Characterization of Tumor-associated Neural Cell Adhesion Molecule in Human Serum

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ABSTRACT

In human serum, at least two molecular species of the neural cell adhesion molecule (NCAM) with molecular weights of 110,000—130,000 and 150,000—180,000, respectively, can be identified by Western blotting. Both are characterized by the absence of epitopes for monoclonal antibodies KD11 and MG5, which specifically recognize intracellular domains of the human NCAM transmembrane isoforms, NCAM-140 and NCAM-180. In contrast to the Mr. 110,000—130,000 molecule also detectable in serum samples from healthy blood donors, the Mr. 150,000—180,000 molecule can no longer be discriminated from the Mr. 110,000—130,000 molecule in Western blotting as well as gel and anion exchange chromatography experiments. The experimental data clearly show that only the embryonic NCAM molecule carrying the poly-α-(2,8)-linked N-acetyleneuraminic acid moiety can be regarded as a specific serum marker for small cell lung cancer.

INTRODUCTION

Lung cancer is currently one of the most prevalent malignant tumors affecting adults and ranks a high position as the cause of cancer-related death in many countries (1). This tumor expresses a wide variety of phenotypes. According to histological criteria and from a clinical point of view, lung cancer is classified into two major groups: SCLC and NSCLC. SCLC accounts for about 20—25% of all lung cancer cases and is characterized by the presence of neurosecretory granules and neuroendocrine differentiation markers. It has an especially poor prognosis due to early and widespread metastatic processes, but it is sensitive to initial chemotherapy and radiation. In contrast, the principal therapy of NSCLC is mainly resection of tumors. A tumor marker which can help to distinguish between NSCLC and SCLC is therefore of utmost clinical importance.

Neuron-specific enolase, an isoenzyme of enolase (EC 4.2.1.11), is known as the most specific tumor marker in SCLC up to now (2). However, false positive results are often obtained from hemolytic specimens because RBC and thrombocytes contain neuron-specific enolase in large amounts (3).

NCAM has also been noted to be a sensitive and relatively specific immunohistochemical SCLC marker (4, 5). As a member of the immunoglobulin superfamily (6), NCAM is normally involved in neuron-neuron as well as nerve-muscle cell interaction. NCAM is a cell surface glycoprotein consisting of a single polypeptide chain. By differential splicing, the use of alternative polyadenylation sites and developmentally regulated posttranslational modifications, a considerable heterogeneity with respect to protein and carbohydrate structure is produced (7). Three major isoforms having almost identical amino-terminal extracellular domains are known: a GPI-anchored form (NCAM-120) (8), an isoform with a smaller cytoplasmic domain (NCAM-140), and one with a larger cytoplasmic domain (NCAM-180) (9). In addition, soluble isoforms of NCAM have been described (10—12). Furthermore, a so-called "embryonic" form (eNCAM) with long chains of PSA added to one or more of the N-glycosylation sites in immunoglobulin-like domain 5 can be differentiated from a so-called "adult" form (aNCAM) whose PSA content is drastically reduced (30% in eNCAM to 10% in aNCAM) (13). The PSA chains of eNCAM are specifically recognized by Mab 735 (14). This epitope is lacking on aNCAM, indicating that PSA chains with polymerization degree >8—9 are not expressed on aNCAM (15). PSA, mainly found on NCAM in fetal brain tissue, influences not only homophilic binding properties of NCAM itself but also bindings of other intercellular adhesion molecules (16).

In a recent study, we presented data about the usefulness of measuring NCAM in serum as a tumor marker in SCLC (17). A good correlation between the serum NCAM concentration and the corresponding clinical status in follow-ups of SCLC patients has been found. Until now, however, only a small amount of information about the structure of the protein found in human serum has been available. Therefore, this study was aimed to investigate tumor-associated NCAM in serum samples in greater detail.

