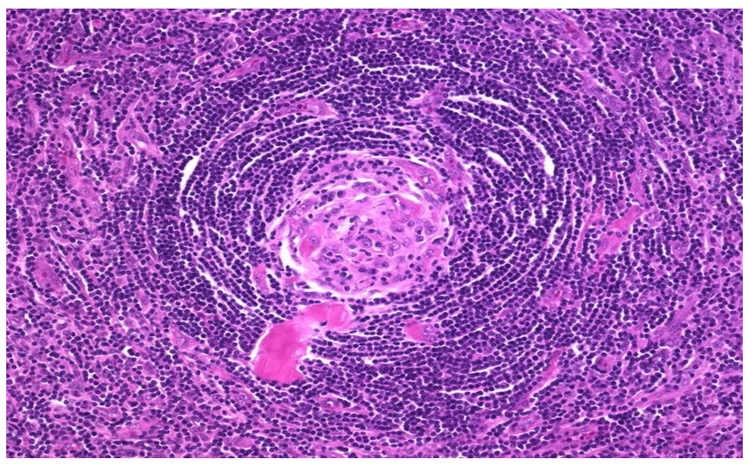
CASTELMAN'S DISEASE – PRESENTATION OF TWO CASES AND LITERATURE REVIEW

V.Goranova-Marinova1, E.Spassov1, K.Sotirova1, D. Dimitrov2, Ch.Stefanov2 St.Goranov1

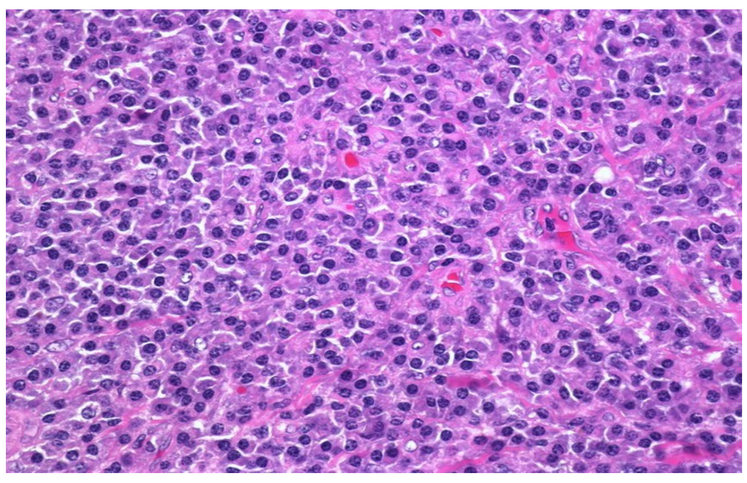
Clinic of Hematology1,
Clinic of Anesthesiology and Intensive Care2
University Hospital "Sv.Georgi"- Plovdiv

BACKGROUND: Castleman disease (CD; angiofollicular lymphoid hyperplasia) is a heterogeneous group of lymphoproliferative disorders of uncertain cause, first described in 1956 by Castleman B. Three histologic variants (hyaline vascular, plasma cell, and mixed) and two clinical types (localized and multicentric) have been described, which comprise at least two distinct diseases with very different prognoses. CD is usually associated with HIV, HHV-8 as well as with number of malignancies, including Kaposi's sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, and POEMS syndrome. Diagnosis is ultimately made by a lymph node biopsy. For the localized type surgical excision is curative while multicentric disease often necessitates aggressive systemic therapy and has a poor outcome.

Hyaline vascular variant



Plasma cell variant



CASE 1. A 41years old female patient presented at the Surgery department in March 2003 with an abdominal tumor mass. The patient noticed a "swelling" in 1998 for the first time. She felt physically healthy and had no other complaints. The CT scan found a solitary retroperitoneal mass, 5x5 cm in size which was surgically removed. Hystological examination proved" CD-plasma cell variant". The laboratory tests of the CBC, DBC, liver enzymes, renal function and proteionogram were within normal ranges. Serological tests for viral infection were negative: CMV IgM(-), EBV (-), HIV (-), HBsAg(-) , HCV(-). Six years later the patient is in good health, on regular follow - up with no data of relapse.

CASE 2.

July 2008:A previously healthy 18-years old boy presented complaining of fever, weakness, nausea, vomiting, abdominal pain and clinical and laboratory findings consistent with acute pancreatitis, peritonitis and sepsis with Pseudomonas Auruguinosa. He was transferred to the Surgical department, where operated. The histological examination of the pancreas confirmed acute hemorrhagic pancreatitis.

