CASE REPORT

Erdheim–Chester disease associated with intramedullary spinal cord lesion

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ABSTRACT. Erdheim–Chester disease (ECD) is a rare non-Langerhans cell histiocytosis. We present a case of a 56-year-old male with ECD. As time progressed, involvement of the orbital fossa, cranial convexity, spinal cord, brain stem, thyroid, lung, retroperitoneum, lower extremity bones and skin were found. Previously reported cases reveal the frequency of ECD with spinal cord involvement is rare. Although this was a presumed diagnosis based on other lesions, our case is the first in which both intramedullary and epidural masses are present.

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Erdheim–Chester disease (ECD) is a rare non-Langerhans cell histiocytosis (LCH). Skin and long bone involvement are often observed in ECD. ECD infiltrates into systemic components which produce protean radiological manifestations. Osteosclerosis at metaphyseal and diaphyseal lesions of long bones on radiographs are a specific finding for ECD. The following extraskelatal sites of lesions have been documented: cardiopulmonary system, intraperitoneal organs, orbital fossa and central nervous system. Spinal cord involvement is very rare. We present a case of ECD associated with spinal cord involvement including intramedullary and epidural lesions.

Case report

A 56-year-old male was admitted to our hospital with left exophthalmos. The patient underwent a total resection of a left orbital tumour. The tumour was a macroscopically yellowish mass and the histological specimen revealed a proliferation of foamy histiocytes associated with the infiltration of lymphocytes and plasma cells, yielding the diagnosis of xanthoma. 2 months later, MRI revealed the recurrent tumour in the left orbital fossa and a new mass in the bilateral cranial convexity. As time progressed, the patient noticed weakness in the left upper and lower extremities and the paresis gradually worsened. Laboratory studies revealed a slight increase in white blood cells, $10\,300\ \mu\text{l}^{-1}$; platelets, $44.7 \times 10^4\ \mu\text{l}^{-1}$ erythrocyte sedimentation rate, 13 mm in

1 h, 36 mm in 2 h; C-reactive protein, $1.1\ \text{mg dl}^{-1}$. The cerebrospinal fluid showed a slight increase in the ratio of polynuclear cells to mononuclear cells, 44/38, $3\ \text{mm}^3$ and protein, $112\ \text{mg dl}^{-1}$. MRI delineated multiple lesions at bilateral cranial convexity, falx, cerebellar tent and left orbital fossa. The tumours displayed low- to isosignal intensity on T_1 weighted images ($T_1\text{WI}$) and low to slightly high signal intensity on T_2 weighted images ($T_2\text{WI}$). A strong homogeneous pattern of enhancement was observed on gadolinium-enhanced (GE)- $T_1\text{WI}$. The small lesions in the brain stem and dentate nucleus of cerebellum showed high signal intensity on $T_2\text{WI}$ and fluid level attenuated inversion recovery (FLAIR) images. We made a pre-operative diagnosis of possible multiple meningioma syndrome, although plasmacytoma, granuloma, hypertrophic pachymeningitis, malignant lymphoma etc were listed for differential diagnosis. An MRI of the cervical spine revealed an intramedullary lesion displayed isosignal intensity on $T_1\text{WI}$, high signal intensity on $T_2\text{WI}$ and a strong homogeneous enhancement pattern on GE- $T_1\text{WI}$ (Figure 1). Open surgical resection of the cranial tumour was conducted. The tumour was a macroscopically yellowish mass. A histological examination showed the tumour was mainly composed of a round nucleus and foamy cytoplasm with positive expression for KP-1 (CD68) and negative expression for S-100 and CD1a, yielding a diagnosis of xanthoma originated from macrophages (Figure 2). Infiltration of plasma cells, eosinophilic cells, lymphocytes and Touton type giant cells were associated. We finally made a diagnosis of ECD. The patient was asymptomatic and was discharged with the spinal lesion remaining. A disturbed gait and numbness of both feet worsened and a follow-up MRI revealed a stable intramedullary lesion in the cervical spine. The extradural mass in the thoracic spine displayed mild high signal intensity on $T_1\text{WI}$, low signal intensity on $T_2\text{WI}$

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Figure 1. Sagittal MRI demonstrates tumour-like lesion (arrows) in intramedullary cervical cord with (a) isosignal intensity in T_1 weighted image, (b) high signal intensity in T_2 weighted image and (c) homogeneous enhancement in contrast-enhanced T_1 weighted image.

and homogeneous enhancement pattern on GE- T_1 WI (Figure 3). Surgical resection of the extradural mass was conducted and a microscopic examination showed the same histological findings as the intracranial lesion. After the patient was discharged, a systemic examination was performed. Radiographs of the lower extremities and the face revealed the osteosclerotic lesions of the tibia and the mandibula. A CT scan of the abdomen revealed a proliferation of connective tissue containing fat tissue in the intraperitoneal and retroperitoneal spaces associated with bilateral hydronephrosis. A CT scan of the chest revealed a calcified mass in the thyroid gland, emphysematous change in the lung and pericardial effusion. Surgical resection of the subcutaneous mass in the left cheek was conducted and the histological diagnosis was

the same as the intracranial lesion. These findings were not contradictory to those corresponding to ECD.

