GFA Protein Reactivity in Nerve Sheath Tumors:
A Polyvalent and Monoclonal Antibody Study

CONSTANCE STANTON, M.D., ELIAS PERENTES, M.D.,
V. PETER COLLINS, M.D., AND LUCIEN J. RUBINSTEIN, M.D.

Abstract. We studied glial fibrillary acidic (GFA) protein immunoreactivity in 30 schwannomas, including two intracerebral examples, 26 neurofibromas and 12 neuromas using the immunoperoxidase method with a polyvalent antiserum (PVAS) and three well-characterized monoclonal antibody (MAB) preparations. Twelve of the schwannomas, including both intracerebral tumors, two of the neurofibromas and none of the neuromas immunostained with PVAS. Except for one schwannoma, all the PVAS-positive tumors were positive with two of the MAB preparations. While both of the intracerebral schwannomas were positive with the third MAB, none of the extracerebral tumors were. Our results suggest that: 1) human nerve sheath tumors contain cells having polypeptides that share epitopes with GFA protein, but 2) these polypeptides differ from astrocytic GFA protein by at least one epitope, and 3) the location of the tumors in relation to the central nervous system may influence GFA protein immunoreactivity.

Key Words: Glial fibrillary acidic protein; Immunohistochemistry; Monoclonal antibodies; Neurofibroma; Neuraoma; Schwannoma.

INTRODUCTION

Glial fibrillary acidic (GFA) protein is the major component of glial cytoplasmic intermediate filaments (1), and its intracellular demonstration has been accepted as characteristic of astroglial histogenesis or differentiation (2–4). However, immunoreactivity to polyvalent GFA protein antisera has also been reported in several cell types outside the central nervous system (CNS). These include non-myelin forming Schwann cells in rat and human peripheral and enteric autonomic nerves (5–8) and in autonomic nerves of rodent, feline and bovine iris (9), enteric glial cells of the rat (10), satellite cells of rat sensory and sympathetic ganglia (5), epithelial cells of mouse crystalline lens (11), Kupffer cells of rat liver (12), cartilage cells of human epiglottis (13), folliculostellate cells of normal and neoplastic human adenohypophysis (14), normal epithelial and neoplastic cells of human salivary glands (8, 15), and neoplastic cells of human peripheral nerve sheath tumors (16–18).

Some of these studies have shown that the antigen(s) recognized by the antisera share properties with astrocytic GFA protein, namely, similar molecular weight by immunoblotting (5, 6, 8, 11, 18). Others have failed to demonstrate the presence of proteins having the biochemical properties of GFA protein and have concluded that the immunoreactivity represented nonspecific crossreactivity with other filamentous

From the Division of Neuropathology, Department of Pathology, University of Virginia School of Medicine, Charlottesville, Virginia (CS, EP, LJ) and the Ludwig Institute for Cancer Research, Stockholm, Sweden (VPC).

Correspondence to: L. J. Rubinstein, M.D., Division of Neuropathology, Department of Pathology, University of Virginia School of Medicine, Charlottesville, VA 22908.

Supported by Neuropathology Training Grant T32 NS7236 from the N.I.N.C.D.S., U.S.D.H.S., by American Cancer Society Clinical Fellowship 86-276 (CS), by a grant from the Fondation Suisse de Bourses de Médecine et Biologie (EP), and by Research Grant CA 31271 from the N.C.I., U.S.D.H.S. (LJR).
proteins or non-immune binding (7, 8, 19). In regard to monoclonal antibodies (MAb), crossreactivity due to epitopes shared by different tissue types (20) or different classes of intermediate filaments (21), and nonspecific binding of non-immune immunoglobulins (22, 23) have become increasingly documented. The problem of the immunoreactivity demonstrated in unexpected cell types with polyvalent antisera is, however, amenable to more precise elucidation when it is compared with that obtained with well-characterized MAb.

Gould et al (18) have recently reported that two human nerve sheath tumors (NST) demonstrating GFA protein immunoreactivity with polyvalent antisera also showed immunoreactivity with MAb. Using a different set of MAb we compared the GFA protein immunoreactivity demonstrable with a polyvalent antiserum in human NST with that obtained with these MAb in 30 schwannomas (two of which were intracerebral), 26 neurofibromas, and 12 neuromas. We present evidence that while some human NST contain protein(s) sharing epitopes with GFA protein, these proteins may differ from astrocytic GFA protein by at least one epitope and that the location of the tumor in relation to the CNS may influence immunoreactivity.

