Clinical features and pathogenesis of scoliosis due to spinal astrocytoma

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Abstract. The aetiology of scoliosis remains unclear. Some studies have focused on the theory of possible muscular imbalance. The role of the spinal cord, which directly innervates the paraspinal muscles, in muscular imbalance has not yet been studied. Spinal astrocytomas often grow on one side of the spinal cord, destroying it asymmetrically. Asymmetrical damage to the spinal cord can lead to asymmetrical changes in paraspinal muscles. The present study investigated the effect of muscular imbalance on scoliosis by observing scoliosis caused by spinal astrocytomas. Patients diagnosed with spinal astrocytomas in a single centre were analysed, and the type and side of the symptoms, sagittal tumour position, scoliosis, end vertebrae and apical vertebrae of scoliosis were recorded. The tumour side was assumed from symptom type and side, and the cross-sectional area of the paraspinal muscles on both sides of the end vertebra was outlined and compared. The incidence of astrocytoma-induced scoliosis was significantly higher in patients with unilateral symptoms. The inferred tumour side was highly consistent with the convex side of scoliosis. The distal vertebral segments of scoliosis were consistent with the spinal cord segments involved in the astrocytomas. The apical vertebrae were more caudal in astrocytoma-induced scoliosis. The cross-sectional area of the multifidus muscle on the convex side of apical-level scoliosis was significantly smaller than that on the concave side. However, no significant differences were observed in the erector spinae muscles. Overall, spinal astrocytomas can cause asymmetric destruction of the corresponding spinal cord segment, resulting in asymmetric atrophy and weakness of the multifidus muscle innervated by the spinal cord segment, thereby causing scoliosis that is convex to the weaker side. This mechanism involves asymmetric lower neuron paralysis of the multifidus muscle. This is a type of scoliosis with several differences from idiopathic scoliosis.

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Introduction

Spinal scoliosis is a 3-dimensional spine and trunk deformity that affects millions of individuals worldwide (1,2). According to its aetiology, it can be divided into the idiopathic, congenital, degenerative and neuromuscular types, among others (3-6). However, this classification method does not reveal more fundamental reasons for scoliosis and has limited significance. The Lenke classification (7), used by spine surgeons to guide surgery, only applies to thoracic and lumbar scoliosis, and is only a morphological classification. Currently, the surgical treatment of scoliosis mainly relies on the fixation and fusion of spinal bones with screw-rod systems (8,9). The operation is challenging, and numerous follow-up problems exist, including chronic pain, growth retardation of the spine and fracture of the screw-rod system (10). Therefore, research on the aetiology of scoliosis is key to the next breakthrough in treatment.

Many studies have focused on the theory of possible muscular imbalance for scoliosis (11-13). Considering the close association between the muscle and the nerves that innervate it, studying the neuromuscular reflex arc cannot be avoided when exploring the mechanism of muscle imbalance. Spinal cord injuries such as poliomyelitis and spinal cord tumours (14,15) can also cause scoliosis. However, the existing literature includes only a few case reports, and there are no articles on the clinical features of scoliosis caused by spinal cord injury. Unlike ependymomas, which are often of central origin and symmetrically disrupt the spinal cord, astrocytomas are characterised by a unilateral origin, asymmetric destruction of the spinal cord, visibility on MRI and the fact that the length of the spinal cord involved with the astrocytoma is clear; therefore, it is a suitable carrier for studying the role of muscle imbalance in scoliosis (16).

The present study analysed cases of scoliosis caused by astrocytoma in a single research centre, and summarised the characteristics and pathogenesis of this type of scoliosis. The incidence of spinal astrocytoma is extremely low, and there is little associated literature due to the lack of knowledge regarding scoliosis caused by spinal astrocytomas. To the best of our knowledge, this study represents the largest sample of

patients with astrocytoma-induced scoliosis currently available for analysis.

