Cerebellar Mass as a Location of Acute Lymphoblastic Leukaemia

ILARIA DESIDERI¹, SILVIA CANOVETTI¹, ILARIA PESARESI², MICHELE CANIGLIA¹, EUGENIO CIANCIA³, CARLO BARTOLOZZI¹, MICHELE PUGLIOLI², MIRCO COSOTTINI^{1,2}

¹Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa; Pisa, Italy

²Neuroradiology Unit, Pisa University Hospital; Pisa, Italy

³Department of Pathology, Pisa University Hospital; Pisa, Italy

Key words: acute lymphoblastic leukaemia, cerebellar mass, MRI, apparent diffusion coefficient

SUMMARY – A 22-year-old man with acute lymphoblastic leukaemia was referred to our observation for headache, cervical pain and sopor. A computed tomography study revealed triventricular obstructive hydrocephalus due to a left cerebellar hyperdense mass impinging on the fourth ventricle. A magnetic resonance study demonstrated an area of hyperintensity on T2-weighted images, hypointensity on T1, restricted diffusivity and contrast enhancement involving the left hemispherical cerebellar cortex and the vermis and causing cerebellar herniation. After surgical excision of the lesion, histological examination revealed an infiltrate of lymphoblastic leukaemia with B cells. Leukaemic intracranial masses are rare. Our report describes a case presenting a cerebellar mass of leukaemic tissue characterized by high cellularity and low apparent diffusion coefficient value comparable to acute ischaemia. Therefore leukaemic intracranial mass has to be considered in the differential diagnosis of cerebellar masses.

Introduction

Leukaemia is the commonest form of childhood cancer and 75% of cases are represented by acute lymphoblastic leukaemia (ALL). Central nervous system involvement in leukaemia is meningeal in the majority of cases, whereas intracranial masses are rare, the common lesion being granulocytic sarcoma or chloroma. We describe a pathologically proven intra-axial cerebellar mass of leukaemic tissue in a patient with ALL, characterized by a very low value of apparent diffusion coefficient (ADC) and by a high cellularity at histological examination.

Case Report

A 22-year-old Caucasian man was referred to our observation for intense headache, cervical pain and sopor. Neurological examination revealed reduced vigilance, confused verbal responses and impaired execution of simple orders.

The patient had a history of acute lymphoblastic leukaemia (ALL) diagnosed three years earlier and promptly treated with chemotherapy. One year after the diagnosis, in 2008, the patient underwent bone marrow transplantation followed by a period of remission until August 2009 when the disease reappeared and the patient was treated with tyrosine-kinase inhibitors that was still ongoing.

Computed tomography (CT) scan revealed triventricular obstructive hydrocephalus due to a cerebellar slight hyperdense infiltrating mass of the left hemisphere impinging on the fourth ventricle (Figure 1).

Neuroradiological assessment was completed with a brain magnetic resonance imaging (MRI) study showing an extended area characterized by hyperintensity on T2-weighted images and hypointensity on T1-weighted images with respect to white matter and restricted diffusivity ($ADC = 0.59 \times 10^{-3} \text{ mm}^2/\text{s}$) mainly involving the left hemispherical cerebellar cortex and the cerebellar vermis. There was vasogenic oedema around the fourth ventricle with minimal exten-

Figure 1 A 22-year-old man with acute lymphoblastic leukaemia. Unenhanced CT scan (A) reveals a slight hyperdense infiltrating mass of the left cerebellar hemisphere with mass effect on the fourth ventricle causing obstructive triventricular hydrocephalus (B).

sion into the contralateral cerebellar hemisphere. The left cerebellar hemisphere was swollen causing compression on the fourth ventricle and the lower portion of the Sylvian aqueduct. This caused triventricular obstructive hydrocephalus and initial protrusion of the left cerebellar tonsil through the foramen magnum and ascending cerebellar herniation through the tentorium. After contrast administration, an intense, inhomogeneous contrast enhancement of the infiltrating tissue was appreciable. Leptomeningeal enhancement around the left cerebellar hemisphere and brain stem was also detected. Cerebellar inflammation or a direct cerebellar infiltration of leukaemia were suspected (Figure 2).

