilateral exophthalmos, double vision, and ocular motility impairment.[27,28] Although DI has been associated with orbital involvement, suggesting an extension of the process from the orbit along the optic nerves and the chiasm to the hypothalamic/pituitary region, evidence on cerebral MRI of pathological lesions in the pituitary or hypothalamus regions is rare. However, DI has been reported in 34% of patients with ECD. Frequently, DI precedes the clinical diagnosis of ECD by 10 or more years, perhaps because MRI seldom detects early abnormalities such as thickening of the pituitary stalk.[13,18,24] Although uncommon, extrapituitary neurological involvement has also been reported infrequently in ECD. The second most common neurological signs in ECD are cerebellar symptoms with ataxia and gait disturbances.[7,29] Nevertheless, the multifocal character of ECD involvement can also produce a wide variety of symptoms and signs, possibly leading to a misdiagnosis of multiple sclerosis with diffuse, multiple, or infiltrative MRI signal abnormalities.[4,14] Spinal neural involvement has also been reported with extra-axial and extradural spinal masses.[22,30] The most usual features, mainly in intracranial ECD, are dural granulomas in the brainstem or cerebellum with encasement of major vessels, including vertebral and basilar arteries.[4,15,31,32] So far only, 27 patients with intracranial lesions have been documented in ECD (Supplementary Table 1).

3. Neuroradiology

Intracranial ECD lesions typically appear hypodense on unenhanced CT scans and have homogeneous contrast-enhancement on post-contrast scans. MRI is more sensitive than CT scans in detecting ECD lesions, revealing even small intracerebral and extracerebral lesions. In most patients who have ECD with DI there is no abnormality of the hypothalamic/pituitary region. Nevertheless, a loss of the posterior pituitary-hyperintensity on T1-weighted MRI with infundibular thickening has been described.[33] A characteristic MRI feature is the prolonged retention of the lesions, even after several days, of gadolinium. This may be due to the abnormal histiocyte content in the intracranial masses. Kujat et al.[4] reported prolonged lesion enhancement 14 days after gadolinium administration. In the patient reported by Martinez,[33] a persistent enhancement was documented in an extra-axial cervico-medullary brainstem lesion after 23 days. The typical MRI signal of the intracranial lesions is a bright hyperintensity on

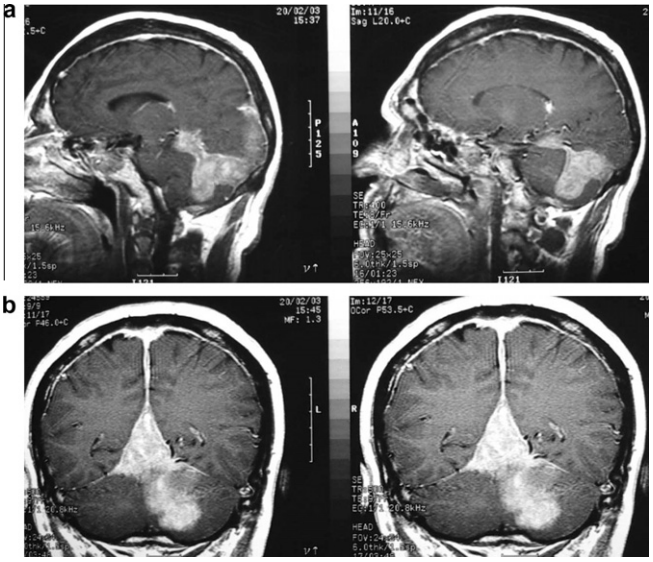

Fig. 2. (a) Sagittal and (b) coronal T1-weighted postcontrast brain MRI showing a homogeneous infra- and supra-tentorial tumor with a dural tail sign at the level of the torcular with encasement of the posterior aspect of the superior sagittal sinus, the straight sinus and transverse sinuses.

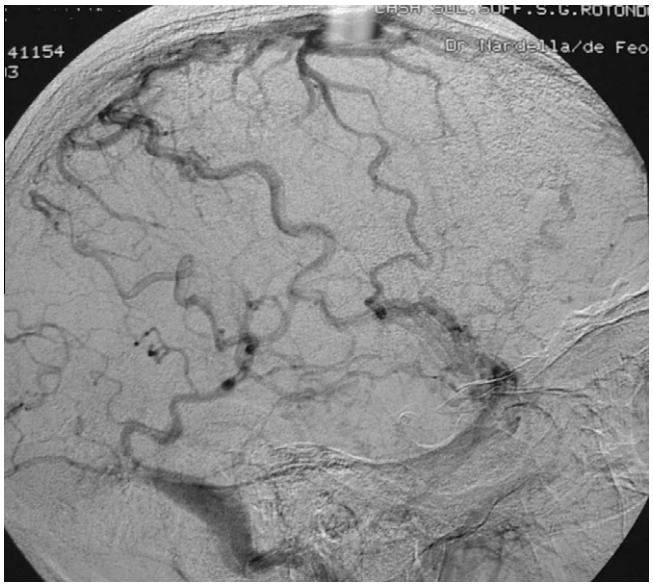

Fig. 3. Lateral cerebral angiography of the patient in Fig. 2 showing a thrombosis of the transverse sinuses, the straight sinus and the posterior superior sagittal sinus, with a narrowed anterior superior sagittal sinus; anomalous anastomotic venous circuits are also present.

T2-weighted sequences.[34,35] In several studies, disease progression from a focal to a diffuse pachymeningitis has been recorded with MRI. Sometimes, the ECD presented on MRI as a homogenous contrast-enhancing lesion with a dural-tail mimicking a meningioma (Fig. 2), while some reports included localization at the falx.[4,10,36–39] Intracranial angiography may show anomalous anastomotic venous circles and no hypervascular tumour stain, with thrombosis of the sinuses (Fig. 3).

4. Pathology

A combination of clinical and radiological features in addition to appropriate biopsy and histopathological analysis provide the