Neuron-Specific Enolase - NSE

Introduction

Enolase is an enzyme involved in glucose metabolism (glycolysis), which catalyzes the conversion of 2-phospho-D-glycerate into phosphoenolpyruvate. Enolase is made up of two out of three existing subunits (α, β and γ subunits), which form the physiologically active enzyme. NSE consists of an αγ or γγ dimer, mostly found in neurons and neuroendocrine tissues. A high concentration of serum γ-enolase (NSE) is detected[1, 2] above all in neuronal and neuroendocrine cell neoplasms (APUD-cells), e.g. bowel and lungs, due to its high tissue specificity. About 20% of all cancer-related deaths in Europe are caused by lung cancer[3], with the highest incidence reported in Hungary[4, 5].

NSE in lung cancer

NSE as marker of choice for small-cell bronchial carcinoma

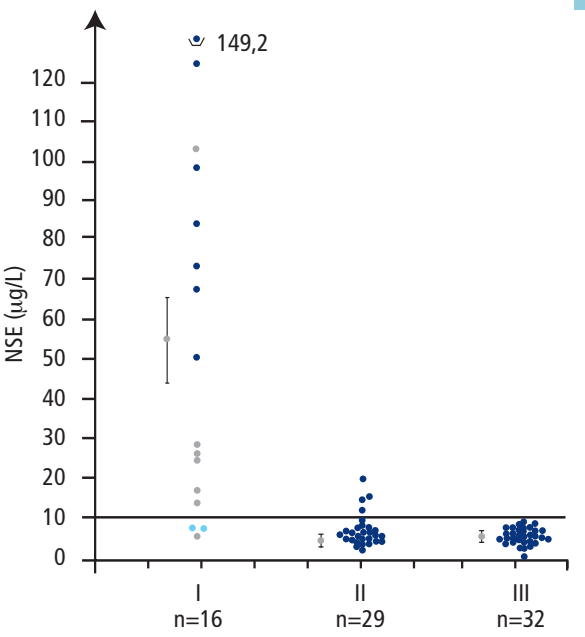
NSE sensitivity in small-cell lung cancer (SCLC) ranges between 60 and 87%[6]. Therefore, NSE is considered a crucial marker for small-cell bronchial carcinoma. NSE is more relevant with respect to other available markers[7] in the differential diagnosis between benign lung disease and non-small-cell lung cancer (NSCLC) or SCLC. NSE correlates well with the tumour size and spread. The course of the disease and its prognosis may be established trustworthy using NSE in both SCLC and NSCLC[8]. The response to treatment can be detected within seven days, because a rapid fall in NSE concentration may be observed 24-72 hours after the initial therapy session in therapy responders[9, 6, 10].

NSE in neuroblastoma

Recommendations as tumour marker for diagnosis and follow-up

Neuroblastoma is the second most frequent malignant cancer among children. Neuroblastomas arise from degenerated cells of the autonomic nervous system and can occur along nerves in the entire human body. The use of NSE as a tumour marker is recommended in the interdisciplinary guideline of the German Cancer Society and the Society for Paediatric Oncology and Haematology[11], since increased serum concentrations of NSE indicate higher probability of the presence of a neuroblastoma. Early neuroblastoma detection is of paramount importance to attain a more benign course of the disease and favorable prognosis. Studies by Zeltzer[12] and Masseron[1] among others seem to indicate that serum values above 30 µg/L are associated with extremely unfavorable prognosis and are especially found in stage III and IV patients. Diagnostic sensitivity on neuroblastoma is 62%[13].

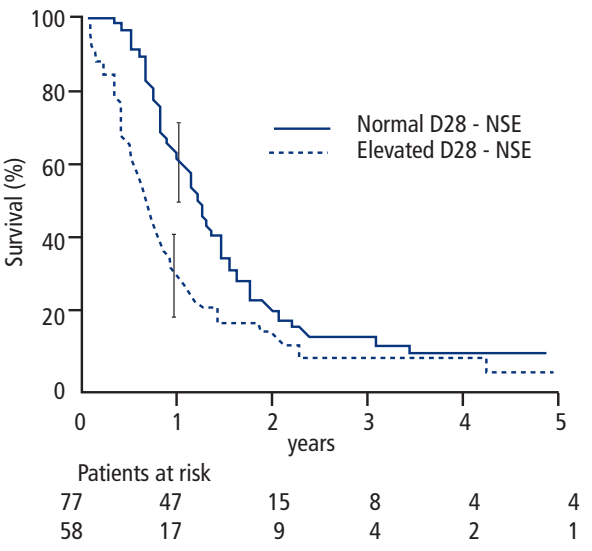
Fig. 1



Pretreatment serum concentrations and mean value (x ± SE) of NSE in patients with SCLC (I), non-SCLC (II), and begin pulmonary diseases (BPD) (III). • Limited disease; • extensive disease; • extensive disease and diffuse metastatic spread