Discussion

ECD named in 1972 by Jaffe [1] was based on two clinical cases presented by Chester [2] and histologically diagnosed by Erdheim in 1930.

More than 390 cases of ECD have been reported worldwide [3]. Histological progress has enabled the differentiation of histiocytes into Langerhans cells, dendritic cell type, with positive expression of S-100 protein and/or CD1a stains and mononuclear cells, macrophage type, with positive expression of CD68 stain. Xanthoma is

Figure 2. Microscopic examination of the resected specimen revealed (a) the histological appearance of proliferation of xanthomatous cells composed of foamy cytoplasm (foamy histiocytes). (b) Foamy histiocytes are immunoactive for KP-1 (CD68) but not for S-100 and CD1a. These foamy cells are considered to originate from macrophage cells, resulting in the diagnosis of non-Langerhans cell histiocytosis.

Figure 3. Comparison between (a) a pre-contrast T_1 weighted image and (b) a post-contrast T_1 weighted image; extradural mass (arrows) in the thoracic spine displayed homogeneous enhancement pattern at the level of the fourth to sixth thoracic vertebrae.

a benign localised disease. It is microscopically composed of foamy cells (or xanthoma cells), which take up fat granules and originated from macrophages. Whereas histiocytosis is a tumour-like infiltrative disease and classified into LCH and non-LCH. ECD belongs to non-LCH and is characterised by xanthogranulomatous infiltration with lipid-laden histiocytes, which are believed to arise from mononuclear macrophage phagocytes.

The cardiopulmonary system, intraperitoneal organs, orbital fossa, skin and central nervous system are listed as extraskelatal sites of the lesions. Neurological involvement is described in less than 30% of cases. Lachenal et al [4] differentiated the neurological involvement pattern into three types: an infiltrative type, a meningeal type and a composite type. The infiltrative lesions on MRI were described as widespread nodules or masses with hyperintensity signals on T_2 WI and GE- T_1 WI, and mainly involved the brain stem and the cerebellum, which caused cerebellar symptoms (ataxia) and/or pyramidal symptoms (diabetes insipidus) [5, 6]. The meningeal lesions on MRI were described as meningioma-like intensity and/or nodular thickening of the dura matter, namely iso- or low signals on T_1 WI and T_2 WI and homogeneous hyperintensity signal on GE- T_1 WI [7, 8]. Therefore, our case was considered to belong to the composite type.

The spinal cord lesion is very rare [4, 9, 10]; it has been observed in only nine patients including our case, and to the best of our knowledge the intramedullary spinal cord lesion presented in this case has not been documented in previous manuscripts. Spinal cord tumours such as astrocytoma, ependymoma, haemangioblastoma, cavernous haemangioma and malignant lymphoma are listed to be differentiated from ECD but considered to be unlikely because the present lesion included less oedema and no cystic component, haemorrhage and flow void. Meanwhile, multiple sclerosis and sarcoidosis are difficult to differentiate using only imaging for diagnosis. Multiple sclerosis usually happens with subacute onset and is accompanied with intracranial lesion, and sarcoidosis rarely happens in the spinal cord in the initial

onset. The present spinal cord lesion has been stable for 2 years, tracing the unique process.

Although a pathological examination was not conducted in our case, Shimada et al [9] reported that the pathological examination of the gadolinium-enhanced intracranial infiltrative lesions of the globus pallidus, putamen and pituitary gland consisted of infiltration of foamy histiocytes and collagenous fibrous tissue with reactive astrocytosis.

ECD is a systemic involvement disease. According to previous reports, the involvement incidences of bone, retroperitoneum, skin, cardiovascular, proptosis and diabetes insipidus were 86%, 59%, 20–36%, 30%, 27–47% and 29–47%, respectively [4, 11]. Our case presented all these involvements except diabetes insipidus, probably because of the long amount of time lapse of this disease.

Conclusion

Although a presumed diagnosis was based on other lesions, we described a case of ECD with spinal cord involvement including intramedullary and epidural lesions. When infiltrative xanthoma is encountered, a systemic image examination should be forwarded, bearing in mind ECD.

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