Is ossification of posterior longitudinal ligament an enthesopathy?

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Abstract The purpose of this study was to investigate the relationship of ossification of posterior longitudinal ligament (OPLL) with enthesis, the site where the posterior longitudinal ligament (PLL) attaches to the vertebral body, by multi-detector CT reconstruction images. Twenty-nine patients with OPLL were studied. According to the plaques' continuity to the vertebral body, OPLL plaques were classified into two categories: "free" and "contiguous". A "broken sign" was defined as a crack between two plaques. The sites where each "contiguous" plaque attached to the vertebral body were then analysed. There were 78 ossified plaques in total, and six were "free". There were eight cases with a "broken sign", including six "free" ones. The site where all 72 "contiguous" plaques attached to the vertebral body included the zone where the PLL entheses was situated, while other zones were included in only part of the plaques. Our conclusion was that there might be no real "free type" ossified plaques, and OPLL could start from entheses, which indicated OPLL could be a kind of *enthesopathy*.

Introduction

Ossification of the posterior longitudinal ligament (OPLL) is characterized by replacement of ligamentous tissue by ectopic new bone formation [1, 2]. It often causes narrowing of the spinal canal, and has been recognized as

one of the causes of cervical myelopathy [3–5]. OPLL is a progressive disease, and it has been reported that the ossification area progresses with time not only after cervical laminoplasty [6, 7], but also without surgery [8]. According to these studies [6–8], young patients with continuous or mixed type OPLL and C3 involvement of ossification had a risk for progression in OPLL following laminoplasty surgery.

The terminology "entheses" or "entheses" means site where tendons and ligaments attach to bone [9, 10]. Two types of entheses can be distinguished by their structure and location. They have recently been called fibrous and fibrocartilaginous entheses, or as periosteal-diaphyseal and chondral/ chondro-apophyseal attachments, respectively [9, 10]. Enthesis of the posterior longitudinal ligament (PLL) was a kind of fibrous or periosteal-diaphyseal entheses [10]. An anatomical study [11] showed that PLL consists of two layers: the superficial layer located just on the dura mater which bridges three or four vertebrae, and the deep layer underlying the vertebra and connecting the adjacent two vertebrae. The fibres of each layer appeared to merge forming a common entheses. Both layers attached to a midline bony septum on the posterior surface of the vertebral body between the superior and inferior margins. This attachment was not always continuous because of deficiencies in the septum in the central third of the vertebral body [11]. It was very interesting, however, that fibrocartilaginous entheses had a similar histological structure to the ossification front of the OPLL, which included four regions: the fibre area, fibrocartilaginous area, calcified cartilage area and bone/ossified area [9, 10, 12]. This similarity indicated that OPLL might start its pathological formation from the site of entheses to other parts of PLL. But the literature rarely focussed on the relationship between OPLL and entheses. The purpose of this study

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was to investigate if the OPLL had any relationship with enthesitis by multi-detector CT reconstruction images.

Materials and methods

Patients

The study included 29 patients (24 males and five females; age range 33–77 years, mean 56.9 years) retrospectively from January 2009 to December 2009. These 29 patients all had OPLL confirmed by lateral cervical X-ray film and CT scan. Patients with spinal infectious diseases and cervical tumours were excluded. The study was approved by the local ethics committee and all patients or their relatives provided informed consent. The detailed information of each patient is listed in Table 1.

Radiographic assessments

Each patient was scanned using a 64-slice multi-detector CT scanner (GE Light Speed VCT). The scan was obtained in an axial plane using a slice collimation of 5 mm, pitch 0.531, 120 KV, 200 mA, bone algorithm (window width 1500, window location 500). The axial images and multi-planar reformats (MPR) of the sagittal images with reconstruction increment of 0.5 mm were used.

These images were blindly read by one experienced spine surgeon and one radiologist.