August 2008. In the post operative period the condition of the patient was complicated with profuse bleeding and the operative site was revisited repeatedly. The patient was admitted to the Intensive care department. ***A rapid decrease of the platelet value from normal to 32x109/l was registered along with prolongation of APTT up to 52", and low AT-III level 62%. Fg and PTT were within normal ranges.*** **From the laboratoray findings**: accelaretd ERS >100mm/h, anemia Hg 113g/l→56g/l, CRP 82 mg/l, ASAT, ALAT, bilirubin, creatinin, urea, uric acid, AP – within normal ranges. **CT scan** ***liver and spleen were enlarged***, initial pleural and pericardial effusions were present. No data of enlarged lymph nodes. A diagnostic search for **autoimmune disease** was done, but all the tests were negative: ANA 1: 40; Anti SS-A52, antiSS-A60; anti –Sm; antiRNP(sm), anti Scl-70; anti Jo-1; anti centromere B; anti SS-B, anti ribosomal P, antimitochonrial autoantibodies, antiphospholipide autoantibodies, anticardiolipine autoantibodies.Serology for **viral infection** was negative: CMV IgM(-), EBV (-), HIV (-), HBsAg(-), HCV(-). At that time all the findings were interpreted in the context of a complicated operation for acute pancreatitis. The patient was treated with antibiotics, haemotransfusions, fresh frozen plasma, platelet transfusions, Novo-seven, AT-III and ***corticosteroids.***

In September for the first time ***bilateral inguinal lymph nodes 1.5 cm*** were found.

In October and November the condition of the patient was temporarily improved, bleeding stopped, he had no fever and was discharged from hospital.

In December 2008 he was hospitalized because of high temperature to 38°C, anuria, diffuse oedema with large pleural and pericardial effusions, enlarged axillar and inguinal lymph nodes.

Laboratoratory findings; Hg 76g/l; WBC 14,2x109/l, platelets18x109/l, creatinin 74, ***total protein 65, albumin 22***, ***IgG 24.9g/l-policlonal***, IgM 0.70, IgA 1,67; serum glucose, bilirubin, ASAT, ALAT, LDH, electrolytes-within referent ranges. **CT scan**: massive pleural effusions, pericardial effusion, ***progressive enlargement of the liver and spleen*** and for the first time ***enlarged paraaortal lymph nodes***, forming a package in the abdomen were described. **Biopsy** from an axillary lymph node was done. The histological exaimination from two independent reviewers revealed: ***Castelman's disease –mixed hyaline vascular/plasma cell type, predominantly plasmacellular***.

At that time the condition of the patient was critical and he died a few days later, before initiating therapy.

DISCUSSION: Two histological variants with distinctive morphological features, and a mixed form between them are described. They do not correlate with the clinical type of the disease. The clinical forms –solitary and systemic have quite different manifestations, evolution , treatment and clinical outcome. The cases we present confirm the above statement.

	Localized form	Multifocal form
Mean age (years)	3-rd decade	6-decade
Clinical signs	Incidental mass effect	Systemic symptoms
Localization	Mediastinum, cervix, abdomen, etc	Multiple lymph nodes
Hystologic type	HV, HV-PC	PC, PC-HV
Treatment	Surgical resection	No consesus, corticosteroids, chemotherapy, radiotherapy
Prognosis	Excellent :100% survival at 5 year	Poor: MS of 30 months
Recurrence after treatment	Extremely rare, related to incomplete resection,	Nearly always
Association	Rarely lymphoma	AIDS,HHV-8, Kaposhi' sarcoma,myeloma, POEMS, NHL

CONCLUSIONS: The variety of clinical symptoms in the systemic form of CD is a prerequisite for broad differential diagnosis, lots of unnecessary laboratory and invasive examinations, late diagnosis and late initiation of treatment. On the other hand the frequent of associations of CD with viral infections, solid neoplasma and other monoclonal gammopathies is another reason for difficult nosological identification. Moreover even after proving the diagnosis there is no consensus treatment so far. Clinitians must rely on their personal judgment and theoretical knowledge. Making the diagnosis of CD and choosing the correct treatment is a real challenge: the joint efforts of hematologists, surgeons, specialist of infectious diseases, pathologists are needed.