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ISOLATED RICHTER'S SYNDROME IN CENTRAL NERVOUS SYSTEM

Case report

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ABSTRACT - Diffuse large cell non Hodgkin's lymphoma associated with chronic lymphoid leukemia (CLL), or Richter's syndrome, is a rare and serious complication. Isolated Richter's syndrome in the central nervous system is very rare; only 12 cases have been reported. We describe a 74-year-old patient with diffuse large cell non Hodgkin's lymphoma in the right frontal region with the appearance of multiform glioblastoma.

KEY WORDS: Richter's syndrome, central nervous system.

Sindrome de Richter isolada em sistema nervoso central: relato de caso

RESUMO - Linfoma não Hodgkin difuso de grandes células em paciente portador de leucemia linfóide crônica (LLC), ou síndrome de Richter, é complicação rara e grave nesta leucemia. Síndrome de Richter isolada no sistema nervoso central é muito rara, tendo sido encontrados apenas 12 casos descritos. Descrevemos paciente de 74 anos, que apresentou linfoma não Hodgkin difuso de grandes células em região frontal direita, simulando glioblastoma multiforme.

PALAVRAS-CHAVE: síndrome de Richter, sistema nervoso central.

The occurrence of a diffuse large cell non Hodgkin's lymphoma in a chronic lymphocytic leukemia (CLL) patient was described by Richter in 1928[1]; this became known as Richter's syndrome after 1964[2]. It is the most serious CLL complication[3]. Isolated Richter's syndrome in the central nervous system (CNS) is very rare, only 12 cases have been described[3-9], 5 of them with isolated leptomeningeal involvment[4,6,9], and the other 7 with parenchimal involvement.

The aim of this paper is to report an additional case with isolated CNS Richter's syndrome with right frontal lobe parenchimal involvement.

CASE

A 74-year-old white male had previously diagnosed CLL, presenting only leucocytosis (lymphocytosis) for 6 years; he had been receiving medical support in another service with occasional use of chlorambucil, when he began to show mental confusion, bewilderment, and gait disorders. Cranial computerized tomography (CT) scan revealed an expansive process in the right frontal region Fig 1A. Extirpation of the lesion was indicated supposing a multiform glioblastoma. Histological examination, however, showed a diffuse large cell non Hodgkin lymphoma. His neurological symptoms improved after surgery, and he attended our hospital on the 15th day post-operative. When admitted, he was in good shape, with rosy complexion, and without adenomegaly or visceromegaly. Neurological examination showed a lucid, conscious and oriented patient, with normal cranial nerves. A slight left hand side hemiparesis with elevated deep tendon reflexes and Babinski sign was present. There were no signs of intracranial hypertension and a fronto-parietal surgical scar was visible. Peripheral blood revealed hemoglobin concentration of 14g/dl, platelet count of 170 x 10^9/l, and leukocyte count of 96 x 10^9/l (94% lymphocytes). Aspirated bone marrow had 60% mature lymphocytes, and bone marrow biopsy revealed a nodular and interstitial pattern of disease involvement. Peripheral blood lymphocyte immunophenotypic findings included CD23(+), CD5(+), CD20(+), CD25(+), CD10(-), CD21(-), CD22(-), CD11c(-), coexpression CD20/5(+), HLA-DR(+), sIgG (+ weak), compatible with B - CLL. Biochemical serum analysis, thoraxic CT scan, and abdominal CT scan were all normal. HIV sorological test was negative. Cerebrospinal fluid (CSF)was

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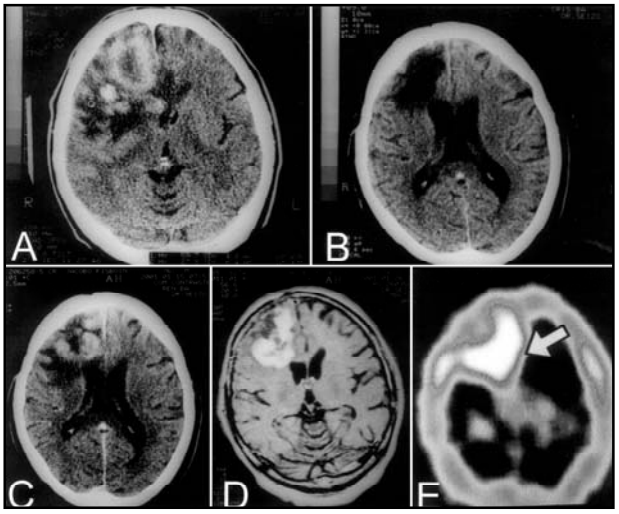

Fig 1. Right side frontal tumoral lesion before (A) and after (B) surgery. Reoccurrence of tumoral mass shown by CT scan (C), MRI (D), and SPECT scan (E).