MATERIALS AND METHODS

Serum Specimens. The serum specimens from healthy blood donors and those obtained preoperatively from SCLC patients were immediately frozen and stored at −20°C. The diagnosis of SCLC was histologically confirmed in all cases. The NCAM concentration in sera from all SCLC patients (nine males and one female, all at extensive stage) was highly increased (512—2368 units/ml measured with eNCAM CIA, described below).

Mabs. Mab 735 (IgG2a, Behringwerke AG) binds specifically to PSA (14, 18).

Murine Mabs BW SCLC-1 and BW SCLC-2 were established against human serum cell lines G0T and MR22 by Dr. Boßlet, Behringwerke AG. The epitopes of these Mabs have been recently identified to be on the extracellular part of NCAM. All these Mabs were purified from hybridoma culture supernatant by protein A-Sepharose column chromatography.

Mab KD11 recognizes the carboxy terminus of the transmembrane isoforms NCAM-180 and NCAM-140, and the epitope of Mab MG5 is encoded by exon 18. Mab 123C3 was generated by Dr. Rob Michalides (the Netherlands Cancer Institute, Amsterdam, the Netherlands) against a membrane fraction of a SCLC autopsy specimen (19), and it recognizes an epitope within the extracellular part of NCAM. Mabs ERIC-1 and MOC-1, which bind also to NCAM, were purchased from Cambridge Research Biochemicals Ltd. (Cheshire, United Kingdom) and MCA Development B.V. (Groningen, the Netherlands).
Netherlands), respectively. Anti-α-fetoprotein, Mab 128 (Behringwerke AG), was used for control purposes. All these Mabs except Mab 735 belong to the IgG1 subclass. Biotin-labeled goat anti-mouse IgG1 and rabbit anti-mouse IgG Fc were bought from Southern Biotechnology Associates, Inc. (Birmingham, AL) and Jackson Immuno Research (West Grove, PA), respectively.

**NCAM Preparations.** NCAM was purified from the culture supernatant of a SCIL cell line, SCIL-SF1, by gel chromatography (Sepharose CL-6B; Pharmacia, Uppsala, Sweden) and was stored at −20°C as NCAM(BW). Some preparations were diluted before storage with pooled human serum in which IgG Fc were bought from Southern Biotechnology Associates, Inc. (Binningham, AL) and Jackson Immuno Research (West Grove, PA), respectively.

Anti-a-fetoprotein, Mab 128 (Behringwerke AG), preparations were diluted before storage with pooled human serum in which IgG Fc were bought from Southern Biotechnology Associates, Inc. (Binningham, AL) and Jackson Immuno Research (West Grove, PA), respectively.

NCAM was removed and stored at −70°C as “soluble” NCAM extract, possibly still containing some membrane-bound proteins. The pellet was resuspended in the same buffer and centrifuged for 20 min. After resuspension of the pellet with extract buffer containing 1% Nonidet P-40 and 0.1% NaN₃ and stirring for 30 min at 4°C, it was again centrifuged (20 min at 4°C and 38,000 × g); the resulting supernatant was stored at −70°C as “crude NCAM extract.”

**Endo neuraminidase Treatment.** Endo N derived from phage K1 specifically cleaves PSA with polymerization degree >8–9 (21). The purification of this enzyme has been described elsewhere (22). Endo N (150 microunits/ml) was incubated with NCAM at 37°C for 30 min. The Endo N treatment was stopped by addition of Endo N inhibitor at a final concentration of 0.1%.

**Immunossays.** For the immunochemical reactivity of NCAM was completely destroyed by heat treatment. After washing with phosphate buffer (pH 7.2), 200 μl of sample or standard were incubated for 1 h at 37°C in the wells of microwell plates previously coated with BW SCLC-1. After washing, 100 μl of BW SCLC-2 conjugated to HRPO were filled into each well and incubated for 1 h at 37°C. The bound enzymatic activity was then determined as described above.

