

The Role of the Immunohistochemical Examination in the Diagnosis of Castleman's Disease

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Castleman's disease is characterized by benign angiolymphoid hyperplasia. There are two clinical forms: the localized form in which one lymph node is affected, often paucisymptomatic, treated by radical surgical excision, without recurrence in most cases, and the multicentric form, characterized by systemic manifestations, polyadenopathy (mediastin, cervical region, abdomen, etc.), organomegaly (e.g. spleen, liver), with a less favorable prognosis than the localized form. The etiology of the disease remains unknown; recent studies suggest the implication of human herpes virus 8 (HHV-8), especially in multicenter forms. We shall present the case of women, aged 23, with Castleman's disease with retroperitoneal localization, who was admitted to the surgery clinic due to abdominal pains. The initial abdominal CT raised the suspicion of a hepatic lobus caudatus tumor, but the anatomical-pathological result confirmed the diagnosis of angiofollicular hyperplasia of the lymph nodes. Diagnostic methods, histological forms, treatment and prognosis aspects of Castleman's disease are described below.

Keywords: Castleman's disease, retroperitoneal hyperplasia, liver tumor

Castleman's disease, or angiofollicular hyperplasia of the lymph nodes, is a rare pathology, first described in 1954 by the American pathologist Benjamin Castleman (1906-1982). The disease presents a continuous interest from both points of view, clinical and scientific. For several decades, some aspects of this disease have been identified due to clinical, paraclinical and bio-molecular researches, but its etiology and pathogenesis have not been elucidated [1,2].

Castleman's disease is manifested by the appearance of a benign nodular tumor located in mediastinum, retroperitoneum and the soft tissues (subcutaneously and intramuscularly) of different body regions, often in the cervical area and the scapular belt. The formation is usually solitary, rarely multiple [3,4].

The diagnosis of Castleman's disease is based on the clinical assessment of the patient and includes: detailed anamnesis, laboratory examinations (IL-6 protein, C-reactive, VSH), histological examination of the affected lymph nodes or suspected formation and imaging examination (radiological, CT, NMR). In recent years, the PET-scanning method (positron emission tomography) is frequently applied. PET may be complemented by CT, in order to assess the metabolic status of the lymph node [5-8].

Experimental part

Clinical case

We shall present the case of a 23-year-old patient with chronic hepatitis B, who was hospitalized in the Hematology Clinic for the investigation of an anemic syndrome. Clinically, the patient presents physical asthenia, scleroretigumentary pallor, pain in the right hypochondrium and the epigastrium. The patient did not receive any medical treatment and does not have history of drug allergy.

The clinical examination revealed a slim, depressible abdomen, with breathing mobility, painful at superficial and profound palpation in the right hypochondrium and epigastrium. In the right hipocampus a pseudotumoral

formation of about 5/7 cm can be palpated. It is painful and immobile on the superficial planes. There is hematologic evidence of moderate iron-deficiency anemia (Hb = 10.1 g%, Fe = 21 µg/dL). The biochemical profile (including liver function tests) was normal. At immunological level, there was determined a AgHbS with a value of 5597. Also, the electrophoresis of serum proteins detected: albumin = 50.40% (low values), gamma globulin = 25.90% (high values). The abdominal-pelvic ultrasound raised the suspicion of tumor of the caudate lobe of the liver: a subhepatic hypheecogenic formation, well-circumscribed, with a size of 55/56/36 mm, in the vicinity of the cave vein, on which it has a mass effect, in a proximity relation with the hepatic artery and the celiac trunk. The MRI confirms the diagnosis of a solid, localized interportocave expansive formation on the topography of the caudate lobe, with dimensions 36/47/54 mm (ap/t/cc), a non-homogeneous structure and a central necrosis area, in a predominantly peripheral T2 hypersignal and T hyposignal, with diffusion restriction and annular contrast enhancement. The formation has a mass effect on the inferior cave vein and the trunk of the portal vein, without thrombosis or signs of invasion at this level.