Definition of “free type”, “contiguous type” and “broken sign”

In order to analyse the relationship between OPLL plaque and vertebral body, we grouped the plaques into two

Table 1 Patients' characteristics and details regarding the evaluation methods

Patient number	Gender	Age (y)	Segments involved	OPLL plaque numbers	With “free type” ossified plaques or no	With “broken sign”
1	M	43	C2,C3,C4,C5,C6	5	No	No
2	M	61	C2,C3,C4	2	No	No
3	M	60	C2,C3,C4,C5	3	Yes	Yes
4	M	52	C5,C6,C7	3	No	No
5	M	74	C4,C5	2	No	No
6	M	44	C2,C3,C5,C6	3	No	No
7	M	55	C6	1	No	No
8	M	65	C3,C4,C5,C6	4	Yes	Yes
9	M	59	C3,C4,C5	2	Yes	Yes
10	M	69	C2,C3,C4,C5,C6	4	No	No
11	M	65	C4,C5,C6	3	No	No
12	M	77	C2,C3,C4	2	No	Yes
13	M	56	C2,C3,C4,C5,C6	4	No	No
14	M	64	C2,C3,C4	1	No	No
15	M	55	C2,C3,C4,C5,C6	3	No	No
16	M	63	C2,C3,C4,C5,C6	5	Yes	Yes
17	F	49	C2,C3,C4,C5,C6,C7	3	No	Yes
18	M	43	C5,C6	2	No	No
19	M	54	C5,C6	1	No	No
20	F	33	C6,C7	2	No	No
21	F	56	C5,C6,C7	4	Yes	Yes
22	M	62	C6	1	No	No
23	M	45	C4,C5	2	No	No
24	M	65	C4,C5,C6	3	No	No
25	F	54	C4,C5,C6,C7	2	No	No
26	F	51	C5,C6,C7	4	No	No
27	M	64	C5,C6	2	No	No
28	M	45	C4,C5,C6	4	Yes	Yes
29	M	67	C6	1	No	No

M male, F female, OPLL ossification of posterior longitudinal ligament

Fig. 1 The “contiguous type” ossified plaque. The neighbour plane showed the ossified plaque contiguous with the vertebral body in the midline layer (**a**). The axial image of the level confirmed that the same plaque continued in the sagittal plane (**b**)

Fig. 2 Broken sign. The *triangle* indicates the location of the crack, and the *arrow* means the direction of the force might cause rupture of the plaque

Fig. 3 Definition of the four zones where the ossified plaque may attach to the vertebral body

categories, “free type” and “contiguous type”, according to the MPR images. “Free type” meant that the plaque was not in contact with the vertebral body in any sagittal plane. On the other hand, “contiguous type” meant that the plaque was in contact with the vertebral body in at least one sagittal plane view. This was further confirmed by the axial images, as shown in Fig. 1.

A “broken sign” was defined as a crack between two OPLL plaques in the sagittal reformatted planes. Moreover, the outlines of the crack should indicate the prior continuity (Fig. 2). This is a novel definition used for first time, with no other mention in the literature.

Analyses of the site where the OPLL plaque is contiguous to the vertebral body

We divided the posterior wall of the vertebral body into four zones: upper/lower midline zone, middle midline zone, upper/lower lateral zone and middle lateral zone, as shown

Table 2 Sites of ossified plaque attaching to vertebral body

	Site	IOPN	Rate of IOPN to TCOPN (72 in total)
<i>IOPN</i> involved ossified plaque numbers, <i>TCOPN</i> total contiguous ossified plaque numbers	Upper/lower midline zone	72	1.000
	Middle midline zone	63	0.875
	Upper/lower lateral zone	38	0.526
	Middle lateral zone	30	0.417

in Fig. 3. According to the anatomical study [11], the PLL enthesis was situated in the upper/lower midline zone in all patients. It might be situated, however, in the middle midline zone in some patients. It could not be situated in the upper/lower lateral zone or middle lateral zone. Then the zones where each ossified plaque attached to the vertebral body were analysed.

