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Case Report: aplastic anaemia and gray matter heterotopias in an autopsy of a 17-year-old puerperal woman

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In this article, we report uncommon findings in an autopsy made at the Pathology Service of Hospital de Clínicas de Porto Alegre (HCPA), in Porto Alegre, Brazil. This autopsy was remarkable for severe bone marrow aplasia (aplastic anaemia), which probably contributed to the cause of death (*Klebsiella sp.* septicaemia), and, as an incidental finding, several gray matter heterotopias in the subcortical white matter, in a pattern compatible with nodular heterotopia. Common findings in autopsy, such as anasarca and pleural effusion, were also present.

CASE REPORT

A 17-year-old patient came to us at the Pathology Service for autopsy. Five months earlier she had delivered a baby via an urgent caesarean section, due to gestational thrombocytopenia, in a hospital in another city, at which she remained hospitalized for 4 months; in this period, the patient received many blood transfusions. Finally, she was referred to HCPA in order to receive a bone marrow transplant from her brother, which was compatible; when she arrived at HCPA, a bone marrow biopsy showed aplastic bone marrow (aplastic anaemia), and the patient started having neutropenic fever, for which she was started on antibiotics; Fanconi anaemia was ruled out at the time as a possible cause. A week later, an abdominal computed tomography showed hepatomegaly and multiple hypodense areas in the liver suggestive of liver abscesses, as well as thickening of the cecum and the ascending colon. Two weeks later, the patient had generalized tonic-clonic seizures, for which she was submitted to a brain magnetic resonance imaging (MRI) that showed multiple microabscesses on the leptomeninges; she was transferred to the intensive care unit (ICU), but developed septic shock by multidrug resistant *Klebsiella sp.* and came to death, being referred thereafter for autopsy.

At autopsy, the patient was found to have anasarca, presenting with ascitis, bilateral pleural effusion, and pericardial effusion. We found two abscesses in the liver, with the largest one measuring approximately 27 cm^3. Both kidneys had alterations compatible with septic shock. The brain was oedematous, with congested blood vessels and parenchymal pallor; a coronal slice of the brain revealed several grayish nodules resembling gray matter (figure 1). On microscopic examination, the nodules showed to be made of cortical neurons distributed in a rudimentary lamination pattern, isolated from the real cortex by white matter in all their sides (figure 2), characterizing thus gray matter heterotopia. At the edge of the coronal slice, four nodules of about 5 mm of diameter each could be identified in the white matter of the brain.

Microscopic examination of bone marrow showed hypocellularity and abundance of hemosiderophages (hemosiderin-laden macrophages), which are classic findings of bone marrow aplasia. Immunohistochemistry of lymph node was positive for CD3, CD68, and lysozyme; weak positive for CD4; and negative for CD20, S100, CD21, CD1a, CD8, and CD34; Ki67 showed low mitotic index. Altogether, the findings were compatible with a reactional

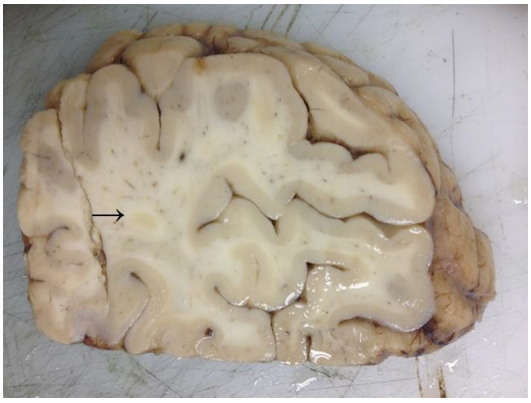

Figure 1: Coronal slicing of brain showing nodular gray matter heterotopy.

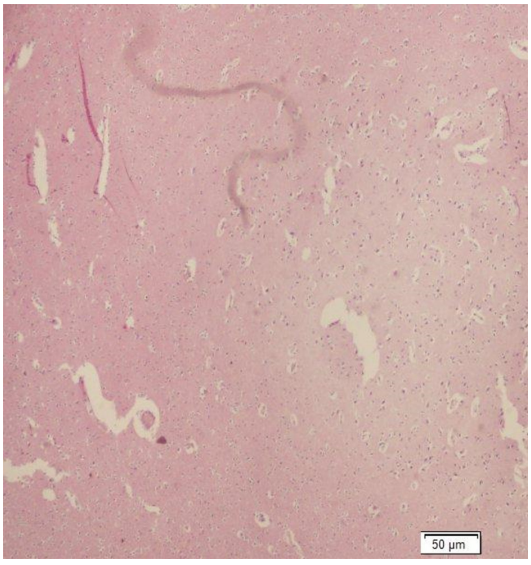

Figure 2: HE staining 40x showing nodular gray matter heterotopy.

condition, discarding the hypothesis of white cell neoplasia contributing to the cause of death.

DISCUSSION

Aplastic anaemia is a rare condition, with an incidence of 2.2 cases per million population[1]. There is no data in the literature about the incidence of puerperal or postpartum aplastic anaemia, probably due to the even greater rarity of this specific condition. As occurred with our patient, septicaemia is the major cause of death of patients with aplastic anaemia[1]. Although the majority of aplastic anaemias are classified as idiopathic, there are several possible aetiologies for this disease. In a recent case-control, multicentre, multinational study of Brazilian and other Latin-American populations, exposure to benzene-derived products, chloramphenicol, and azithromycin in the year before the onset of the disease was associated with a greater odds ratio for its development[2]. Our patient, however, presented no such exposures, as far as we know, nor did she have any finding pointing to a defined cause for her bone marrow aplasia, for which we classified her as an idiopathic case.

Nodular heterotopia, specially its subcortical type, is not a particularly rare incidental finding in autopsies, even in the ones not related to neurological alterations, although there is currently no prevalence estimation in the literature. Although there is no data regarding subcortical nodular heterotopia, paraventricular nodular heterotopia (a subtype that is morphologically and possibly functionally related to the subcortical one) is strongly related to epilepsy[3], and patients usually have a history of refractory seizures. Our patient, as far as we know from her clinical history, did not suffer from epilepsy, nor did she have, at autopsy, other malformations, which makes her case distinctive in that her nodular heterotopias were asymptomatic casual findings. It is remarkable that the heterotopias were not found in the brain MRI to which the patient was submitted, presumably due to their small size; conversely, we actively searched for signs of microabscesses in all meningeal surfaces, but were unable to find any, which suggests that they may have resolved with the antibiotics given to the patient, or may have been taken for heterotopias or other anatomical structures.

In medicine, it is said that one should always follow Occam`s principle: the simpler, the better; however, there is currently no data either linking aplastic anaemia to nodular heterotopia of the gray matter or establishing a possible common cause for the two condition. Thus, we have to admit that two rare findings presented together in the same patient, which makes this case report remarkable.

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