The patient underwent urgent endoscopic ventriculostomy to reduce intracranial hypertension. Five days after surgery, control CT scan demonstrated normalization of the supratentorial ventricular system and the disappearance of transependymal resorption of cerebrospinal fluid (CSF). Seven days after CSF shunt, intense headache, vomiting and psychomotor impairment recurred so the patient underwent suboccipital craniotomy with surgical excision of the cerebellar lesion. Histological examination on the surgical specimen showed an infiltrate of lymphoblastic leukaemia with B cells (Figure 3).

Discussion

Leukaemias are a heterogeneous group of haematologic malignancies resulting from neoplastic proliferation of haematopoietic cells at an undifferentiated or partially differentiated stage of maturation^{1,3}. Leukaemia is the commonest form of childhood cancer and 75% of cases are represented by acute lymphoblastic leukaemia (ALL)¹. The proliferation of leukaemic cells can have a profound effect on haematopoietic stem cells and normal cells of the immune system. As a result, leukaemia can cause anaemia, alterations in haemostasis and a tendency for infections^{1,3}.

Leukaemic cells can infiltrate virtually any anatomic location. In the past, central nervous system (CNS) complications of leukaemia were rarely seen due to the rapid course of the disease; more recently, advances in imaging techniques and improved treatment such as aggressive polychemotherapy, intrathecal cytostatic prophylaxis and cranial irradiation, have prolonged survival and the frequency of CNS complications has increased reaching an incidence of 25-50%^{1,2,4}.

Uncommonly, CNS involvement is the first manifestation of systemic leukaemia. More frequently, the CNS is involved in patients with

A

B

C

Figure 3 A 22-year-old man with acute lymphoblastic leukaemia. A) Small enlargement 25 $\times$ coloured with haematoxylin-eosin shows cerebellar architecture and the neoplastic infiltration, mainly localized in the meninges and in molecular and granular layers. The box enlargement 250 $\times$ shows neoplastic cells organized in the typical “starry sky” aspect. B) Immunostaining for CD20, specific for B cells. C) Immunostaining for TdT, specific for blastic cells.

known acute leukaemia or in patients believed to be in remission following antileukaemic therapy. The exact method by which leukaemic cells permeate the CNS is unknown but haematogenous mechanisms as well as direct spread from adjacent involved bone marrow are assumed³.

The cerebral location of leukaemia can be parenchymal although the majority of cases are meningeal. Infiltration of the meninges by leukaemic cells may affect the dura, the leptomeninges or both and may be diffuse or focal. Meningeal involvement can be identified on CT and more easily on MR images as abnormal enhancement of the meninges and nerve roots but cytological or pathological confirmation are often necessary for diagnosis.

Several conditions mimic meningeal leukaemia and have to be considered for differential diagnosis: infectious or inflammatory menin-

gitidis as well as irritation from intrathecal chemotherapy, haemorrhage or meningeal fibrosis may be associated with abnormal leptomeningeal enhancement in the absence of leukaemic involvement³.

Although rare, intracranial masses may occur in the course of leukaemia. Granulocytic sarcoma (chloroma) is a mass composed of primitive precursors of the granulocytic cells, which include myeloblasts, promyelocytes and myelocytes². Chloroma mainly affects patients with myelogenous leukaemia but it may appear also in patients with other myeloproliferative disorders most commonly involving bone, periosteum, soft tissue, lymph nodes, and skin, although it can occur anywhere throughout the body^{1,5}.

Granulocytic sarcoma or other leukaemic masses may arise in the CNS within the brain parenchyma or may have a dural implant. Dural-based granulocytic sarcoma may be indis-

tinguishable from meningioma and manifests with signs of increased intracranial pressure or mass effect³. Leukaemic intracranial masses must be differentiated from several solid lesions related to leukaemic disease: radionecrosis caused by the combination of chemotherapy and radiation therapy or secondary tumours induced by radiation therapy, like sarcoma, meningioma and glioblastoma. Moreover, the infectious complications of immunosuppression like Candidiasis and Aspergillosis have to be considered in leukaemic patients.

