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LETTER TO THE EDITOR

An unusual cause of diplopia

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Case report

We here report the case of a 51-year-old man who was admitted in our neurology unit to explore a sudden onset of diplopia. Upon clinical examination, the patient showed signs of intrinsic and extrinsic right third nerve palsy, which had developed over a couple of days, without any associated pain or visual acuity loss. Clinical examination was otherwise normal. Angio-CT scanner, brain MRI and MRA were normal, as was the neck Doppler. MRI included high-resolution sequences, and no meningeal or third nerve enhancement was observed after Gadolinium contrast medium injection (Fig. 1). Peripheral blood counts were normal. Due to a strong history of autoimmune disorders (pericarditis, uveitis, Grave-Basedow thyroiditis, vitiligo), biological signs of active inflammatory disorders were looked for but there was none, with the exception of slightly increased sedimentation rate (28 mm/h) and C-reactive protein (14.6 mg/L). The patient was under Acenocoumarol for a recent pulmonary embolism, and L-Thyroxin. Past treatment included corticosteroids, colchicine, and radioiodine ablation of the thyroid. Analysis of the cerebrospinal fluid (CSF) showed a moderate increase in protein levels, and increased numbers of white blood cells (23/mm^3). Those cells were identified as 92 % of myeloid blasts (Fig. 2). A bone marrow biopsy revealed an infiltration by 29 % of myeloblasts, confirming the diagnosis of acute myeloid leukaemia (AML). Cytogenetic and molecular analyses revealed a *t*(9;11)(p22;q23) rearrangement of MLL(KMT2A/MLLT3) gene, as well as trisomy 3 (EVI1, 3q26). An ^{18}F-fluorodeoxyglucose PET-CT was performed and did not reveal any other extra medullary localisation.

Patient was treated with Aracytin (100 mg/m^2 for 7 days) and Daunorubicin (90 mg/m^2 for 3 days) with intrathecal injection of Methotrexate, Aracytin and corticosteroids (on day 1, 4, 6, 8, and 25), a treatment with which microscopic and molecular complete remission was achieved. Remission was consolidated with high dose Aracytin and intrathecal injection of Methotrexate, Aracytin and corticosteroids, before mini-haploidentical bone marrow transplantation, in the absence of a better donor, was performed. Third nerve palsy recovered over 3 weeks, 9 days after the beginning of chemotherapy, and no recurrence of diplopia or oculomotor impairment was reported during the follow-up (5 months).

Discussion

AML is the most common leukaemia in adults, with an incidence of 1.2/100,000/year in patients under 65 y.o. [1]. Clinical presentation is usually related to pancytopenia, with an association of shortness of breath, asthenia, bruises,

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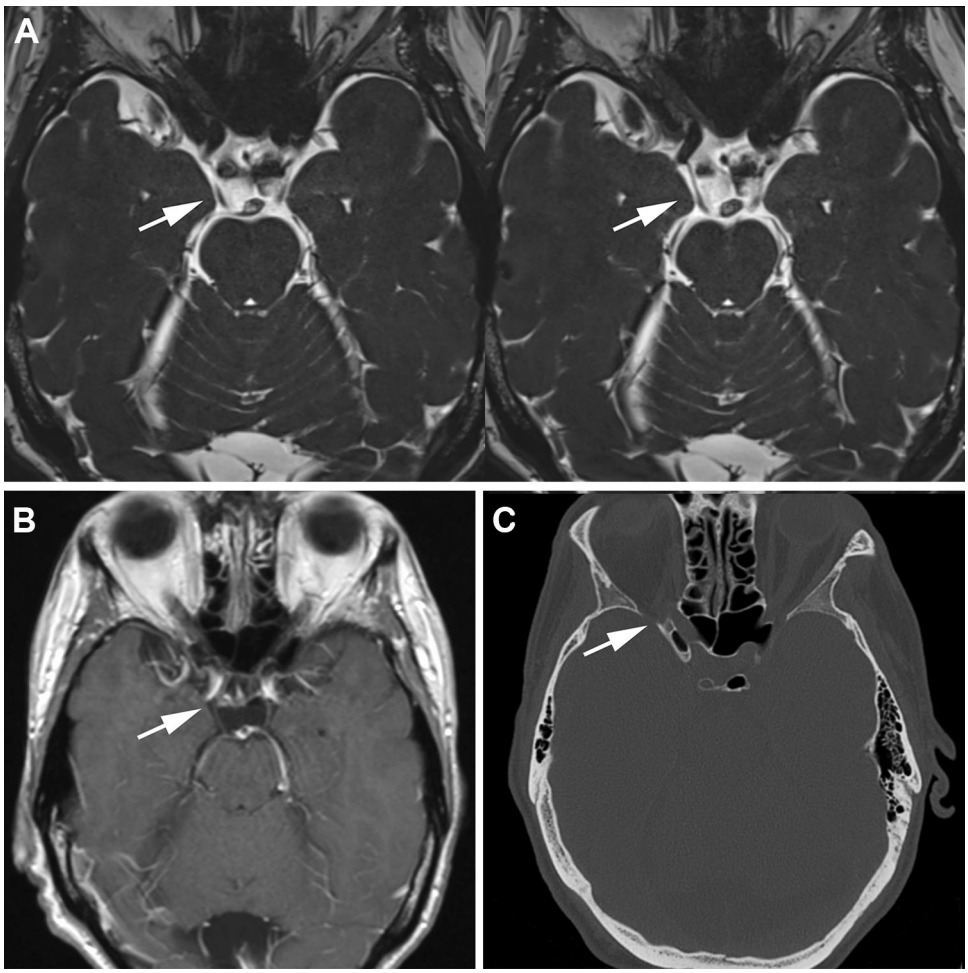

