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Letter to the Editor

Long-bones involvement in generalized crystal-storing histiocytosis

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Crystal storing histiocytosis (CSH) is a rare histiocytic disorder, first described in 1978 [1], often associated with plasmacytic or lymphoid hemopathy. CSH is characterized by the infiltration of various organs by histiocytes CD68 (+), CD1a (-) with the accumulation of abnormal intracytoplasmic material, which has a crystal appearance. These crystals are generally composed of light chains of immunoglobulins. The bone marrow is the most frequently affected site, although involvements of various organs have been described [2]. CSH is a non-clonal, reactive histiocytosis that was not included in the revised classification of histiocytoses [3]. The diagnosis is difficult for pathologists. The clinical and radiological phenotype may be very similar to that of other histiocytoses, in particular the L group. We describe a case of CSH initially presenting with limbs pain and a multi-systemic infiltration including pachymeningitis, pleural and long bones involvement. A 73-year-old woman with a past history of IgG kappa monoclonal gammapathy was referred for asthenia, weight loss and bone pain of the limbs.

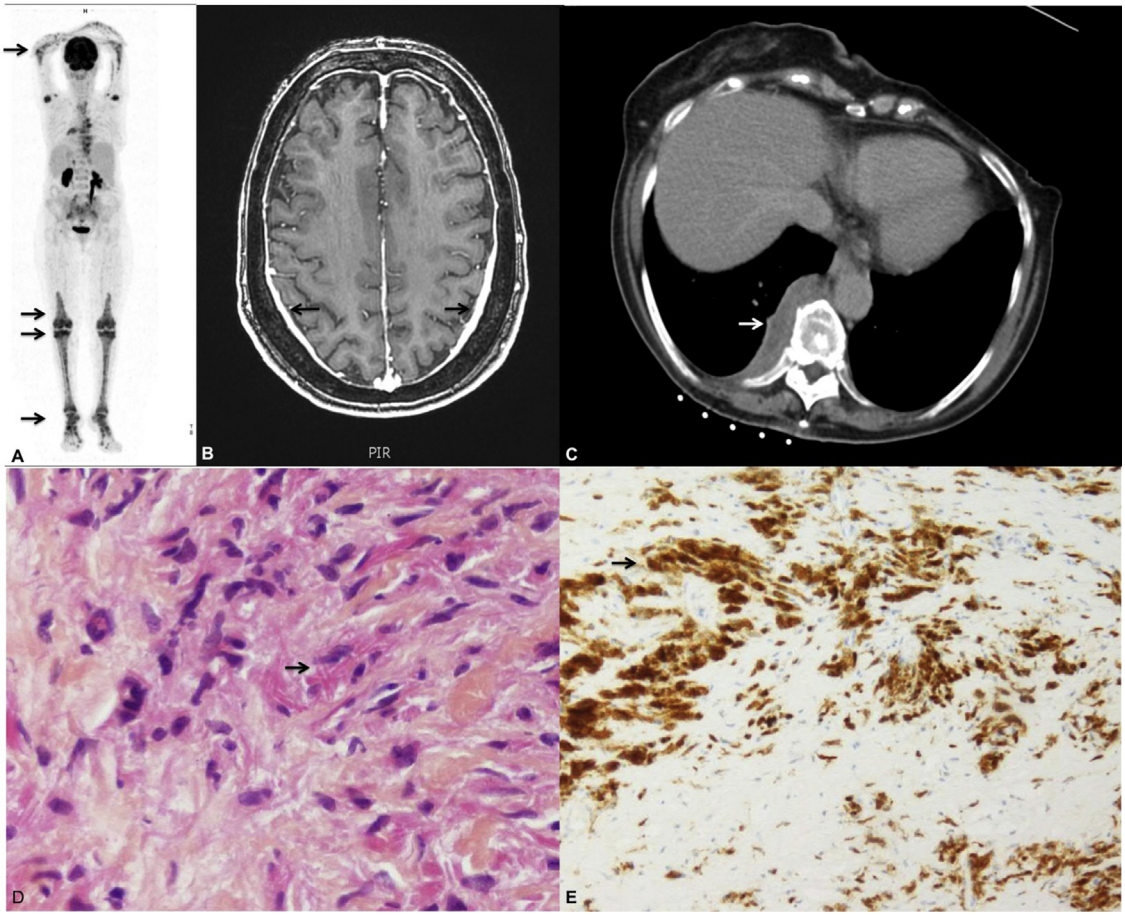

Fig. 1. Radiological and pathological presentation of crystal storing histiocytoses. A. 18 Flurodeoxyglucose positron emission tomography showing long bones hypermetabolisms. B. Pachymeningitis in brain MRI. C. Pleural mass (chest CT scan). D. Hematoxylin eosin staining of the pleural biopsy showing crystal inclusion in the cytoplasms of histiocytes. E. immunohistochemistry of the pleural mass with CD68 antibodies, the histiocytic cells are marked.

