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Original contributions

Fascin expression in 90 patients with glioblastoma multiforme

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Abstract Fascin is a protein that serves to aggregate F actin into bundles that rearrange the cytoskeleton and promote cellular motility. Fascin has been linked to the invasive behavior of some tumors. Fascin immunohistochemical analysis was performed in 90 glioblastoma multiforme, including 53 males and 37 females (mean age, 58.3 years). All patients had tumors that demonstrated positive fascin staining. Nineteen tumors showed more than 75% positive staining tumor cells, 14 tumors had more than 50% to 75% staining, 23 tumors had more than 25% to 50% staining, 26 tumors had more than 5% to 25% staining, and 8 tumors had less than 5% staining. In comparison, 9 of 11 low-grade astrocytomas had 50% or less staining for fascin. Eight of 10 anaplastic astrocytomas had more than 50% fascin staining. All gliomas studied expressed fascin by immunohistochemistry. Higher grade tumors generally expressed a greater degree of fascin staining. There was no obvious correlation with the extent of staining and survival among glioblastoma multiforme. Fascin may play a role in tumor cell infiltration.

Keywords: Glioblastoma multiforme; Fascin; Astrocytoma; Anaplastic astrocytoma; Brain tumor

1. Introduction

Intercellular interaction and the interaction of cells with matrix play an important role in the organization and stabilization of tissue [1]. This stabilization maintains the cells in a nonmigratory state. The neoplastic transformation of cells involves a switch to a migratory state that enables tumor cells to invade and potentially metastasize [1]. This process is still not completely understood.

The changes in motility behavior of malignant cells require complex rearrangements of the actin cytoskeleton that involves multiple actin-binding proteins [1]. One of these proteins is fascin, a 55-kDa globular protein, which serves to aggregate F actin into well-ordered parallel bundles [2-4]. These bundles are concentrated in cell protrusions, rearranging the cytoskeleton and promoting cellular motility [1-7]. The notion that fascin functions in cell protrusions has been reinforced by studies of actively migrating cultured cells, where fascin is localized to the leading edge of motile cells [2-4]. Antibodies reactive with actin-binding fascin domains inhibit the binding of fascin and prevent cell spreading and migration [2-4]. These data indicate that fascin is necessary for migration and may be required for the control of migratory behavior [2-4].

Fascin has been studied in a variety of different types of tumors. It has been linked to the invasive behavior of breast carcinoma [8,9] and colonic adenocarcinoma [1]. Analysis of tumor markers using tissue microarray in pancreatic and biliary carcinomas identified fascin upregulation with transition from carcinoma in situ to invasive carcinoma, implying a role in neoplastic progression [10-12].

There is a limited literature, however, focused on the expression of fascin in gliomas. Recently, Peraud et al [13] studied fascin expression in astrocytomas, and an association between fascin expression and higher World Health Organization (WHO) grade was reported. We studied the expression of fascin in high-grade astrocytomas to assess whether fascin immunoreactivity correlates with outcome.

2. Materials and methods

Institutional review board approval was obtained before the commencement of the study. The surgical pathology files were searched for cases in which a diagnosis of glioblastoma multiforme (GBM) (WHO grade IV) was rendered. Tumors resected between 1995 and June of 2004 were included in the study. In addition, 11 low-grade astrocytomas

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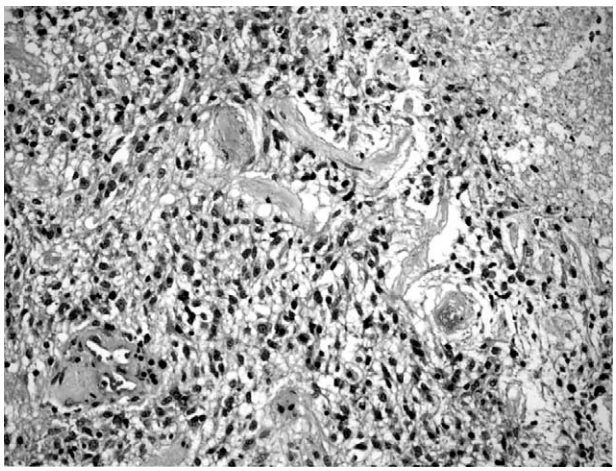

Fig. 1. High-magnification appearance of typical GBM characterized by increased cellularity, nuclear pleomorphism, and necrosis (hematoxylin-eosin, intermediate power magnification).