MATERIALS AND METHODS

Material was obtained from 30 schwannomas (15 from the acoustic nerve, 11 from spinal nerve roots or peripheral nerves, 1 subcutaneous, 1 from theellar area, and 2 intracerebral schwannomas), 26 neurofibromas (22 cutaneous, 3 from spinal nerve roots or peripheral nerves, 1 from the acoustic nerve), and 12 neuromas (9 traumatic, 3 Morton's). Theellar schwanna, previously reported by Goebel et al (24), the two intracerebral schwannomas and one peripheral nerve schwannoma originated from the case referral collection of one of us (LJR). The rest of the material was obtained from the Department of Pathology at the University of Virginia School of Medicine. One schwannoma was obtained at autopsy; the remainder were surgical specimens.

All specimens were formalin-fixed, paraffin-embedded, and sectioned at 5–6 micrometers (μm). The storage time of the material ranged from weeks to years and had no effect on the immunoreactivity.

Four anti-GFA protein antibody preparations were used: a) polyvalent rabbit antiserum (to be called henceforth PVAS), courtesy of Dr. L. F. Eng, Stanford University, Stanford, California; b) a “cocktail” of three mouse IgG2b-kappa MAb (2E1E9, 1B4D9, 4A11), courtesy of Dr. D. D. Bigner, Duke University, Durham, North Carolina (25, 26); c) 2E1E9 (one of the MAb in the “cocktail”) (26), also courtesy of Dr. D. D. Bigner; d) C9, a mouse IgG1-kappa MAb prepared by one of us (VPC) (27).

All sections were deparaffinized in xylene for ten minutes (min). Sections studied with the C9 MAb were delipidized in chloroform for 24 hours before proceeding with the next step, as this was noted to improve the immunoreactivity. Pretreatment with trypsin did not improve reactivity with any of the antibodies and was not routinely performed. Following rehydration in graded methanols (C9 MAb) or ethanol (all others) to water and blockage of endogenous peroxidase activity with hydrogen peroxide (0.5% in methanol for 30 min) immunohistochemical staining was performed using the peroxidase–antiperoxidase (PAP) method of Sternberger et al (28). For the PVAS, a three-step reaction was carried out with all reagents diluted in 0.05 M Tris buffered saline (pH 7.6) containing 1% normal goat serum. For the MAb a four-step reaction was used with reagents diluted in 0.05 M Tris buffered saline (pH 7.6) containing 1% normal swine serum. Before application of the primary antibody all sections were saturated in 10% normal serum for ten min (goat) or 15 min (swine). The sections were incubated overnight at 4°C with the primary antibodies used at the following dilutions; a) PVAS (1:1,400), b) “cocktail” (12.5 μg/ml = total of all three MAb), c) 2E1E9 (12.6 μg/ml), d) C9 (1:25). Linking antibodies were goat anti-rabbit immunoglobulins (Cooper Biomedical, Malvern, PA) (1:50) for ten min following PVAS, or rabbit anti-mouse immunoglobulins (Dako, Santa Barbara, CA) followed by swine anti-rabbit immunoglobulins (Dako) for 15