**SDS-PAGE and Immunoblotting.** Serum samples were usually preincubated 1:5 or 1:10, respectively, with PBS. Then, samples were kept at 65°C for 10 min with the same volume of 12.5 mM Tris buffer containing 35 mM sodium dodecyl sulfate, 0.08 mM EDTA, and 32.4 mM 1,4-dithiothreitol. For silver staining, sample buffer without 1,4-dithiothreitol was used. Electrophoresis was then performed on SDS-containing polyacrylamide gels (PhastGel, gradient 4–15; Pharmacia, Uppsala, Sweden) at 12°C and 250 V using a PhastSystem (Pharmacia). After separation, the gel was immediately silver stained with PhastGel silver kit (Pharmacia) according to the modified method of Heukeshoven and Dernick (23) recommended by the manufacturer.

**Western blotting experiments, separated proteins were transferred to nitrocellulose membranes (0.2 μm, Pierce, Rockford, IL) in Tris/glycine buffer (2.5 mM Tris, 192 mM glycine, and 20% methanol) at 15°C and 25 mA using a semi-dry transfer method on Phast Transfer (Pharmacia). Non-specific binding sites were blocked for 1 h at room temperature in 20 mM Tris buffer containing 137 mM NaCl and 0.1% Tween 20 (pH 7.6; TBS-T) with 5% bovine serum albumin. After washing with TBS-T, immunostaining was then performed with preformed Mab 735 (1 μg/ml in TBS-T for 2 h at room temperature), Mab 123C3, or ERIC-i (approximately 0.5–1 μg/ml in TBS-T for 2 h at room temperature), followed by an incubation step with biotinylated goat anti-mouse IgG1 (0.03 μg/ml in TBS-T for 1 h at room temperature). Then, after washing with TBS-T, the membrane was incubated with 60 ng/ml of streptavidin conjugated to HRPO for 30 min at room temperature. An enhanced chemiluminescence detection system (ECL, Amersham, Buckinghamshire, United Kingdom) was used. For molecular weight determination, ECL protein molecular weight markers (GIBCO BRL, Gaithersburg, MD) were used.

**Gel Filtration Chromatography.** Samples were diluted 1:1.5 with PBS (pH 7.2) and centrifuged for 3 min at 900 × g before application; 200 μl of sample were applied to a prepacked column (Superose 6 HR/10; Pharmacia). A high performance liquid chromatography system (Merck/TOSHIBA D-6000) was run with a flow rate 0.5 ml/min of PBS containing 350 mM NaCl, 1 mM EDTA, and 0.05% NaN₃ (pH 7.2). Fractions were collected every 1 min for 60 min and analyzed by using the immunossays described above. If a concentration step was needed, fractions were concentrated about 20-fold with Centricon 10 centrifugal microconcentrators (M, 10,000 molecular weight cutoff; Amicon, Danvers, MA). Every two runs, the column was calibrated with aldolase (M, 158,000), catalase (M, 232,000), ferritin (M, 440,000), and thyroglobulin (M, 669,000) (Gel filtration calibration kit; Pharmacia).

**Anion Exchange Chromatography.** For anion exchange chromatography, a Mono Q column (Mono Q HR/5; Pharmacia) was used. The running buffer was 20 mM HEPES buffer (pH 7.0; flow rate, 0.4 ml/min). A gel filtration (Sephadex G-25M column; Pharmacia) or a dialysis step (overnight at 4°C followed by a centrifugation for 3 min at 2500 × g) with 20 mM HEPES (pH 7.0) was performed before 500 or 200 μl of samples, respectively, were applied to the column. A linear gradient of high ionic strength buffer, 20 mM HEPES containing 1 mM NaCl, (pH 7.0), was started at 10 min after sample application and ended after 60 min. Fractions were collected every min for 70 min and immediately analyzed with the immunossay or immunoblotting methods described above.

