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## High grade endometrial stromal sarcoma: An update

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Low-grade endometrial stromal sarcomas constitute the majority of endometrial stromal neoplasms; they frequently contain Lohromosomal rearrangements that result in JAZF1-SUZ12 fusion or other equivalent genetic fusions. The tumors that have variably been referred to as "high-grade endometrial stromal sarcomas" are more uncommon and are more clinically aggressive than their low grade counterparts. The new WHO 2014 classification essentially defined the latter by the presence of YWHAE-NUTM2A/B (YWHAE-FAM22A/B) fusions. Overall, the diagnostic approach to high grade endometrial stromal sarcomas by pathologists has undergone a significant evolution in the past several decades. In this presentation, this historical evolution is reviewed in detail, with a description of current diagnostic criteria, limitations of current classification schemes and a proposal that incorporates all currently available data.

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## Estimation of time since death using the cholesterol levels in peripheral nerve

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**Introduction:** Many years ago, we studied the post-mortem modifications of the peripheral nerves investigating the structural and ultrastructural alterations of the nervous fibers. We also investigated the paranodal demielinization by a computer assisted system connected to an optical microscope and we observed a positive correlation between the paranodal demielinization and the time after death. The paranodal demielization segment grew according the time from the death. The statistical elaboration of the results showed an interesting perspective in the estimation of post-mortem interval (PMI) with a possible error of 2, 4, 8 hours within 12, 24 and 48 hours after the death, respectively. These observations moved us to investigate the post-mortem lipid metabolism of nervous fibers; so, considering the peripheral nervous tissue composition, we studied the cholesterol variations in peripheral nerve at different time after death.

**Method:** Samples of median nerve were collected during forensic autopsy when we knew circumstances and time of death. Fragments of approximately 1 cm were collected in test tubes and samples were kept at -20°C until analysis. Cholesterol (CHOL) quantification was performed on aliquots of about 50 mg of collected nerves, added with  $\alpha$ -cholestane standard solution, used as internal standard. Samples were incubated with 1M KOH at 65°C for 1 hr, then kept at room temperature and added with 2 mL of bidistilled water, prior of purification by mean of liquid/liquid extraction with n-hexane. Organic fractions were dried under nitrogen stream and dissolved in 500 µL of ethyl acetate; 10 µL aliquots were used for gas chromatographic/ mass spectrometric (GC/MS) analysis, after derivatization with BSTFA (reaction at 70°C for 20 min). CHOL quantification in median nerve was performed by means of a calibration curve in the range (9.25-150) ng/µL.

**Result & Discussion:** 36 samples were collected at different intervals after death from male and female subjects 25-53 years old, without neurological diseases. An increased cholesterol concentration has been recorded in all enrolled subjects. The cholesterol increment with time –after – death can be explained with the catabolic post mortal processes of nerve (cholesterol is the main constituent of myelin), with the lysis of lipidic membrane and with the structural modifications of peripheral nerve. The obtained data, although preliminary, showed a positive correlation between a cholesterol concentration in median nerve samples and the time after death. Significant increased levels of cholesterol also have been observed in samples collected after only two hours. The cholesterol variation seems to follow a linear regression but results have to be confirmed by the anlysis of a large number of samples, possibly collected from the same subject, at more intervals of time.

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