### TABLE 1
GFA Protein Immunoreactivity in Nerve Sheath Tumors

<table>
<thead>
<tr>
<th>Location</th>
<th>PVAS</th>
<th>Monoclonal antibody “cocktail”</th>
<th>2E1E9</th>
<th>C9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schwannomas</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 18</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acoustic (9)</td>
<td></td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Spinal root*/peripheral nerve (7)</td>
<td></td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Sellar† (1)</td>
<td></td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Subcutaneous (1)</td>
<td></td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acoustic</td>
<td></td>
<td>+</td>
<td>+‡</td>
<td>+§</td>
</tr>
<tr>
<td>Acoustic‖</td>
<td></td>
<td>+</td>
<td>+‡</td>
<td>+§</td>
</tr>
<tr>
<td>Acoustic</td>
<td></td>
<td>+ QNS</td>
<td>QNS</td>
<td>-</td>
</tr>
<tr>
<td>Acoustic</td>
<td></td>
<td>+ QNS</td>
<td>QNS</td>
<td>-</td>
</tr>
<tr>
<td>Acoustic</td>
<td></td>
<td>+</td>
<td>+‡</td>
<td>+§</td>
</tr>
<tr>
<td>Acoustic</td>
<td></td>
<td>+</td>
<td>+‡</td>
<td>+§</td>
</tr>
<tr>
<td>Spinal root</td>
<td></td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Spinal root‖</td>
<td></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Spinal root‖</td>
<td></td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Spinal root</td>
<td></td>
<td>+</td>
<td>+‡</td>
<td>+</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td></td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td></td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

| **Neurofibromas** |      |                                 |       |    |
| N = 26            |      |                                 |       |    |
| Negative          |      |                                 |       |    |
| N = 24            |      |                                 |       |    |
| Cutaneous (22)‖    |      | -                               | NT    | NT |
| Spinal (1)        |      | -                               | NT    | NT |
| Acoustic (1)      |      | -                               | NT    | NT |
| Positive          |      |                                 |       |    |
| N = 2             |      |                                 |       |    |
| Spinal root‖      |      | ++                              | ++    | +  |
| Spinal root‖      |      | +                               | +     | -  |

| **Neuromas**      |      |                                 |       |    |
| N = 12            |      |                                 |       |    |
| Negative          |      |                                 |       |    |
| N = 12            |      |                                 |       |    |
| -                  |      | NT                              | NT    | NT |

—, no reaction; +, isolated positive cells; ++, small areas containing several positive cells; ++++, large areas where most cells were positive. NT, not tested; QNS, insufficient tissue.

* Two of these tumors are from one patient with neurofibromatosis—a spinal root tumor and a recurrence at the same level.
† Case reported by Goebel et al (24).
‡ Fewer cells positive than with PVAS.
§ Fewer cells positive than with "cocktail."
‖ All three tumors from one patient with neurofibromatosis; the second spinal root tumor is a recurrence.
¶ One patient with neurofibromatosis with three negative large cutaneous neurofibromas and one positive spinal tumor.

min each after the MAb. Dilutions of 1:15 were used following C9 and 1:50 following the other MAb. Rabbit PAP complex (Dako) was applied for 20 min at 1:100 for C9 and 1:200 for the others. Reactions were developed in freshly-prepared 3,3'-diaminobenzidine tetra-hydrochloride (Sigma), 5.0 mg in 6.5 ml of 0.05 M Tris buffered saline (pH 7.6) containing 0.015% hydrogen peroxide, and counterstained with Harris's hematoxylin. All steps following the primary antibody were performed at room temperature.

All material was studied first with the PVAS. Only those cases which were positive were

*J Neuropathol Exp Neurol, Vol 46, November, 1987*
evaluated further with MAb. Each positive case was studied with each MAb, except for two schwannomas for which this was not possible due to limited availability of tissue: these were studied with the PVAS and the C9 MAb only.

As positive controls autopsy and surgical specimens of reactive and neoplastic astrocytic tissue were used. As negative controls, normal rabbit serum, mouse myeloma nonspecific IgG2b-kappa immunoglobulins (courtesy of Dr. D. D. Bigner), and mouse myeloma non-specific IgG1-kappa immunoglobulins (Sigma, St. Louis, MO) were substituted for the PVAS, the “cocktail” and the 2E1E9 MAb, and the C9 MAb, respectively. Controls were run in parallel with test slides.

RESULTS

The results are summarized in Table 1.

In the positive control cases PVAS produced a reliable intense staining of reactive and neoplastic astrocytes. Twelve of 30 schwannomas were PVAS-positive: 6/15 acoustic, 4/11 spinal nerve root or peripheral nerve tumors, and both intracerebral schwannomas. The subcutaneous and sellar area schwannomas were negative. Two of 26 neurofibromas (both spinal nerve tumors) were PVAS-positive. All the cutaneous neurofibromas, one spinal nerve root neurofibroma and the neurofibroma from the acoustic nerve were negative. All neuromas were PVAS-negative. Except for the difference in immunoreactivity, PVAS-positive tumors were histologically indistinguishable from PVAS-negative tumors.