Patients and methods

Patients. The medical records of all patients diagnosed with spinal astrocytoma at a single research centre (Peking University Third Hospital, Beijing, China) between January 1990 and October 2022 in both inpatient and outpatient settings were retrospectively reviewed. The inclusion criteria were as follows: Patients diagnosed with spinal astrocytoma (including pilocytic astrocytoma, anaplastic astrocytoma and glioblastoma) according to pathological examination who underwent spinal X-rays before surgery. Patients with no clear tumour segments on imaging or medical records were excluded. Scoliosis was defined as a Cobb angle of >10˚ for the two vertebral bodies on the coronal plane of the spine (3).

The following details were obtained from each medical record: Demographic details, initial side and type of symptoms, duration of the disease, sagittal tumour location, presence of scoliosis and astrocytoma pathological grade (World Health Organisation Neuropathological Classification) (17-22). In addition, where scoliosis was present, the convex side, end vertebrae and apical vertebrae of the scoliosis were recorded.

The study was conducted in accordance with the tenets of the Declaration of Helsinki, and the Ethics Committee of Peking University Third Hospital (Beijing, China) approved the study.

Clinical symptom classification and tumour side inference. Initial clinical symptoms were divided into two main types: Strength and sensory disturbances. Furthermore, the patient's symptoms were characterised as unilateral or bilateral. If the patient's initial symptom was a unilateral sensory disturbance, the tumour would be on the opposite side of the sensory disturbance side. On the other hand, if the patient's initial symptom was unilateral decreased muscle strength, the tumour would be located on the same side of weakness.

Evaluation of the paraspinal muscles. If the patient had scoliosis, the cross-sectional areas of the multifidus and erector spinae muscles on both sides of the apical level of the scoliosis were assessed using MRI. The slice thickness was 4 mm, with a 0.1-mm gap between each slice. The field of view for the scan was 150x163 mm, with 128x256 matrices. The bilateral cross-sectional areas of the multifidus and erector spinae muscles at the apical level were measured by outlining the fascial boundary of the muscle using Image J (ver. 1.3; National Institute of Health), as described by Shafaq *et al* (23).

Pathology and diagnosis. All tumours were examined pathologically. This was consistent with the latest World Health Organisation Neuropathological Classification at the time of diagnosis (17-22).

Statistical analysis. R4.0.3 statistical software (University of Auckland) was used for the statistical analysis. For continuous data, the Shapiro-Wilk normality test was used to determine the normality of the sample data. If it conformed to the normal distribution, it was expressed as the mean ± standard deviation, and the comparison between the two groups was performed using the independent sample t-test; if it did not conform to the normal distribution, the median (lowest to highest value) was used, and the Wilcoxon test was used for comparison between the two groups. A paired sample t-test was used to assess the cross-sectional area of the paraspinal muscles on both sides. Categorical data are statistically described as n (%), and comparisons between groups were performed using the χ^2 test. $P<0.05$ was used to indicate a statistically significant difference.

Table I. Patient data summary.

Variables	Value
No. of patients	189
Mean age ± SD, years	40.69±14.8
Sex, n	
Male	94
Female	95
Side of symptoms, n	
Unilateral	119
Bilateral	70
Type of symptoms, n	
Sensory disturbance	75
Strength disturbance	114
Mean duration of disease ± SD, months	11.6±13.6
Tumor sagittal location, n	
Cervical	50
Cervicothoracic	35
Thoracic	54
Thoracolumbar	28
Lumbar	14
Full length	8
Pathological grade, n	
1	31
2	116
3	29
4	13
Scoliosis, n	
Yes	106
No	83

Results

A total of 189 patients (94 men and 95 women) met the inclusion criteria. The mean patient age was 40.69±14.8 years (range, 6-84 years), while the mean duration of the disease before diagnosis was 11.6 months. A total of 119 patients had unilateral onset and 70 had bilateral onset. Overall, 80 patients had a sensory impairment and 118 had a motor impairment. The astrocytoma was located in the cervical spine in 50 patients, in the cervicothoracic spine in 35 patients, in the thoracic spine in 54 patients, in the thoracolumbar spine in 28 patients and in the lumbar spine in 14 patients. The tumour invaded the entire

Table II. Comparison of patients with unilateral and bilateral symptoms.