Fig. 1 On the patient's MRI, no abnormalities are found along the *right* third nerve tract, either at the cisternal level (**a**), or superior orbital fissure (**c**). No enhancement is seen after Gadolinium contrast medium injection (**b**)

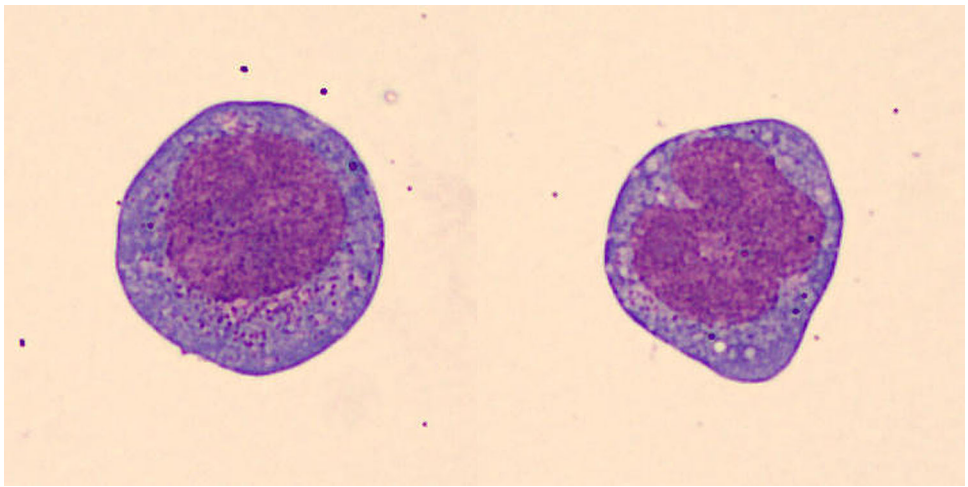

Fig. 2 Two of the myeloid blasts identified in the CSF

ecchymosis, external bleeding, and infections. Almost all patients have circulating blasts at the time of diagnosis.

Central nervous system (CNS) involvement is estimated to occur in less than 5 % of the patients all stages combined, less than in acute lymphoid leukaemia (ALL). Risk factors for CNS involvement include high white blood cell counts, elevated lactate dehydrogenase, and some specific chromosomal abnormalities [2].

To the best of our knowledge this is the first case of AML presenting exclusively as a neurological disorder

without myeloid sarcoma or peripheral blood abnormalities. One similar case was reported in an ALL, where the patient showed signs of meningeal irritation and a tetrapyramidal syndrome. The peripheral blood count and smear were normal, as well as the bone marrow aspiration. Blasts were only found in the CSF, then in the bone marrow biopsy [3]. In all other cases where a neurological sign was the first signs of AML, either peripheral blood count was abnormal (anaemia, circulating blasts…), or a myeloid sarcoma was found, sometimes years before systemic signs of the disease (e.g. [4]).

For these reason, AML is understandably not mentioned as a cause of diplopia. Third nerve palsy can occur secondary to nuclear or fascicular lesion, compression in the subarachnoid space, at the tentorial edge, in the cavernous sinus, or in the orbit, due to vascular (ischemic or haemorrhagic), traumatic, solid neoplastic, infectious, inflammatory aetiologies, or increased intracranial pressure [5]. None of these aetiologies was found in this case. In our opinion, AML could have caused this third nerve palsy either by a minute compression at the superior orbital fissure level, non-reachable with our MRI, or by a microvascular event at the time neuromeningeal infiltration occurred. Of course, we cannot formally exclude that the diplopia and AML diagnosis are unrelated, but the fact we excluded other aetiologies, the timing of occurrence and resolution, and resolution after chemotherapy are in favour of a causal relationship.

Conclusion

Our case illustrates an exceptional cause of diplopia, as our patient had a right third nerve palsy as the only sign of AML. Blasts were initially found in the CSF, and the peripheral blood counts and smear, and the MRI were normal. To our knowledge, it has not been reported in the literature before, as the few cases of cranial nerves presentation of AML were all accompanied by peripheral blood count or MRI abnormalities. It demonstrates the importance of a complete and systematic work up of neurological signs, including CSF cytopathology.

Compliance with ethical standards

Conflict of interest The authors do not report any conflict of interest.

Ethical approval This manuscript does not contain any studies with human participants or animals performed by the authors. The management of this patient was in no way modified by the redaction of this report.

Informed consent For this type of study formal consent is not required. Data were anonymized as required by the Medical and Faculty Ethics Committee of the University of Liege.

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