The patient is transferred to the Surgery Clinic, in order to establish the therapeutic course. An exploratory laparotomy was carried out after an adequate preoperative preparation and an adenopathic block was identified at celiac trunk level, with a size of approximately 60/45/55



Fig. 1. Ecographic appearance of the massive tumor formation on the portal vein

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mm. There was performed the ablation of the adenopathic block with control hemostasis.

The macroscopic adenopathic block shows 6 nodular formations with smooth integral capsule, a solid white-yellowish appearance on the section and a slightly low consistency.

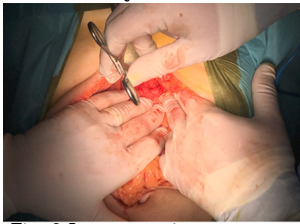


Fig. 2 Intraoperative appearance of the tumor formation

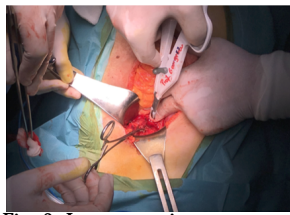


Fig. 3. Intraoperative appearance of the adenopathic block before completing the ablation

The definitive diagnosis was established on the basis of the histopathological paraffin examination, which revealed the hyaline - vascular type of Castleman's disease. There was carried out the microscopic examination of multiple



Fig. 4. Macroscopic appearance of the adenopathic block

fragments of a partially wiped lymph node with absent medullary and subcapsular sinuses and numerous lymphoid follicles dispersed throughout the entire lymph node area, uneven, with preserved polarization and present mantle area, some of them hyperplastic with doubling aspects of the germinal centers. There were also large areas of dense interstitial fibrosis and venule hyperplasia with high endothelium in the interfollicular areas, as well as other 5 lymph nodes with preserved structure. The morphological aspects suggest Castleman's disease. The immunohistochemical examination confirms the aforementioned diagnosis according to the following specific markers: CD20 positive in lymphocytes B at lymphoid follicle level and in the interfollicular areas; CD 23 positive in follicular dendritic cells at the level of germinal centers; BCL2 negative in the lymphoid follicles, but positive in many lymphocytes in the interfollicular area; CD79a positive in lymphocytes B and plasmocytes, CD138 positive in many plasmocytes in the interfollicular areas; CD 15 positive in the rare granulocytes; CD 30 slightly positive in the rare activated lymphocytes B.



Fig. 5. Macroscopic appearance of the adenopathic block after sectioning

The immediate postoperative progression of the patient was favorable, being discharged on the 7th postoperative day with a good overall condition.

Results and discussions

The disease was described for the first time in 1954 and 1956 by Castleman as a benign localized volume increase of the lymph nodes. Castleman's disease is rare and affects between 100,000 and 200,000 people in the United States. [9,10] From a clinical point of view, the disease manifests

itself in two forms: localized or multicentric. In the case of our patient, the lymph node damage was localized and of hyaline-vascular type (a type that most commonly affects young people).

Castleman's disease is an atypical, benign lymphoproliferative disorder characterized by hypervascular lymphoid hyperplasia with distinct mechanism and unknown etiology. Abundant evidence indicates that a viral infection can have a significant contribution to the disease. Our patient had chronic hepatitis B.

In this disease, tumor masses are very vascularized, which means that embolization prior to extirpation can reduce intraoperative bleeding and facilitate the excision. In our case, there was no need to carry out a preoperative embolization, the surgical intervention was successful, without intraoperative incidents that might carry hemorrhagic risk [11].

The hyaline - vascular type is preferentially localized in the case of young patients and our patient was 23 years old. Clinical manifestations are poor and, at biological level, it is possible to observe a moderate anemia, a mild VHS increase and polyclonal hypergammaglobulinaemia, stigmas that are quickly corrected after a complete exeresis. The patient came back one month after the intervention for clinical and biological reassessment. The results are favorable and without haematological changes.

Conclusions

Unfortunately, paraclinical explorations are not specific to Castleman's disease and the certainty diagnosis remains the histological one. Castleman's disease must be differentiated from lymphomas or reactive hyperplasia of the lymph nodes. Identifying the histological variant is mandatory for the administration of an appropriate treatment, as well as for prognosis in patients with Castleman's disease.

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