**Western Blotting.** For Western blotting experiments, separated proteins were transferred to nitrocellulose membranes (0.2 μm, Pierce, Rockford, IL) in Tris/glycine buffer (2.5 mM Tris, 192 mM glycine, and 20% methanol) at 15°C and 25 mA using a semi-dry transfer method on Phast Transfer (Pharmacia). Non-specific binding sites were blocked for 1 h at room temperature in 20 mM Tris buffer containing 137 mM NaCl and 0.1% Tween 20 (pH 7.6; TBS-T) with 5% bovine serum albumin. After washing with TBS-T, immunostaining was then performed with preformed Mab 735 (1 μg/ml in TBS-T for 2 h at room temperature), Mab 123C3, or ERIC-i (approximately 0.5–1 μg/ml in TBS-T for 2 h at room temperature), followed by an incubation step with biotinylated goat anti-mouse IgG1 (0.03 μg/ml in TBS-T for 1 h at room temperature). Then, after washing with TBS-T, the membrane was incubated with 60 ng/ml of streptavidin conjugated to HRPO for 30 min at room temperature. An enhanced chemiluminescence detection system (ECL, Amersham, Buckinghamshire, United Kingdom) was used. For molecular weight determination, ECL protein molecular weight markers (GIBCO BRL, Gaithersburg, MD) were used. For molecular weight determination, ECL protein molecular weight markers (GIBCO BRL, Gaithersburg, MD) were used.

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RESULTS

Western Blotting. For molecular weight determination, six serum specimens from SCLC patients (tumor sera) and six samples from healthy blood donors (normal sera) were examined by immunoblotting with Mab 735. None of the normal sera showed any activity (Fig. 1A). In contrast, all blots of tumor sera exhibited a relatively broad band representing a protein with a molecular weight of 150,000–180,000. This band could not be found in samples treated with Endo N (Fig. 1B).

Two bands, one at \( M_r = 110,000–130,000 \) and a second at \( M_r = 145,000–185,000 \), were detected in Western blots with Mabs 123C3 (Fig. 2) and ERIC-i (data not shown). After Endo N treatment, the upper band disappeared, and a relatively higher signal of the lower band was obtained. Normal sera showed only one faint band at \( M_r = 110,000–130,000 \).

Epitopes on Different NCAM Preparations. To evaluate the epitopes on the embryonic NCAM form, Mab 735 specifically binding to long chains of PSA was used as capture antibody in the eNCAM ELISA. No eNCAM could be found in normal sera. In specimens from SCLC patients, however, NCAM isoforms expressing the epitopes of Mabs 735, BW SCLC-i, BW SCLC-2, 123C3, and MOC-1, but not those of Mabs KD11 and MG5, were identified (Fig. 3A).

Concerning tumor sera, similar results were obtained with a second assay system, the e/aNCAM ELISA, which allows the additional detection of aNCAM (Fig. 3B). Normal sera also contained molecules which were recognized by BW SCLC-1, BW SCLC-2, MOC-1, and 123C3, but not by Mab 735, KD11, and MG5.

For control purposes, NCAM(BW), “soluble” and “crude” extract from human brain and crude extract of cultured cells (TE 671), were investigated by using the same immunoassays (Fig. 3; Table 1). In crude extract from human brain, NCAM isoforms existed with epitopes for all Mabs including KD11 and MG5. Mab KD11 also
bound to NCAM from cell line TE 671. In contrast, NCAM(BW) and soluble NCAM from human brain showed a similar epitope distribution as the tumor-associated NCAM from serum specimens, no epitopes for KD11 and MG5.

**Chromatography.** Six tumor sera, three normal sera, and two different NCAM(BW) preparations (diluted in heated human serum) were subjected to gel filtration chromatography to evaluate the relationship between molecular size and epitope distribution (Fig. 4A). NCAM from tumor sera detected by eNCAM CIA was found in fractions Fr.24—29 (314—715 kDa) with a main peak at Fr.25 (582—645 kDa). Using the NCAMpep assay, one relatively broad peak around Fr.28 (408—473 kDa) was observed. Identical results were obtained with NCAM(BW). For comparison, human IgG was eluted at Fr.30—31.

