Intracerebellar granulocytic sarcoma. A case report

Sarcoma granulocitico intracerebellare. Descrizione di un caso

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Summary
Granulocytic sarcoma is a form of extramedullary leukaemia. The intraparenchymal localisation is extremely rare. We report a case of cerebellar granulocytic sarcoma occurring in a 43 years old woman without any precedent medical history. The diagnosis of granulocytic sarcoma was established by neoplastic cells findings through morphological and immunohistochemical studies. The patient died few days after surgery. There are still no conclusive treatment strategies for this entity; however, early antileukemic chemotherapy seems to lower the probability of developing systemic disease and thus prolong survival.

Introduction
Granulocytic sarcoma (GS) or chloroma is a tumor mass of myelolasts or immature myeloid cells occuring in an extramedullary site or in bone. The tumor mass may precede or occur concurrently with acute or chronic myeloid leukaemia or with other types of myeloproliferative disorders or myelodysplastic syndromes. We report herein a case of cerebellar GS without meningeal or skull invasion.

Observation
A 43-years-old female without precedent medical history presented during september 2004 with dizziness, weight loss, headache and vomiting. Physical examination revealed an important hepatosplenomegaly. Her neurological examination was normal. All laboratory findings were within normal range mainly hemoglobin, erythrocytes, thrombocytes, leucocytes and peripheral blood smear. Axial computerized tomography showed an intraparenchymal mass of the right cerebellar hemisphere and the vermis containg hemorragic foci. There was a heterogenous enhancement after contrast administration (Fig. 1). The mass was resected through suboccipital craniectomy.

Histological examination showed a diffuse infiltrate of medium-sized to large cells, often with interspersed eosinophilic myelocytes. The neoplastic cells showed various stages of maturation; they had round to folded nuclei, and moderate amount of cytoplasm. A fine granularity was seen in some cells. Mitotic figures were abundant (Fig. 2).

Immunohistochimical study used myeloperoxidase, lysozyme, chloroacetate esterase, leucocyte common antigen and CD68. It demonstrated diffuse positive staining of the tumor cells with myeloperoxidase, lysozyme and chloroacetate esterase. Reactivity of tumour cells with leucocyte common antigen and CD68 was focal (Fig. 3). These results were compatible with granulocytic sarcoma. The patient died few days after surgery.

Discussion
Granulocytic sarcomas are rare extramedullary tumors composed of immature granulocytic precursors. Origi-
nally described in 1811 by Burns, the term “chloroma” was first used in 1853 to refer to the green color of the tumor caused by high content of myeloperoxidase. However, because of up to 30% of these tumors can be white, gray, or brown, Rappaport renamed them GS in 1966.

The most common sites of occurrence are the orbit and skin followed by bone, paranasal sinuses and epidural areas. Central nervous system and genitourinary system involvement contribute to only 3-8% of the total number of GS lesions. The cerebellum is a rare site of GS infiltration. To our knowledge, there had been nine cases of cerebellar GS described, four of which were children. Our case is thus the tenth. In addition, intracranial GS without meningeal or skull invasion is extremely rare.

The exact pathogenesis of intracranial granulocytic sarcoma is still unclear. Numerous theories were proposed. Azarelli et al. suggested that leukemic cells may pass from the bone marrow of the skull to the dura, and then to the subarachnoidal space. However, this theory does not explain intraparenchymal without apparent skull and meningeal invasion. Saper et al. explained the formation of leukemic nodules without meningeal invasion in patients with blast crisis by leukostatic plugging of small cerebral vessels during extreme leukocytosis. However, white blood cells counts are close to normal in most of the patients and thus, leukemic nodules fail to explain the pathogenesis of intraparenchymal GS. In some cases, GS occur as primary tumors in patients without evidence of concomitant hematologic disorder, and most of them progress to overt systemic leukemia within months. Ho et al. suggested that rests of embryonic central nervous system cells capable of hematopoietic differentiation could undergo malignant transformation and that intraparenchymal GS might develop in patients without systemic hematologic disease.

The tumor can present before, simultaneously with or after the diagnosis of acute myeloid leukemia. Nevertheless, leukemia almost always develops after an interval of weeks to years if systemic treatment is not given. Rarely GS may represent the first sign of blastic transformation of myelodysplastic syndrome or chronic myeloproliferative disorder.

The presenting syndromes of cerebellar GS include convulsions, cerebellar deficits, headache, hemiparesis and aphasia.

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**Fig. 1.** Axial computerized tomography: Intraparenchymal mass within the right cerebellar hemisphere and the vermis containing hemorrhagic foci.

**Fig. 2.** Granulocytic sarcoma: Tumor showing myeloid cells in different stages of maturation. Note variable size and lobulated nuclei. (HE x 100).

**Fig. 3.** Immunohistochemical staining of the tumor showing immunoreactivity to antomyeloperoxidase.
On computerized tomography and MRI, the tumor is homogeneous iso-attenuated or slightly hyper-attenuated. The lesions are hypo- or iso-intense on T1-weighted and T2 weighted images with marked, homogenous enhancement following contrast administration. These studies may allow the distinction of intra-cranial GS from haematomas and abcesses but is difficult to differentiate from olidendroglioma, metastasis, medulloblastoma and lymphoma.

Histopathologically, GS is composed of myeloblasts and neutrophils and neutrophil precursors. There are three major types based on degree of maturation: blastic, immature and differentiated type. The blastic type is composed mainly of myeloblasts, immature type of myeloblasts and promyelocytes and the differentiated type of promyelocytes and more mature neutrophils. Immunohistochemical positive staining with antibody to myeloperoxidase, lysozyme, chloroacetate esterase, CD68 and negativity with CD20 and CD30 proves the diagnosis.

Cytogenetic analysis may demonstrate a translocation t (8;21) (q22; q22) or t (16; 16) (p13; q22). GS is commonly misdiagnosed as lymphoma, particularly in cases without a history of leukemia.

The differential diagnosis includes sarcoma-like tumors with unusual features and lymphomas. An adequate immunohistochemistry should be applied to confirm the diagnoses.

The usual management of cerebellar GS includes surgical excision, radiotherapy, intrathecal and/or systemic chemotherapy.

References