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Überörtliche Berufsausübungsgemeinschaft
MVZ · Dr. Eberhard & Partner Dortmund

Laboratoriumsmedizin Dortmund

LabmedLetter

MVZ Dr. Eberhard & Partner Dortmund
Postfach 10 10 40
44010 Dortmund
Brauhausstraße 4
44137 Dortmund
www.labmed.de
info@labmed.de
mikro@labmed.de
Labor:
Tel.: 0231 · 95 72 - 0
Fax: 0231 · 57 98 34
Mikrobiologie:
Tel.: 0231 · 95 72 - 5100
Fax: 0231 · 55 34 62

Laboratory information 3/2017

Progastrin releasing hormone (ProGRP): Improved differential diagnosis of lung cancer subtypes

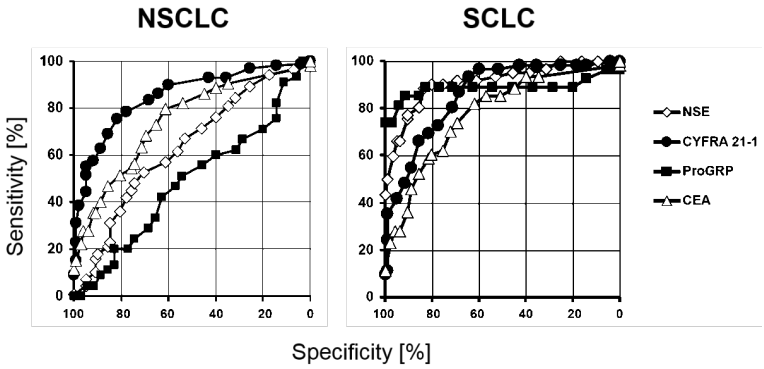
Medical background

Lung cancer is one of the leading and deadliest malignancies worldwide, representing about 15% of all new diagnosed cancers every year. Depending on the histological cell type, lung cancer can be classified into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC accounts for around 80% of all new lung cancer cases, with SCLC making up the remaining 20%. It is critical to distinguish between these two subtypes at initial presentation, since they differ in their treatments and prognoses. The NSCLC is curable by surgery in the early stages, while the SCLC is the more aggressive variant with high tumor growth and early metastatic spreading which requires an intensive chemo-therapy and radiotherapy. However, relapse is seen in most patients, especially due to acquired resistance to chemotherapy.

A large panel of tumor markers is available for the diagnosis of lung cancer. Mostly, carcinoembryonic antigen (CEA), CYFRA 21-1, squamous cell carcinoma antigen (SCCA), tissue polypeptide specific antigen (TPS) and neuron-specific enolase (NSE) are the markers of choice. However, they all are far apart from being ideal tumor markers as they lack sensitivity and specificity. Furthermore, none of them allows a reliable performance to distinguish between the two types, since high levels of these markers can be found both in SCLC and NSCLC. NSE is suggested to be even more valuable for the detection of SCLC compared to NSCLC (see ROC graphic plot).

Since SCLC is seen as a disorder of neuroendocrine tissue differentiation, a precursor of the neuropeptide gastrin releasing peptide, the progastrin releasing peptide (ProGRP), has recently been identified as promising new marker for SCLC. ProGRP and the processed GRP have been described to function as growth-stimulator in an autocrine fashion and may be responsible for the aggressive growth and poor prognosis of SCLC patients with high serum levels. Although NSE was historically the recommended tumor marker for SCLC, studies confirmed that ProGRP is increased particularly in the early stages of SCLC. Though it should be considered as the biochemical marker of choice for SCLC, much more useful than NSE as it supports quick and accurate discrimination between SCLC and NSCLC ensuring an early diagnosis and a faster decision on appropriate therapeutic intervention.

At cut-offs corresponding to a high specificity of 95%, the sensitivity of ProGRP was 78.4 %, while that of NSE was only 48.6% to detect SCLC. ProGRP accurately discriminates between NSCLC and SCLC at 97.7% specificity and sensitivity of 75.7%, while NSE presented obviously lower sensitivity of only 37.8%. The assay distributor (Roche Diagnostics) has worked out a cut-off at 85.7 pg/ml, which provides 95% specificity and a sensitivity of 80%. ProGRP is rarely increased in malignancies other than SCLC or in benign conditions, except in renal failure, neuroendocrine tumors (NET) and medullary carcinoma of the thyroid (MCT). Thus, we recommend to take care in interpreting ProGRP results in patients with an eGFR below 30 ml/min/1.73 m.



Prospectively, ProGRP surely cannot relieve NSE, since up to 20% of all patients suffering from SCLC express either NSE or ProGRP. Preliminary studies suggest changes in ProGRP blood levels show excellent correlation with the therapeutic responses in SCLC patients. Hence, ProGRP could be highly beneficial in combination with NSE in monitoring the therapy and patients' follow-up of established SCLC.

Method and turnaround time

Electro-chemiluminescence immunoassay (ECLIA);
daily analysis, results same or next working day

Material

EDTA or lithium heparin plasma preferred, about 1 ml.
Stable for 24 hrs. at 2-8°C, in addition please freeze at -20 °C, serum should be separated immediately and kept frozen at -20 °C.

Reference intervals & cut-offs

< 63 pg/ml

Contact

Dr. rer. nat. Falko Strotmann: strotmann@labmed.de

Literature

1. Molina et al. ProGRP: A New Biomarker for Small Cell Lung Cancer. EJCMO (2009) 1, 25-32.
2. Nisman et al. The Diagnostic and Prognostic Value of ProGRP in Lung Cancer. Anticancer Research 29: 4827-4832 (2009
3. Korse et al. Multicenter evaluation of a new progastrin-releasing peptide (ProGRP)