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The C-reactive protein level was 51 mg/L (normal value < 5 mg/L). The ^{18}Fluorodeoxyglucose (FDG) positron emission tomography (PET) showed hypermetabolism of the long bones of the limbs, right side of spine, pelvis, right retroperitoneal area and adrenal glands (Fig. 1). A brain MRI disclosed pachymeningitis (Fig. 1) with osteosclerosis of the sphenoid and maxillary sinuses. The osteomedullar biopsy displayed a proliferation of plasma cells, with a kappa monotype. Pleural biopsy displayed the presence of histiocytes CD68 (+) CD1a (-) PS100 (-). A second biopsy was performed and intracellular crystals of immunoglobulins were then seen within the cytoplasms of the histiocytes, leading to the diagnosis of CSH (Fig. 1). In this patient, the first sign of the disease was bone pains in the lower limbs, a common finding in other histiocytoses such as Erdheim-Chester disease (ECD), which is a rare non-Langerhans cell histiocytosis of the L group. Long bone uptake was suggestive of ECD and the biopsy showed CD68 (+) CD1a (-) histiocytes, a finding that is consistent with ECD [4]. In the second pleural biopsy, the pathologist revised the diagnosis to CSH. In CSH, the histiocytes are often in aggregates with intracellular needle-like appearance and/or refringent inclusions [5] and this may be difficult to diagnose. The intracellular formation is almost always formed of kappa light chains [6]. The mechanism of storage is unknown. Two forms of CSH have been described, localized and generalized. The most common organs affected are bone marrow, liver, lymph nodes, spleen and kidneys. In the present case, long bones uptakes in ^{18}FDG PET scan were suggestive of ECD [7]. The associated diseases in CSH are predominantly plasma cell disorders (88%) associated with monotypic κ light chain. In ECD, a high frequency of associated hematologic malignancies (in particular myeloproliferative disorders) have been described [8], but an underlying B-cell lymphoma or clonal plasmacytic neoplasm is more often found in CSH [2]. Clinical presentation of CSH includes limbs bone pain. As in the presented case, CSH may be difficult to distinguish from other histiocytoses, including ECD. Presence of monoclonal gammapathy, absence of the *V600E* mutation in the *BRAF* gene, which is present in almost 70% of cases of ECD, and inclusions within the cytoplasms of the histiocytes, constitute red flags and should prompt interaction with the pathologist to search CSH. Thus, rheumatologists may be aware of clinical and ^{18}FDG PET scan presentations of CSH.

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Author's contribution

All the authors contributed to drafting/revising the manuscript for content and study design, as well as analysis and interpretation of the data.

A.M. and F.C.-A. contributed to the acquisition of data.

Ph.M. provided the PET images.

F.Ch. provided the histopathological images.

FCA, JH and ZA coordinated the study.

All the authors approved the final submitted version

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Terashima K, Takahashi K, Kojima M, et al. Kappa-type light chain crystal storage histiocytosis. Acta Pathol Jpn 1978;28:111–38.
[2] Dogan S, Barnes L, Cruz-Vetrano WP. Crystal-storing histiocytosis: report of a case, review of the literature (80 cases) and a proposed classification. Head Neck Pathol 2012;6:111–20.
[3] Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016;127:2672–81.
[4] Cohen-Aubart F, Emile JF, Carrat F, et al. Phenotypes and survival in Erdheim-Chester disease: Results from a 165-patient cohort. Am J Hematol 2018;93:E114–7.
[5] Fang H, Chiu A, Reichard KK. Crystal-storing histiocytosis in bone marrow: a clinicopathologic study of eight cases and review of the literature. Am J Clin Pathol 2018;149:148–63.
[6] Lebeau A, Zeindl-Eberhart E, Muller EC, et al. Generalized crystal-storing histiocytosis associated with monoclonal gammopathy: molecular analysis of a disorder with rapid clinical course and review of the literature. Blood 2002;100:1817–27.
[7] Haroche J, Cohen-Aubart F, Rollins BJ, et al. Histiocytoses: emerging neoplasia behind inflammation. Lancet Oncol 2017;18:113–25.
[8] Papo M, Diamond EL, Cohen-Aubart F, et al. High prevalence of myeloid neoplasms in adults with non-Langerhans cell histiocytosis. Blood 2017;130:1007–13.

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