Variables	Unilateral symptoms	Bilateral symptoms	P-value
No. of patients	119	70	
Age, years	40.08±16.19	41.73±12.11	0.426
Sex, n			0.337
Male	56	38	
Female	63	32	
Type of symptoms, n			0.194
Sensory disturbance	43	32	
Strength disturbance	76	38	
Mean duration of disease ± SD, months	10.8±11.5	13.0±16.5	0.240
Tumor sagittal location, n			0.196
Cervical	35	15	
Cervicothoracic	22	13	
Thoracic	38	16	
Thoracolumbar	14	14	
Lumbar	6	8	
Full length	4	4	
Pathological grade, n			0.242
1	23	8	
2	67	49	
3	19	10	
4	10	3	
Scoliosis, n			0.012[a]
Yes	75	31	
No	44	39	

[a]P<0.05.

length of the spine in 8 patients. Among all the patients, 57.1% had scoliosis (Table I).

The patients were divided into two groups according to whether their initial symptoms were unilateral or bilateral. There was no statistical difference in the baseline indicators between the two groups, but the incidence of scoliosis in the unilateral onset group was significantly higher (Table II).

The details of the patients with scoliosis with complete information are listed in Table III. The inferred tumour side was highly consistent with the convex side of scoliosis. According to classic anatomical studies, in early human embryos, the spinal cord has the same length as the spine, and each spinal cord segment is consistent with the corresponding vertebral bone. However, in the process of growth, the growth rate of the spine is faster than that of the spinal cord. Therefore, in adults, spinal cord sections do not precisely correspond to the corresponding vertebral bones (24). The corresponding rules are listed in Table IV. The sagittal position of the astrocytoma and scoliosis end vertebra follow the same rules. Three typical cases are shown in Fig. 1: A C2 to C7 segment tumour caused C3 to T1 segment scoliosis, a C7 to T7 segment tumour caused T3 to T10 segment scoliosis and a T7 to T11 segment tumour caused T10 to L3 segment scoliosis. Unlike idiopathic scoliosis, the apical vertebrae were generally in the middle of the scoliosis, and the apical vertebrae were more caudal to this scoliosis type. In some cases, the apical vertebra was the caudal end vertebra. Morphologically, the vertebral bodies of idiopathic scoliosis line up similarly to a 'c' shape, whereas the vertebral bodies of astrocytoma-induced scoliosis in the present study lined up similarly to an 'L' shape with a larger angle. The morphology of this scoliosis type in the cervical, thoracic and lumbar spine is shown in Fig. 2.

Of the 106 patients with scoliosis, 12 did not undergo an MRI scan in the cross-section of the end vertebra, while the distal vertebral paraspinal muscles of the remaining 94 patients were delineated and analysed. The cross-sectional area of the multifidus muscle on the convex side of the apical-level scoliosis was significantly smaller than that on the concave side. There was no significant difference in the cross-sectional area of the erector spinae muscles between the convex and concave sides of the apical vertebrae (Table V).

Discussion

Scoliosis affects millions of individuals worldwide; however, the pathogenesis remains unclear (25,26). Anatomically, the spine consists of vertebral bodies and intervertebral discs, which are mechanically passive and rigid. Several muscles, which are mechanically active and retractable structures, are attached to the spine. Logically, only asymmetrical

Table III. Details of tumors and scoliosis in patients with complete information.