The number of PVAS-positive cells in NST was variable; in some cases, there were large areas where most cells were positive (designated +++ in Table 1; Fig. 1A); in other cases focal positivity was observed in multiple small areas (++; Fig. 1B), or there was staining in cells forming small clusters or in isolation (+; Fig. 1C). In most cases there were focal collections of several positive cells, especially noticeable in the perivascular areas (Fig. 1D) and longitudinally-sectioned fascicles (Fig. 1B). When compared to the cranial nerve tumors, intracerebral and spinal tumors tended to have a higher proportion of positive cells. Cells in both Antoni A and Antoni B areas were positive. The positive cells displayed the characteristic morphology of Schwann cells (Fig. 1B, C) and some were present in Verocay bodies (Fig. 1E). Individual cells exhibited reactivity in both perikarya and cell processes, the staining being either homogeneous or delicately fibrillar. Although some tumors, especially neurofibromas, showed a diffuse light brown nonspecific staining of their fibrous elements, this did not interfere with the ready evaluation of the immunopositive tumor cells.

The reaction obtained with the “cocktail” on the astrocytic control material was virtually identical with that obtained with the PVAS in regard to staining intensity and the number of positive cells. Only one NST (a spinal nerve root schwannoma) of the 12 PVAS-positive NST was negative when tested with the “cocktail.” In seven NST, including the two intracerebral schwannomas, there were fewer positive cells than with the PVAS. The “cocktail” closely replicated PVAS in the remaining four NST, including both PVAS-positive neurofibromas.

In the astrocytic control tissue, immunostaining with the 2E1E9 MAb (one component of the “cocktail”) was in general slightly less intense and demonstrated fewer positive cells than that with the “cocktail.” In NST the staining intensity was, likewise, usually slightly diminished when compared to that of the “cocktail.” In eight of 12 NST the number of cells stained was almost identical with that of the “cocktail,” but in four NST fewer cells were stained.

All the astrocytic control tissues were positive with the C9 MAb, especially in large gemistocytic reactive and neoplastic astrocytes. However, the immunoreactiv-
Fig. 1. A. Low-power view of a schwannoma demonstrating large areas where most cells are positive (++++ positivity). Immunonegative blood vessel in the center. Immunoperoxidase staining for GFA protein using the PAP method with polyvalent antiserum. Counterstaining with hematoxylin. ×75. B. Immunostaining of a neurofibroma demonstrating positivity in cells forming a longitudinal fascicle (++ positivity). Immunoperoxidase staining for GFA protein using the PAP method with polyvalent antiserum. Counterstaining with hematoxylin. ×270. C. Isolated positive cell in a schwannoma (+ positivity) displaying typical Schwann...
GFA PROTEIN REACTIVITY IN NERVE SHEATH TUMORS

It was in every case less marked in intensity and in regard to the number of positive cells than that obtained with the PVAS or the “cocktail,” and sometimes less and never more intense than that obtained with the 2E1E9 MAb. Pretreatment with trypsin did not improve MAb C9 reactivity. Both intracerebral schwannomas stained with the C9 MAb (Fig. 1F), but less intensely than with the PVAS. None of the extracerebral NST, including the intensely PVAS-positive tumors, was positive with the C9 MAb.

All the reactions performed with the nonspecific mouse myeloma IgG1-kappa and IgG2b-kappa immunoglobulins were negative and without any background staining.

DISCUSSION

In this study we demonstrated GFA protein immunoreactivity with PVAS in neoplastic cells of human NST, including two very rare intracerebral examples. Further testing of the PVAS-positive cases with the well-characterized MAb of the “cocktail” confirmed this reactivity. However, the intracerebral schwannomas, which were histologically identical with the extracerebral ones, were positive with the C9 MAb while the other NST were negative. These findings raise two questions: a) Why did NST which were positive with PVAS and the “cocktail” fail to exhibit immunostaining with C9, which has been shown to recognize astrocytic GFA protein? b) Why did intracerebral and extracerebral schwannomas react differently with respect to C9? Before addressing these issues, the GFA protein immunoreactivity of peripheral nerve elements in normal and non-neoplastic conditions needs to be briefly considered.