Two tumor sera were further examined after Endo N treatment. The complete digestion of PSA by Endo N was confirmed because no activity could be measured with eNCAM CIA any more. With NCAMpep ELISA, a higher and sharper peak could be now detected around Fr.28. In normal serum, no activity was found using the eNCAM CIA, and the concentration of NCAM measurable with the NCAMpep ELISA was also very low. Therefore, pools of every six fractions were prepared and concentrated about 20-fold. The activity was mainly detected in the fifth pool (Fr.25—30). Then each single fraction from Fr.25 to Fr.36 was concentrated under the same conditions. The highest activity was detected in Fr.28.

Better separation of NCAM isoforms and IgG was obtained with anion exchange chromatography using the Mono Q column. Three tumor sera, three normal sera, and three different NCAM(BW) preparations were examined. IgG and human serum albumin were eluted in Fr.3—5 and Fr.35—36, respectively.

As shown in Fig. 4B, NCAM eluted between Fr.43 and 51 (640—800 mM NaCl). For all tumor sera and NCAM(BW), two peaks (Fr.44—45 and Fr.49, corresponding to 660—680 mM and 760 mM NaCl) were detected with NCAMpep ELISA. The second peak was in the identical fraction as the only peak found by eNCAM CIA. After Endo N treatment, this peak disappeared in both assay systems, and the first peak around Fr.45 showed a higher activity. In normal serum, NCAM was only found around Fr.45 using NCAMpep ELISA.

![Fig. 4. A, gel filtration of human serum specimens on Superose 6 column. After centrifugation, the samples were applied to the column and eluted with PBS containing 350 mM NaCl (pH 7.2). B, anion exchange chromatography of human serum samples on a Mono Q column. The specimens were applied to the column after buffer exchange into running buffer, 20 mM HEPES (pH 7.0) by Sephadex G-25M filtration or dialysis overnight. Endo N treatment was performed for 2 h at 37°C (A) or overnight at 4°C during dialysis (B). NCAM concentration was measured both using eNCAM CIA for specific determination of the embryonic form and NCAMpep ELISA for detecting eNCAM and aNCAM. NS, serum from healthy blood donor; SCLC, serum from SCLC patient.](#)
DISCUSSION

NCAM is one of the best known intercellular adhesion molecules. The expression of this glycoprotein, as studied by immunohistochemical as well as Western blotting techniques, occurs not only in neural but also in tumor tissues or in some cell lines derived from neuroectodermal malignancies (24–27). NCAM is normally found as a surface antigen, but increased NCAM concentrations have also been recently described in sera from SCLC patients (17). This indicates NCAM is a potential serum tumor marker in SCLC. The aim of this study was to characterize the tumor-associated NCAM molecule from serum specimens.

Two molecular forms of NCAM were found in sera from SCLC patients by Western blotting. After Endo N treatment, the Mr 150,000–180,000 band recognized by Mabs 735, 123C3, and ERIC-1 disappeared, and the Mr 110,000–130,000 band, only detectable with the Mabs 123C3, and ERIC-1, became more intensively stained. The differences in migration of the two molecules found in serum specimens on SDS-PAGE and the fact that only the higher-molecular-weight form was recognized by Mab 735 indicate that these two molecular forms differ at least by the presence of PSA. From the estimated molecular weight of Mr 110,000–130,000, serum NCAM is suspected to be an isoform without intracellular domain. This hypothesis is further supported by the lack of reactivity with Mabs KD11 and MG5, which recognize epitopes on the intracellular domain. Our current data do not allow us to differentiate between the GPI-linked isoform (Mr 120,000–125,000) or a secreted isoform (Mr 110,000–115,000). Preliminary experiments did not show an elevation of NCAM concentration in supernatants of cultured SCLC SF1 cells after treatment with phosphatidylinositol phospholipase C (data not shown). We are speculating that these cells do not express GPI-linked NCAM. Only one tumor serum (Fig. 2; SCLC 1341) showed two bands in the range of Mr 110,000–130,000, one prominent band (Mr 110,000–125,000) and an additional faint band (Mr 125,000–130,000). These two bands may represent two different isoforms or possibly are the result of a technical artifact.