Patient no.	Sex	Age, years	Initial symptom side	Initial symptom type	Inferred tumor side	Scoliosis convex side	Duration of disease, months	Tumor sagittal location	Scoliosis end vertebrae	Scoliosis apical vertebrae	Pathological grade
1	F	45	L	Strength disorder	L	L	12	C0-T1	C2-T1	C7, T1	4
2	M	40	L	Strength disorder	L	L	2	C2-6	C3-T2	C7	3
3	F	20	R	Sensory disorder	L	L	6	C2-7	C3-T1	T1	1
4	F	24	R	Sensory disorder	L	L	3	C3-5	C4-T2	C7	3
5	M	41	L	Strength disorder	L	L	24	C3-L2	T7-L5	L2-3	2
6	F	40	L	Strength disorder	L	L	9	T10-11	T10-L4	L1	2
7	F	41	R	Sensory disorder	L	L	36	T1-2	C6-T3	T2-3	2
8	M	54	L	Strength disorder	L	L	60	C5-T2	/	/	2
9	M	31	R	Sensory disorder	L	L (cervicothoracic); R (thoracolumbar)	24	C6-T5	C3-T5 (cervicothoracic); T5-L1 (thoracolumbar)	C7, T10	1
10	M	60	R	Strength disorder	R	R	36	C2-T1	C2-T3	T1-2	2
11	F	18	R	Strength disorder	R	R	2	T7-11	T10-L3	L1-2	2
12	M	67	R	Strength disorder	R	R	1	C3-5	C2-6	C4	3
13	F	29	R	Strength disorder	R	R	6	C4-6	C5-T1	C6-7	2
14	F	12	L	Sensory disorder	R	R	12	C7-T7	T3-10	T8	2
15	F	19	R	Strength disorder	R	R	24	T2-6	T2-9	T5	2
16	F	45	L	Sensory disorder	R	R	2	T4-6	T5-8	T6-7	2
17	F	42	R	Strength disorder	R	R	18	T5-7	C6-L2	T5-6	2
18	M	26	R	Strength disorder	R	R	0.5	T6-10	T9-L2	T12, L1	1
19	M	40	R	Strength disorder	R	L	6	C5T1	C4-T5	T1-2	2
20	M	13	R	Strength disorder	R	L	2	T11-12	T12-L5	L3-4	2
21	M	39	L	Strength disorder	L	R	3	C4T2	C4-T1	C7T1	1
22	M	49	L	Strength disorder	L	R	12	T2-5	T3-T7	T6	3
23	M	41	Bilateral	Strength disorder	-	R	3	C4-5	C4-6	C6	1
24	M	13	Bilateral	Sensory disorder	-	R (thoracic); L (thoracolumbar)	48	T3-L2	T3-T11 (thoracic); T11-L5 (thoracolumbar)	T8, L4	1
25	M	21	Bilateral	Strength disorder	-	R (thoracic); L (thoracolumbar)	60	T4-11	T7-T11 (thoracic) T11-L4 (thoracolumbar)	T9, L4	2
26	F	58	Bilateral	Sensory disorder	-	R	12	C6-T4	C6-T6	T4	3
27	M	48	Bilateral	Sensory disorder	-	L	4	T12-L1	L1-5	L3	2

L, left; R, right; C, cervical; T, thoracic; L, lumbar.

Table IV. Association between the location of the spinal cord segments and the vertebral segments.

Vertebral segment	Number of segments difference	Spinal cord segments
C1-4	+0	C1-4
C4-T3	+1	C5-T4
T3-6	+2	T5-8
T6-9	+3	T9-12
T10-12	Variable	L1-5

C, cervical; T, thoracic; L, lumbar.