Fischbach et al. *Cancer* 1989

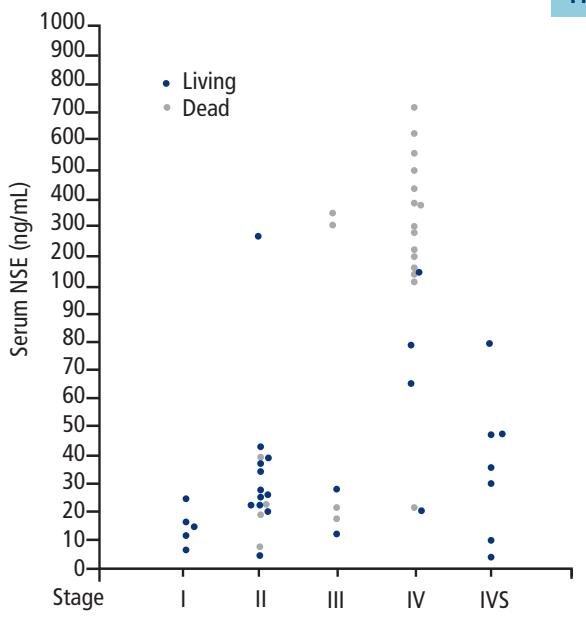
Fig. 2



Overall survival of patients with small cell lung carcinoma is shown, according to the serum neuron specific enolase value measured on Day 28 after chemotherapy (D28-NSE)

Fizazi et al. *Cancer* 1998

Fig. 3



Serum NSE levels at diagnosis by stage in 54 patients with 2 or more years of follow-up with life status (survival). Disease-free survival was 79% (27/34) below and 10% (2/20) above the level of 100 ng/mL which was used to calculate the prognostic value of the test

Zeltzer et al. *Cancer* 1986

NSE in APUDomas and seminomas

Improved correlation with clinical course

APUD-cells originate from the neural crest and are cells which take up amines and are capable of decarboxylation. APUDomas form several tumours of different origin in the human body. These tumours are mostly of neuroendocrine origin, show a relatively slow growth and synthesize NSE in large amounts in serum.

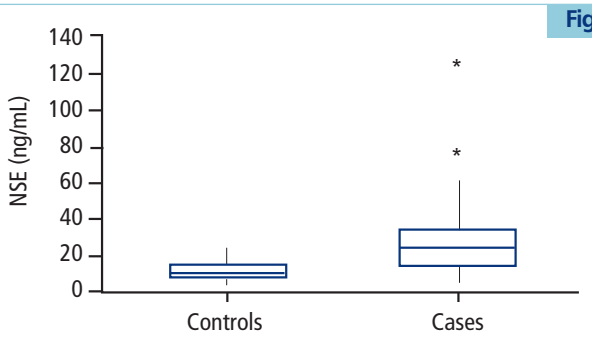
Diagnostic sensitivity on APUDomas is 34%[14].
Germ-cell tumours are the commonest tumours among men in the age group of 20 to 40 years. They represent overall 1% of all neoplasms with increasing incidence in the last 40 years[15]. About 40-60% of seminomas are considered as the most frequent germ-cell tumours. NSE determination is of help in metastatic seminomas, although AFP and β-hCG are usually recommended as tumour markers, because increased NSE concentration is found among 68-73% of patients[16, 17].

NSE in neurological impairment

Identification and prognosis of traumatic brain injury

Due to high tissue specificity of γ-enolase, brain injury can be identified by the enzyme release in the cerebrospinal fluid or blood. In particular, studies in children[18, 19, 20] as well as adults[21, 22] seem to indicate that increased NSE in serum or cerebrospinal fluid can lead to improved diagnostic and prognostic evaluation of the clinical course of the disease.

Fig. 4



Box plots showing distribution of biomarker concentrations in controls versus cases with and without ICH. The horizontal line in each box represents the median concentrations. Asterisks represent outliers. NSE; p, 0.001 between groups

Berger et al. J *Neurosurg* 2005

Summary

- NSE differentiates between benign and malignant disease and shows disease progression in small-cell bronchial carcinoma.
- Decreased NSE concentrations are generally indicative of successful treatment. If NSE concentrations are unaltered or increased, treatment strategy must be changed.
- NSE is a valuable diagnostic marker for neuroblastoma.
- Increased NSE concentrations for APUDomas and seminomas indicate metastatic disease.