Schlaepfer et al (29) studied normal formalin-fixed, paraffin-embedded spinal nerve roots and reported that while astrocytic processes, and hence GFA protein, in the nerve entry zone extended for short distances into the endoneurium, no GFA protein immunostaining could be detected distal to that zone. Other workers who have attempted to elicit GFA protein immunoreactivity in peripheral nerves have likewise been unable to obtain positive staining in formalin-fixed, paraffin-embedded tissue (4, 17, 30). In neuromas that were similarly processed, no immunoreactivity was found with PVAS in the present study, or by Trojanowski et al (31) using a MAb. It should be emphasized that studies which have documented GFA protein immunoreactivity in peripheral nerves have relied on fresh or frozen tissue (5–8). This reactivity was localized to non-myelin forming Schwann cells (5) and was found to increase following injury to the nerve (6, 7). More recently Eng (4) reported that in normal rat sciatic nerve GFA protein makes up 0.01% (5 ng/80 μg) of the total protein and 0.04% (20 ng/50 μg) of the total cytoskeletal protein. These very small amounts of antigen may well have contributed to the difficulty of detecting GFA immunoreactivity in peripheral nerve, especially when relatively less sensitive immunohistochemical techniques have been used. Formalin fixation may have com-
pounded the problem by altering the protein structure or by blocking what little antigen is present.

Human NST have been investigated by quantitative immunoelectrophoresis designed to compare the amount of GFA protein in the tumors to that in normal brain. Jacque et al (32) did not detect any "significant" GFA protein in 19 neurinomas. In four of these tumors the "insignificant" amount present was considered to be "a biochemical index of contamination by neighboring tissue." Rasmussen et al (33) discovered "trace amounts" of GFA protein in nine neurinomas. The results reported in both studies can be interpreted as consistent with the presence of very low concentrations of GFA protein in these tumors.

In a number of previous reports describing immunoperoxidase staining with polyvalent antisera on formalin-fixed, paraffin-embedded tissue, immunostaining of NST was stated to be negative in a small number of tumors tested (34, 35). The "atypical presence" of GFA protein in one of six neurinomas was first reported by Tascos et al (16). Subsequently Memoli et al (17) reported that seven of ten schwannomas, four of eight neurofibromas and none of six malignant schwannomas were GFA protein-positive. The staining pattern obtained in the present study was similar to the one they described, but the proportion of positive cases in our study was lower. Recently Gould et al (18) reported that two of 12 "typical benign schwannomas" were positive, but one "ancient schwannoma," two "cellular schwannomas," four malignant schwannomas and six neurofibromas were negative. With freshly frozen specimens they also studied the same tumors by indirect immunofluorescence, using three separate MAb which were different from those we employed. The two schwannomas noted by Gould et al (18) to be positive by the PAP method were again positive with all three MAb. Furthermore, these two tumors were shown to contain a protein which comigrated with human brain GFA protein on two-dimensional gels, and GFA protein was also shown to be present in tumor homogenates by immunobLOTS.

Our results with a "cocktail" of three MAb that have been well-characterized (25, 26) and reported to recognize phylogenetically conserved regions of GFA protein (26) are in agreement with those of Gould et al (18) in that they confirm the presence of GFA protein immunoreactivity in NST with MAb, thus substantiating the findings observed with polyvalent antisera. In our study, only one PVAS-positive schwannoma did not stain with the "cocktail": the PVAS-binding in this case could have been nonspecific, but this is unlikely in view of the positive results obtained with the "cocktail" in all the other tumors. Alternatively, the sections of the tumor that were stained with the "cocktail" may not have included any reactive cells, as they were obtained from another level in the tissue block. Using the same "cocktail" with the avidin--biotin method at a dilution of 75 μg/ml following trypsinization of the tissues, McLendon et al (25) reported that the four schwannomas they tested were negative.

Given the focal nature of the staining of NST with anti-GFA protein antibodies, the variability of the findings reported to date with both polyvalent antisera and MAb is not surprising, considering the relatively small number of tumors studied to date. However, the collective results demonstrating GFA protein immunoreactivity in formalin-fixed NST by the immunoperoxidase technique suggest that the concentration of the protein must be higher in at least some neoplastic Schwann cells than in normal Schwann cells.

