CASE REPORT

Erdheim-Chester disease with isolated craniocerebral involvement

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SUMMARY

Erdheim-Chester disease (ECD) is a rare non-Langerhans form of histiocytosis with distinctive radiographic and pathological features. Intracranial involvement is further a rarity, usually producing diabetes insipidus or cerebellar-brainstem symptoms. We report a 40-year-old man presenting with recurrent secondarily generalised seizures. An MRI scan of the brain revealed multiple enhancing intracranial masses in frontal, temporal and parietal regions. Biopsy from the left frontotemporal lesion confirmed it to be a rare case of ECD. The patient received a short course of corticosteroids initially and subsequently remained well-controlled on antiepileptic therapy alone. A repeat MRI of his brain showed significant resolution of lesions. Osteolytic lesions in the skull vault were detected during follow-up which also disappeared. Interestingly, there was no involvement of long bones or any other system even after 12 years of follow-up.

BACKGROUND

Erdheim-Chester disease (ECD) is rare as such and isolated central nervous system (CNS) involvement is still rarer. Even after long-term follow-up (of 12 years) our patient neither had CNS relapse nor other system involvement. In ECD bone involvement is usually osteosclerotic type, whereas cranial bone involvement in our patient was osteolytic type. There was very good response with short course of steroids in our patient.

CASE PRESENTATION

A 40-year-old man presented to us in September 2000 with a 1 year history of recurrent right partial to secondarily generalised seizures and occasional mild diffuse headache. There was no history of vomiting, incoordination, unsteadiness, visual impairment, bone pains, polyuria, fever or tuberculosis in the past. General physical, other system and neurological examination was unremarkable.

INVESTIGATIONS

Routine haemogram and biochemistry were normal except for elevated erythrocyte sedimentation rate (ESR, 50 mm in the first hour). Serum HIV was negative, Venereal Disease Research Laboratory test was non-reactive and serum ACE level was normal. His ECG, chest x-ray, two-dimensional echo of heart, ultrasound abdomen and EEG were normal. His contrast CT scan of head followed by contrast MRI brain showed multiple nodular enhancing lesions of varying size in bitemporal, bifrontal and left parietal lobes with perilesional oedema in some without

meningeal enhancement (figure 1). Cerebrospinal fluid analysis was normal.

We then proceeded with biopsy from left frontotemporal lobe lesions which revealed multiple nodular aggregates of histiocytes with characteristic linear nuclear grooves, inflammatory cells including eosinophils and lymphocytes with granuloma formations and multinucleated giant cells. The cytoplasm of the latter was strongly positive for HAM-56 macrophage stain, but was negative for CD1-a and S-100 protein confirming the diagnosis of ECD. After the confirmation of ECD a complete skeletal survey especially of long bones, high resolution CT of chest and contrast CT of abdomen was performed which was unremarkable.

DIFFERENTIAL DIAGNOSIS

Langerhans cell histiocytosis (LCH), sarcoidosis.

TREATMENT

He was treated with steroids (short course) and antiepileptic drugs.

OUTCOME AND FOLLOW-UP

He remained under regular follow-up and his seizures were well controlled with carbamazepine alone. Repeat contrast MRI brain done 1 year later revealed significant resolution of frontal, temporal

Figure 1 Contrast MRI brain showing multiple nodular enhancing lesions of varying size with perilesional oedema in some, in bitemporal and frontal lobes.

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Figure 2 A repeat contrast MRI brain done 1 year after the presentation revealed significant resolution of frontal, temporal and parietal lesions.

and parietal lobe lesions (figure 2). But, later on, contrast MRI brain done in February 2003 revealed multiple focal lesions in the skull vault showing areas of osteolysis and abnormal enhancement in the frontal, parietal and occipital bones and abnormal enhancing soft tissue in the right petrous, temporal bone involving the external auditory canal, middle ear cavity and mastoid bone (figure 3). However, these lesions showed complete resolution spontaneously in follow-up contrast MRI brain done in September 2005. During the last follow-up in August 2012, nearly 12 years after the presentation, the patient

Figure 3 Abnormal enhancing soft tissue seen in right petrous, temporal bone involving external auditory canal, middle ear cavity and mastoid bone.

Figure 4 Follow-up contrast MRI brain repeated in August 2012, 12 years after the presentation did not reveal any fresh parenchymal lesions.

was completely asymptomatic and no fresh intracranial parenchymal lesions were detected on contrast MRI brain (figure 4). Skeletal survey for cranium and long bones and detailed investigations to look for any other systemic involvement were unremarkable.