xanthochromic, with 10 erythocytes/mm^3, 7 leucocytes/mm^3 (95% lymphocytes; 5% monocytes), 203mg/dl protein, 49mg/dl glicosis, and negative Nanquin ink. Simultaneous diagnosis of CLL and diffuse large cell non Hodgkin lymphoma of the CNS were established (Richter's syndrome). The patient received chlorambucil (4mg/day, continuous use), intrathecal chemotherapy (methotrexate = 12mg, cytarabine = 70mg, dexamethasone = 2mg - once a week for 3 consecutive weeks), plus radiotherapy of the right cerebral hemisphere (total of 3600 cGy within 4 weeks). CT scan after radiotherapy showed no tumor remnants in CNS, and revealed only a local porencephalic cyst (Fig 1B). Treatment of CNS lymphoma was stopped but treatment of CLL continued (chlorambucil). Five months later the same neurological symptoms reappeared. A slightly xanthochromic CSF showed 39 erythrocytes/mm^3, 2 leucocytes/mm^3, 412 mg/dl protein, 52 mg/dl glicosis, and negative Nanquin ink. Imaging of CNS by CT scan, magnetic resonance imaging (MRI), and cerebral perfusion with Sestamibi-99mTc (SPECT scan) revealed tumor relapse in the right frontal region [Fig 1C,D, E]. The choice was right frontal lobectomy, performed without incident. He was discharged receiving dexamethasone (4 mg/day), acetazolamide (500 mg/day), and carbamazepine (400 mg/day). He presented good evolution, practically free of neurological sequels (with only brief periods of mental confusion). He died at home while sleeping on the 14th day post-operative, before any other adjuvant therapy.

DISCUSSION

Richter's syndrome occurs in at least 1 to 10% of CLL cases[6], and is the most serious complication of this disease[3]. The usual presentation is sudden clinical deterioration, assymetric adenomegaly, esplenomegaly, fever, weight loss, increased lactate dehydrogenase, and monoclonal gammopathy. Although extra-nodal involvement is possible, isolated topography is extremely uncommon[5,6,8]. In the 12 CNS cases, the lesion was meningeal in 5, and parenchimal in 7, as in our patient.

The malignant characteristics of cerebral large cell lymphoma probably resulted in a neurorradiological aspect similar to multiform glioblastoma. Lymphoma of cerebral parenchima is very serious. Our patient died only 7 months after surgery, radiotherapy, and intrathecal chemotherapy.

There is evidence that prolymphocytic CLL transformation, blastic CLL crisis, and blastic transformation of low grade non Hodgkin lymphomas can present closely related manifestations, signifying neoplastic progression. Thus the malignant cells in the cerebral lymphoma of our patient could have developed as a subclone of his CLL[4,8,9].

REFERENCES

1. Richter MN. Generalized reticular cell sarcoma of lymph nodes associated with lymphatic leukemia. Am J Pathol 1928;6:285-299.
2. Lortholary P, Boiron M, Ripault J, Manus A, Bernard J. Leucémie lymphoïde chronique secondairement associée à une réticulopathie maligne (syndrome de Richter). Nouv Rev Fr Hematol 1964;4:621-644.
3. O'Neill BP, Habermann TM, Banks PM, O'fallon JR, Earle JD. Primary central nervous system lymphoma as a variant of Richter's syndrome in two patients with chronic lymphocytic leukemia. Cancer 1989; 15: 1296-1300.
4. Lane PK, Townsend RM, Beckstead JH, Corash L. Central nervous system involvement in a patient with chronic lymphocytic leukemia and non-Hodgkin´s lymphoma (Richeter´s syndrome), with concordant cell surface immunoglobulin isotypic and immunophenotypic markers. Am J Clin Pathol 1988;89:254-259.
5. Bayliss KM, Kueck BD, Hanson CA, Matthaeus WG, Almagro UA. Richter's syndrome presenting as primary central nervous system lymphoma: transformation of an identical clone. Am J Clin Pathol 1990;93:117-123.
6. Robertson LE, Pugh W, O´Brien S, et al. Richter´s syndrome: a report of 39 patients. J Clin Oncol 1993;11:1985-1989.
7. Mahé B, Moreau P, Bonnemain B, et al. Isolated Richter's syndrome of the brain: two recent cases. Nouv Rev Fr Hematol 1994;36:383-385.
8. Gilles FJ, O´Brien SM, Keating MJ. Chronic lymphocytic leukemia in (Richter´s) transformation. Sem Oncol 1998;25:117-125.
9. Agard G, Hamidou M, Leautez S, Garand R, Grolleau JY. Localisation neuroméningée d´um syndrome de Richter. Rev Méd Interne 1999;20:64-67.