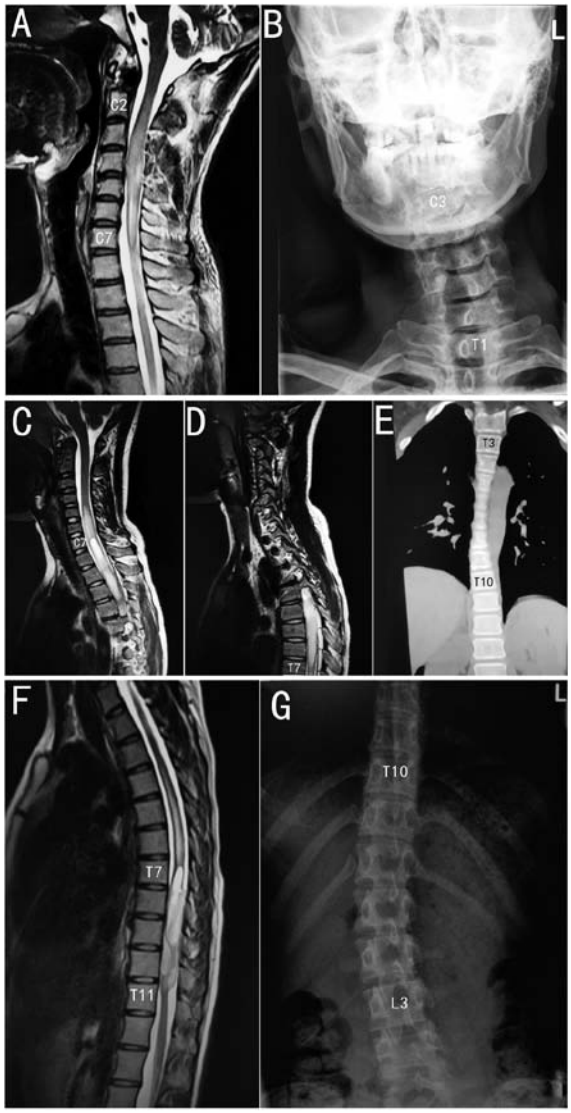

Figure 1. Three typical cases showing the association between the spinal tumour location and scoliosis location. (A) A C2 to C7 segment tumour that caused a (B) C3 to T1 segment scoliosis. (C and D) A C7 to T7 segment tumour that caused a (E) T3 to T10 segment scoliosis. (F) A T7 to T11 segment tumour that caused a (G) T10 to L3 segment scoliosis.

contraction of the muscle can lead to spinal curvature. This is the case with side bending under physiological conditions

Table V. Cross-sectional area of the deep paravertebral muscles at the apical vertebrae.

Muscle	Concave side, mm^2	Convex side, mm^2	P-value
Multifidus muscles	302.5±117.4	250.2±103.4	0.001[a]
Erector spinae muscles	614.8±255.3	559.7±237.6	0.128

[a]P<0.05.

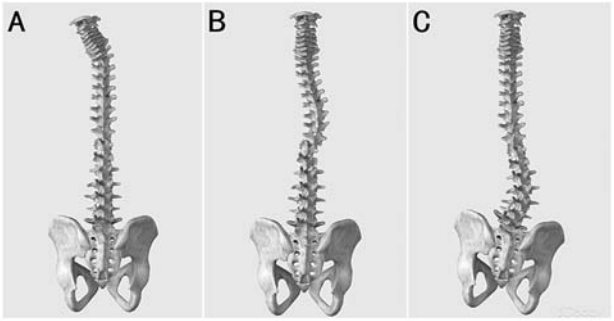

Figure 2. Morphological depiction of astrocytoma-induced scoliosis in the (A) cervical, (B) thoracic and (C) lumbar spine. The vertebral bodies of astrocytoma-induced scoliosis line up in an 'L' shape with a larger angle, and the apical vertebrae are more caudal to this scoliosis.

and should be the same with scoliosis under pathological conditions. Previous studies have provided a basis for this hypothesis. Electromyography shows increased activity on the convex side of the curve (27), and the spine becomes silent when surgically fused or braced (28). Histological studies have shown disproportionate slow-twitch vs. fast-twitch fibres in the paravertebral muscles in cases of scoliosis (29,30). When assessing how the asymmetrical activation or weakness of the paravertebral muscles is caused, research has mainly been focused on the role of the cerebrum, brain stem and cerebellum (31-34), but no consensus has been reached. The role of the spinal cord and spinal nerves, which directly innervate the paraspinal muscles, in muscular imbalance has not yet been studied.