NCAM with a molecular weight of 110,000–130,000 can also be detected in serum from healthy blood donors. This NCAM species did not react with the Mabs KD11 and MG5, indicating the absence of the intracellular domain. In addition, this molecule was not recognized by Mab 735, neither in Western blots nor in ELISA, which indicates the absence of PSA. Krog et al. (12) reported that only Mr 110,000 and Mr 115,000 isoforms of NCAM could be found in rat plasma and that these NCAM isoforms were not recognized by Mab OB11, which is believed to bind to an intracellular domain common to the transmembrane molecules.

Hirano et al. (28) evaluated sera from SCLC patients with a sandwich radioimmunoassay using Mabs which bind to cluster 1 antigens. In contrast to our findings (17), they concluded that cluster 1 antigen, which has been recently identified as NCAM (29), was not useful as a serum SCLC marker. The most distinctive feature of tumor-associated NCAM in serum, however, is not so much the increase of total NCAM concentration as the appearance of polysialylated eNCAM. Therefore, an immunoadsays detecting tumor-associated NCAM should be specific for the so-called PSA-rich embryonic NCAM molecule.

For control purposes, several other NCAM preparations were also investigated. In crude extract from human brain and some other animal species, NCAM isoforms exhibiting epitopes for KD11 and MG5 were found. On the contrary, the soluble isoform from adult human brain appears to be similar to both NCAM from SCLC patients and healthy blood donors with respect to KD11 and MG5 epitopes. NCAM(BW), which we used as calibrator material for quantitative measurements, showed almost identical characteristics as tumor-associated PSA-rich serum NCAM derived from SCLC patients.

For determination of NCAM serum concentration, we established two immunoenzymes, eNCAM CIA and NCAMpep ELISA. Using NCAMpep ELISA, all human NCAM isoforms are detected because both BW SCLC-1 and BW SCLC-2 recognize peptide epitopes on the extracellular domain of NCAM. In contrast, when eNCAM CIA was used, only the embryonic NCAM forms could be measured. The results obtained by gel chromatography as well as anion exchange chromatography confirmed that NCAM can be found in at least two molecular forms in serum samples from SCLC patients, the Mab 735-reactive molecule with long chains of PSA and a second form without PSA. After Endo N treatment, the peak corresponding to polysialylated NCAM disappeared, and the peak representing NCAM without PSA increased in both chromatographic separation techniques. As shown in the Western blotting experiments, the only difference between the two NCAM specimens in serum appears to be the presence or absence of PSA.

The molecular weight of about Mr 400,000–600,000 estimated by gel chromatography can be interpreted by the formation of dimers, because NCAM has homophilic binding properties. This was also reported by Krog et al. (12). These authors showed that purified soluble NCAM from rat brain formed dimers. Elution behavior on Superose 6 does not correspond to molecular weight but to molecular size. PSA residues represent large hydrated regions leading to an increased volume. This might also be a reason for the discrepancies in molecular weight estimations of NCAM by gel chromatography in comparison to SDS-PAGE.

Furthermore, PSA is said to play an important biological role. Although the homophilic binding site appears to be on the third immunoglobulin-like domain (30), PSA chains which are located on the fifth immunoglobulin-like domain affect the binding ability of NCAM (13). The highly sialylated NCAM molecule exhibits reduced adhesive properties, whereas the less sialylated NCAM promotes adhesion (16). Therefore, NCAM without PSA presumably binds to the same molecular structure more rapid than to the polysialylated NCAM. This appears to be the reason that after Mono Q chromatography, only two, not three, peaks were detected with NCAMpep ELISA. Characteristic features of tumor cells are invasion and metastatic growth. Cells may control their binding properties by changing the length of N-acetylgaluraminic acid chains. An increased production of polysialylated NCAM may lead to a reduced fixation of cells so that more tumor cells can be released into vascular or lymphatic circulations. Our recent data showed a good correlation between the serum NCAM concentration and the corresponding clinical status of SCLC patients (17). From this point of view, the detection of NCAM in serum, especially the embryonic form of NCAM, might be of prognostic relevance.

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REFERENCES


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