DISCUSSION

ECD is a rare non-Langerhans form of histiocytosis characterised radiologically by osteosclerosis of long bones and pathologically by xanthogranulomatous infiltrate.¹ Clinical spectrum ranges from an asymptomatic focal process to fatal systemic disease. While skeletal involvement is highly specific characterised by symmetric, bilateral osteosclerosis of long bones,² extraskeletal manifestations like cardiovascular and pulmonary involvement, xanthelasma, CNS, retroperitoneal and adrenal infiltration are seen in approximately half of ECD patients.¹

CNS involvement in the form of dural or parenchymal infiltrates is rare. Diffuse or localised, the latter tends to involve the cerebellum, brainstem, hypothalamus/pituitary and cerebrum. Most frequent CNS manifestations are diabetes insipidus, cerebellar features, orbital lesions and extra-axial masses involving the dura.¹ ECD needs to be differentiated from LCH on the basis of immunohistological and microscopic characteristics of histiocytes. Histiocytes in ECD are CD-68 positive, CD-1a negative and do not immunostain for S-100 protein and OKT6. In LCH, CD-1a is positive and electron microscopy reveals Birbeck granules.³ However, these two diseases may coexist, and cases of double infiltration with mixed LCH and ECD have been reported.⁴

ECD is a rare non-Langerhans form of histiocytosis that was first described by Jacob Erdheim and William Chester in 1930 and the term ECD was coined by Jaffe in 1972.⁵ ECD is characterised by xanthomatous infiltration of tissues by foamy histiocytes and differs from LCH in terms of clinical features as well

as immunohistological and microscopic characteristics of the histiocytes.⁶ ECD has been diagnosed in all age groups, but it is most common in adults with a slight male preponderance.¹

In patients with ECD, skeletal involvement is considered to be highly specific typically presenting with bone pains and the disease is frequently characterised by bilateral symmetric long bone osteosclerosis.² However, in our patient, there was an involvement of cranium alone. About half of the patients have extraskeletal manifestations, including xanthelasma, interstitial lung disease, cardiovascular involvement, retroperitoneal infiltration with periaortic fibrosis and perineural and/or urethral obstruction, renal failure and exophthalmos¹ which were all absent in our patient clinically as well as on investigations. Though we could not perform electron microscopy owing to the lack of resources, negative staining for S-100 protein and CD-1a strongly favoured the diagnosis of ECD in our case which are positive in LCH.⁶

Neurological symptoms are rare in ECD.⁶ The most frequent CNS manifestations of ECD are diabetes insipidus, cerebellar features and symptoms that are related to extra-axial focal mass lesions and may lead to severe disability or death,⁷ but our patient presented with seizures and mild headache only. In ECD, patchy meningeal thickening or well-circumscribed meningioma-like dural mass lesions—can be seen. Johnsona *et al*⁸ reported a case of ECD presenting as multiple extraaxial lesions that appeared similar to meningiomas involving the parasellar region, torcula and orbits, whereas our patient had multiple cranial vault lesions. Usually skeletal lesions are osteosclerotic in ECD and involve long bones of extremities; however, facial and/or skull bone thickening can be seen in upto 80% of the cases.¹ A study done by Drier *et al*¹ showed osteosclerosis with diffuse thickening of the skull vault in 26% of the patients, whereas, in our patient, cranial vault lesions were osteolytic in nature. Osteolytic lesions are infrequently associated with ECD and they were found in only 5–8% of patients. These lesions were in the flat or long bones and were usually concurrent with the typical osteosclerotic appendicular lesions.⁵

Previously reported intra-axial mass lesions in ECD have mainly involved the infratentorial space including the brainstem, cerebellum and middle cerebral peduncles,⁹ but our patient did not have involvement of any of these structures. However, lesions can also be seen in the cerebral hemispheres and the basal ganglia⁹ as in our case where lesions were predominantly in the frontal, temporal and parietal lobes.

Isolated CNS involvement in ECD is a rare entity. Adem *et al*³ reported a patient who presented after first seizure and his MRI revealed high signal intensity abnormalities involving both the hippocampi which could explain his seizure, but additionally he also had involvement of the cerebellar tonsils, pons, mammillary bodies and pituitary stalk though he did not have any brainstem, cerebellar features or diabetes insipidus. However, radiographs of the lower extremities showed abnormalities. Rushing *et al*¹⁰ reported a case with a first isolated occurrence of intracranial ECD mimicking a primary brain tumour who presented with seizure and had a well-circumscribed temporoparietal mass on imaging, but long-term follow-up was not available to rule out other system involvement. Conley *et al*¹¹ also reported a case of an autopsy proven ECD with isolated CNS involvement that presented with a large suprasellar mass but succumbed within a few months after the onset of illness. To the best of our knowledge, probably ours is

the first case report of ECD with long-term follow-up of 12 years having isolated craniocerebral involvement who presented with seizures alone and without any evidence of other system involvement.

To conclude, our case with biopsy proven ECD had many atypical and interesting features. He had isolated CNS involvement clinically which is rare and presented only with seizures. Though many earlier reported cases presenting with seizure alone showed cerebellar, brainstem and pituitary involvement radiologically, our patient did not have involvement of the same. Involvement of bones in ECD including facial and skull bones is usually in the form of osteosclerotic lesions, whereas our patient had osteolytic lesions in the cranial bones which resolved in follow-up imaging making it further a rarity.

Learning points

- Erdheim-Chester disease (ECD) though rare should be differentiated from Langerhans cell histiocytosis clinically, radiologically and histopathologically including immunohistochemistry.
- ECD can manifest as isolated CNS syndrome with cranial cerebral involvement.
- ECD can have osteolytic lesions.
- The prognosis of ECD patients can be good despite multiple intracranial parenchymal lesions.
- Patient can remain asymptomatic for long time without any relapse and other system involvement with good clinical outcome.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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