Castleman Disease, Hyaline-vascular Variant: Clinical and Histological Features of 12 Patients

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Introduction. Castleman disease (CD) is a rare (less than 100 cases diagnosed yearly worldwide) benign lymphoid hyperplasia. Classification includes the classical CD or hyaline-vascular subtype (HV-CD) and much less frequent plasma cell variant that has no specific histological features. Median age is 33 years. Tumour is localised in 90% patients, mediastinum is the most frequent site (60–75%), followed by neck (20%) and mesenterial (10%) lymph nodes. Extranodal lesions of extremities, abdominal organs and retroperitoneum, lungs and pleura, meninges and othershave been reported. Localised CD progresses slowly, the tumour could measure up to 15 cm or more. 50–90% patients are asymptomatic or suffer from local symptoms only; accidental finding is common. Multicentric CD is associated with AIDS and aggressive course. Aetiology is unclear, CD is considered to represent an atypical immune reaction with IL-6 hyperproduction as a key factor.

Histology of HV-CD is specific: atypical "burnt-out" follicles, massive vascularisation and hyalinosis, loss of normal lymphoid stroma. The foremost differential diagnosis is with lymphoid neoplasms and reactive lymph node hyperplasia. Surgery is effective in 90–95% cases of localised CD, other options have proved unsuccessful. Intensive anti-retroviral therapy and experimental protocols have been used in patients with multicentric disease.

Materials and methods. Cases of HV-CD diagnosed between 2000 and 2012 in the National Centre of Pathology, Pauls Stradins Hospital Institute of Pathology and Children's Clinical University Hospital were retrospectively studied. The patients' documentation and histology were reviewed to define relevant clinical and histological features and to evaluate the efficiency of diagnostic procedure.

Results. 12 proven cases of HV-CD were found during the study period, returning the yearly incidence 0.42/million population. 6 patients were male and 6 female, age was 15–69 (mean – 36.3). 11 patients had localised disease, multicentric CD was diagnosed in one HIV+ case. Most common tumour site was neck (5 cases), followed by retroperitoneum (4), mediastinum (2) and thigh (1). Tumour size varied from 2.5 × 1.5 cm till 10 × 8 cm. In 5 patients the tumour was found accidentally, in 4 patients it had existed for many years (4–21). Local symptoms were found in 4 cases, 4 patients presented with systemic symptoms and 2 with biochemical alterations. All 11 localised tumours were completely surgically extirpated; no relapses have occurred during the observation time and systemic symptoms resolved. The patient with multicentric CD was transferred for antiviral treatment.

The HV-CD diagnosis was proven by histology and immunohistochemistry in all cases, the staining protocol included CD3, CD20, bcl2, Ki67 and CD21 as the backbone with variable additions. The most constant histological features were "burnt-out" germinal centres, hyperplastic mantle zones forming concentric circles – "onion-like" structures, prominent interfollicular vascularisation and loss of sinuses and other stromal elements of normal lymphoid tissue (all cases), followed by hyalinosis (11 cases), follicles invaded by blood vessels – "lollypop" (10), hyperplasia of CD21+ follicular dendritic cells (7) and multiple germinal centres within single mantle (7). Combination of specific features and immunohistochemistry assured confident diagnosis in all cases.

Conclusions. CD is a very rare disorder in Latvian population, still, one should be aware of it as a differential diagnosis; there remains a high probability of missed patients. Our series were similar to literature data by clinical and histological features. Surgery provided excellent results, making precise diagnosis paramount for CD patients.