Spinal astrocytoma is a malignant tumour that occurs in the spinal cord and causes damage to the neurological function of the corresponding segment of the spinal cord (35); it is unilateral in origin, visible on MRI and characterised by a clear length of involvement in the spinal cord (16). Patients with spinal astrocytoma have asymmetric damage to the spinal cord, which can lead to asymmetrical changes in the paraspinal muscles. The present study investigated the effect of muscular imbalance in scoliosis by observing scoliosis caused by spinal astrocytomas. In this study, astrocytomas with unilateral initial symptoms were more likely to develop scoliosis, and the inferred tumour side was consistent with the convex side of scoliosis. In addition, the distal vertebral segments of scoliosis were consistent with the spinal cord segments (not the vertebral segments) involved in astrocytomas. This confirms that

asymmetrical weakness of the paraspinal muscles on one side is a cause of scoliosis, and the cause of muscle weakness is lower motor neuron paralysis due to spinal cord injury. For the same reason, symmetrical weakness of the paraspinal muscles on both sides is less likely to cause scoliosis, similar to bilateral symptoms, although the muscles are also paralysed. Some patients with initial bilateral symptoms also had scoliosis as the tumour had asymmetric invasion, which further contributed to the asymmetric injury of the spinal cord, although the tumour involved both sides. In some patients, the inferred side of the tumour was opposite to the convex side of scoliosis, which may be since the compensatory space in the spinal canal was too small, and the tumour with a noticeable mass effect directly caused injury to the contralateral side, although the tumour was located on the convex side. Furthermore, the present study found that the cross-sectional areas of the multifidus muscles on the two sides of the apical vertebrae in patients with scoliosis were different on MRI, which also provided a basis for the hypothesis that the scoliosis was caused by atrophy of one side of the muscle, to be precise, the deep short segment muscle on the side of the tumour. A previous study showed that in patients with idiopathic scoliosis, concave-side muscle atrophy is more severe, which is inconsistent with the findings of the present study (36). This finding suggests that there may be more than one pathogenesis of scoliosis. Asymmetrical activation and asymmetrical weakness may be different mechanisms of different scoliosis types (37).

In summary, the differences between the scoliosis type presented in the current study and idiopathic scoliosis are as follows: i) Morphologically, the vertebral bodies of idiopathic scoliosis line up like a 'c' shape (38), whereas the vertebral bodies of astrocytoma-induced scoliosis line up like an 'L' shape. ii) The apical vertebrae of idiopathic scoliosis are often located in the middle of the curve (39). By contrast, the apical vertebrae in astrocytoma-induced scoliosis tend to be caudal to the curve. iii) Degeneration of the paravertebral muscles on the concave side of idiopathic scoliosis is more apparent (21), while degeneration of the paravertebral muscles on the convex side of astrocytoma-induced scoliosis is more obvious. These differences indicate that astrocytoma-induced scoliosis is different from idiopathic scoliosis. The present study found that the essence of scoliosis caused by astrocytoma is lower neurone paralysis of the deep paravertebral muscles caused by spinal cord injury. Given the difference between idiopathic scoliosis and scoliosis due to spinal astrocytoma, we believe that idiopathic scoliosis is caused by excessive contraction of the concave paraspinal muscles, as the upper neurone spastic paralysis of the concave muscle is caused by a spinal cord lesion. Of course, this is merely a hypothesis and requires further evidence.

The present study has a few limitations. First, the sample size was relatively small. Second, some of the findings were descriptive studies and not controlled studies. These findings require further validation in controlled trials with larger sample sizes.

In conclusion, spinal astrocytomas can cause lower neuron paralysis of the paraspinal multifidus muscles, which is innervated by the corresponding spinal cord segment affected by the tumour, resulting in scoliosis that is convex to the paralysed side. Astrocytoma-induced scoliosis is a type of scoliosis with several differences from idiopathic scoliosis.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

YS made substantial contributions to study conception, designed the study and was involved in drafting the manuscript. HZ performed the statistical analysis. SBH took the MRI images and analyzed the data. CLY performed data analysis and interpretation. QQM repeated the analysis to ensure it was correct. CCM provided suggestions for research design and reviewed the article. JY reviewed the article and helped with the data analysis. All authors read and approved the final manuscript. YS, HZ, SBH, CLY, QQM and JY confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Peking University Third Hospital (Beijing, China).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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