(LGA) (WHO grade II), 10 anaplastic astrocytomas (AA) (WHO grade III), and 5 normal brain controls were comparatively evaluated. Histological materials were reviewed in all cases, and the original diagnosis was confirmed, using the most recent WHO classification [14]. Cases included for study had paraffin blocks available and suitable for immunohistochemical staining. In each case before 1999, a representative block was selected, and tissue from the blocks was arranged in a tissue microarray. For the tumors diagnosed after 1999, a representative block was selected, and immunohistochemical stains were performed on unstained slides.

Immunohistochemical staining with fascin antibody (1:20 dilution; Dako, Carpinteria, Calif) was performed in all cases using an automated immunostainer (Ventana ES, Tucson, AZ). Positive and negative controls were used with each immunostain. Fascin immunohistochemical positivity

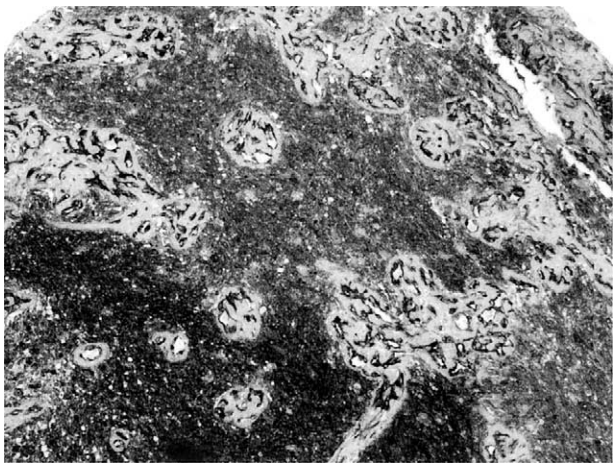

Fig. 2. Pattern of fascin expression in a GBM (WHO grade IV tumor) evaluated as 5+ staining (>75%) (fascin, intermediate power magnification).

Table 1
Correlation of fascin immunostaining and clinical features of GBM (WHO grade IV), AA (WHO grade III), and LGA (WHO grade II)

Tumor type	Age mean (range) (y)	No. of male/ female	No. of radiation therapy/ chemotherapy	Fascin positivity
LGA (WHO grade II)	39.1 (9-83)	5/6	4/6	5+ (2)
				4+ (0)
				3+ (3)
				2+ (4)
				1+ (2)
AA (WHO grade III)	59.3 (45-77)	4/6	6/4	5+ (7)
				4+ (1)
				3+ (1)
				2+ (1)
				1+ (0)
GBM (WHO grade IV)	58.3 (11-83)	53/37	67/42	5+ (19)
				4+ (14)
				3+ (23)
				2+ (26)
				1+ (8)

<5% = 1+, >5%-25% = 2+, >25%-50% = 3+, >50%-75% = 4+, and >75% = 5+.

of tumor cells was graded as follows: no staining = 0, less than 5% = 1+, 5% to 25% = 2+, more than 25% to 50% = 3+, more than 50% to 75% = 4+, and more than 75% = 5+.

Medical records were reviewed in each case for pertinent clinical information: age and sex of the patient, clinical symptoms, location of tumor, extent of initial resection, administration of adjuvant chemotherapy or radiation therapy, tumor recurrence, and status at most recent follow-up. The relationship between fascin immunostaining and outcome was examined.

3. Results

Ninety patients with a diagnosis of GBM (53 men and 37 women) were included in the study. Patients ranged in

Table 2
Correlation of fascin immunostaining and status at follow-up of GBM (WHO grade IV)

Fascin positivity	Follow-up, mean (range) (mo)	No. and status at follow-up
5+ (19)	9.4 (1-20)	1 ANET
		1 AWT
		17 DWT
4+ (14)	11.2 (0.5-29.5)	2 ANET
		1 AWT
		11 DWT
3+ (23)	12.6 (1-55.5)	2 ANET
		2 AWT
		19 DWT
2+ (26)	10.6 (1-23.5)	2 ANET
		1 AWT
		23 DWT
1+ (8)	13.8 (4-24.5)	1 ANET
		7 DWT

<5% = 1+, >5%-25% = 2+, >25%-50% = 3+, >50%-75% = 4+, and >75%=5+.