The results obtained with the C9 MAb are more difficult to explain. All astrocytic controls and both intracerebral schwannomas were positive with this MAb, but the
PVAS-positive extracerebral schwannomas (which were also "cocktail"-positive) were C9-negative. Positive reactions with this MAb were generally less intense than that obtained with PVAS or the "cocktail." This possibly reflects the effect of formalin fixation, which may alter or block the epitope recognized by C9 (VPC, unpublished data). However, since all astrocytic controls showed C9-positivity, blockage of the epitope by formalin-fixation and subsequent paraffin-embedding is unlikely to be the complete explanation. An alternative hypothesis is that the concentration of available C9 epitope in NST may be lower than that detectable by the PAP method. However, some of the extracerebral NST that were intensely PVAS- and "cocktail"-positive (thus suggesting that they had relatively high concentrations of antigen) did not stain with C9. The pattern of the results using C9 with the NST and the controls is best interpreted as indicating that a) the C9 epitope is present in astrocytic GFA protein, but distinct from those epitopes recognized by PVAS and the "cocktail"; and b) it is present in intracerebral schwannomas, but absent in extracerebral schwannomas.

Jessen et al (5) reported that Schwann cells of rat sciatic nerve that were positive with a polyclonal GFA protein antiserum were negative with a well-characterized MAb, GFAP-3 (36). This led them to conclude that GFA protein is a heterogeneous group of polypeptides that are antigenically different in the PNS and the CNS. In this context it is interesting that the five schwannomas and five neurofibromas studied by Trojanowski et al (31) were all negative using a mouse IgG2a MAb specific for glial cells. Although the number of their cases was small and although it is not known whether any of those NST would have been PVAS-positive, it is possible that their MAb likewise recognizes an epitope on astrocytic GFA protein that is not present in the PNS. The C9 epitope could similarly be restricted to the CNS, thus explaining how it could be present in astrocytic GFA protein but absent in PVAS-positive extracerebral schwannomas. This does not, however, account for the C9-positivity found in the intracerebral schwannomas, unless these tumors contained antigens shared by astrocytic GFA protein, including the C9 epitope.

Our observation that intracerebral and extracerebral schwannomas, which are histologically identical, are distinct in their antigenicity as demonstrated by their C9 immunoreactivity is of interest. The only other difference between these tumors was their location. The intracerebral schwannomas were surrounded by glial cells, some of which were directly contiguous with the tumors. In one of the intracerebral schwannomas the Antoni B areas which were in close proximity to the CNS tissue were intensely immunostained with all GFA protein antibody preparations, including C9. Consideration should therefore be given to the hypothesis that Schwann cells are able to take up astrocytic GFA protein in the same manner as has been postulated to occur in some of the stromal cells of cerebellar hemangioblastomas (37). However, the topographical distribution of the immunoreactivity did not, as a rule, support this hypothesis. Alternatively, hormonal or growth factors released from CNS tissue or other factors in the microenvironment may influence the expression of GFA protein in Schwann cells, as has been shown to occur in astrocytes in vivo (38) and in vitro (39). Whatever the mechanism, the results reported here indicate that intracerebral schwannomas include a relatively large number of cells containing astrocytic GFA protein or an antigenically similar material.

In summary, several conclusions may be drawn: a) human NST contain cells having polypeptides that share some epitopes with GFA protein; b) outside the CNS these polypeptides may be antigenically distinct from astrocytic GFA protein by at least one epitope; c) the location of the tumors in relation to the CNS may alter the
pattern of immunoreactivity in neoplastic Schwann cells; and d) the pattern of immunoreactivity in neoplastic Schwann cells may differ from that of their non-neoplastic counterparts. The results of this study reinforce the caution with which unexpected immunoreactivity should be interpreted, even when affinity-purified polyclonal antisera and well-characterized monoclonal antibodies are employed in the study of well-established tumor entities.

ACKNOWLEDGMENT

The authors thank Mrs. Elisabeth Perentes for technical assistance.

REFERENCES


(Received 21 November 1986/Accepted 12 March 1987)
MS86-113