Although leukaemic infiltration can affect any part of the brain parenchyma, we have found only one reported case of cerebellar involvement in a patient with acute myelomonocytic leukaemia. In this case the patient was studied only with CT examination that showed a contrast-enhancing infiltrating mass localized in the left cerebellopontine angle. The lesion disappeared with radiation therapy and intraventricular chemotherapy and post-mortem examination revealed scattered macrophages, giant astrocytes and atypical oligodendroglia with absence of leukemic cells⁶. However, we have not found any case of cerebellar infiltra-

tion in acute lymphoblastic leukaemia. Our patient had a pathologically proven intra-axial cerebellar localization of ALL with contiguous leptomeningeal involvement. The non-specific hyper and hypointensity on T2 and T1-weighted images was associated to a strong enhancement and mainly a very low ADC value. The ADC value ($0.59 \times 10^{-3} \text{ mm}^2/\text{s}$) within the lesion is comparable than that reported for acute ischaemia ($0.57 \times 10^{-3} \text{ mm}^2/\text{s}$)⁷ and lower than that reported for lymphomas ($0.78 \times 10^{-3} \text{ mm}^2/\text{s}$)⁸, high grade ($0.96 \times 10^{-3} \text{ mm}^2/\text{s}$) and low grade gliomas ($1.19 \times 10^{-3} \text{ mm}^2/\text{s}$)⁹. As proved at pathological examination, the cerebral localization of ALL is characterized by a high density of pathological lymphocytic cells and reduced intercellular space, supporting the notion that the ADC value inversely correlates with the tissue cellularity¹⁰.

The present case report demonstrates that isolated infiltration of cerebellar parenchyma may occur in ALL. ALL localization must be considered in the differential diagnosis in the presence of a solid cerebellar mass and diffusion-weighted imaging could aid in orienting the diagnosis.

References

- 1 Ulu K, Töre G, Bayrak A, et al. MRI of central nervous system abnormalities in childhood leukemia. *Diagn Interv Radiol.* 2009; 15 (2): 86-92.
- 2 Vázquez E, Lucaya J, Castellote A, et al. Neuroimaging in pediatric leukaemia and lymphoma: differential diagnosis. *Radiographics* November. 2002; 22 (6): 1411-1428.
- 3 Ginsberg LE, Leeds NE. Neuroradiology of leukemia. Review article. *Am J Roentgenol.* 1995; 165 (3): 525-534. doi: 10.2214/ajr.165.3.7645463.
- 4 Wolk RW, Masse SR, Conklin R, et al. The incidence of central nervous system leukemia in adults with acute leukemia. *Cancer.* 1974; 33 (3): 863-869. doi: 10.1002/1097-0142(197403)33:3<863::AID-CNCR2820330336>3.0.CO;2-1.
- 5 Suzer T, Colakoglu N, Cirak B, et al. Intracerebellar granulocytic sarcoma complicating acute myelogenous leukemia: a case report and review of the literature. *J Clin Neurosci.* 2004; 11 (8): 914-917. doi: 10.1016/j.jocn.2003.12.018.
- 6 Saper CB, Jarowski C. Leukemic infiltration of the cerebellum in acute myelomonocytic leukemia. *Neurology.* 1982; 32 (1): 77-80. doi: 10.1212/WNL.32.1.77.
- 7 Yamada N, Satoshi I, Sakuma T. Value of diffusion-weighted imaging and apparent diffusion coefficient in recent cerebral infarctions: a correlative study with contrast-enhanced T1-weighted imaging. *Am J Neuroradiol.* 1999; 20 (2): 193-198.
- 8 Akter M, Hirai T, Makino K, et al. Diffusion-weighted imaging of primary brain lymphomas: effect of ADC value and signal intensity of T2-weighted imaging. *Comput Med Imaging Graph.* 2008; 32 (7): 539-543. doi: 10.1016/j.compmedimag.2008.06.001.
- 9 Lee EJ, Lee SK, Agid R, et al. Preoperative grade of presumptive low grade astrocytomas on MR imaging: diagnostic value of minimum apparent diffusion coefficient. *Am J Neuroradiol.* 2008; 29 (10): 1872-1877. doi: 10.3174/ajnr.A1254.
- 10 Kono K, Inoue Y, Nakayama K, et al. The role of diffusion-weighted imaging in patients with brain tumors. *Am J Neuroradiol.* 2001; 22 (6): 1081-1088.

Mirco Cosottini, MD
Department of Translational Research
and New Technologies
in Medicine and Surgery
Unit of Neuroradiology, AOUP
University of Pisa
Via Paradisa 2
56124 Pisa, Italy
Tel.: + 39 050-992443
Fax: + 39 050-992127
E-mail: mircocosottini@libero.it