Statistical analyses

Interclass correlation (ICC) was used to evaluate the inter-observer reliability among two observers, one spine surgeon and one radiologist. The kappa statistic was used to evaluate the inter-observer reliability of the determination of attachment type. The kappa reference value of 0.5 was chosen as an indication of moderate agreement and 0.8 as an indication of substantial agreement. For statistical analysis of results, SPSS statistical software was used.

Results

The kappa value of inter-observer reliability was 0.849. It proved that the evaluation had high reliability.

As shown in Table 1, there were 78 ossified plaques in 29 cases. Of the 78 plaques, there were six “free” plaques, which were not in contact with the vertebral body in any sagittal plane. The other 72 plaques were contiguous with the posterior wall of the vertebral body. Meanwhile, there was a total of eight patients with a “broken sign” according to the sagittal reconstructed images. Interestingly, all six

“free” plaques also had a “broken sign” with adjacent plaques. As to the zones in which each plaque attached to the vertebral body, the upper/lower midline zone was involved in all 72 “contiguous” plaques, the middle midline zone in 63 of them, the upper/lower lateral zone in 38, and the middle lateral zone in 30. The results are listed in Table 2. Briefly, all the plaques were contiguous to the vertebral body in the upper/lower midline zone, while only part of the plaques were contiguous to the vertebral body in the other three zones. Figure 4 demonstrates a case of early stage OPLL, which indicated that only the upper/lower midline zone was involved.

Discussion

The “broken sign” is a novel concept used for the first time in our studies. It seems likely that with the development of OPLL, especially when extending axially, the motion range of the cervical spine was restricted by the ossified plaques [13]. It would be reasonable to expect that the motion of the cervical spine might cause rupture of the plaques, just like a stress fracture.

This study demonstrated that most ossified plaques were contiguous, while all free plaques had a “broken sign”. Moreover, all of the contiguous plaques attached to the vertebral body in the site of the “upper/lower midline zone”, where enthesis is located. Based on these two results, an inference, that there might be no real “free type” ossified plaque, and all of “free type” plaques were originated from rupture of a whole plaque, could be drawn.

Fig. 4 A case of early stage ossification of posterior longitudinal ligament (OPLL). Axial plane (a) combined with reformatted sagittal plane (b) of CT scan indicated an ossified plaque which only involved the lower midline zone of the C7 vertebral body. The arrow indicates the ossified plaque

Meanwhile, as suggested previously [11], PLL enthesis could only be situated in the upper/lower midline zone and the middle midline zone, but never in the upper/lower lateral zone or the middle lateral zone. This could mean that all ossified plaques had a “root” to the vertebral body in the location of the PLL enthesis. Although the plaques also contacted the vertebral body in other zones, it could be the result of extending from the enthesis site. It is unfortunate that this study lacks the support of histological evidence, because it is always difficult to obtain the en bloc OPLL specimen with the posterior wall of the vertebral body in surgery. Fortunately, some other studies have reported [12, 14] that ossification always has a direct contact with cortical bone, and that OPLL plaque was contiguous with the ligamentous enthesis to the vertebral body and to the deep layer of the PLL. Animal studies [15–17] also confirmed that the PLL was replaced by bony tissue forming an osseous bridge contiguous to the enthesis. Interestingly, another study [18] on ossification of the ligamentum flavum had a similar conclusion that ossification was found to start in the superior margin of the lamina, where the enthesis was located.

The results of this study were consistent with the conclusion that the OPLL might originate from the location of an enthesis. It would be helpful to get a better understanding of the origination and development of OPLL. Moreover, it is indicated that OPLL could be actually a kind of *entheseophyte*, or *entheseopathy*, as diffuse idiopathic skeletal hyperostosis (DISH) [19–21] and ankylosing spondylitis [19, 21, 22]. Enthesopathy had been considered as rheumatic or metabolic disorders for a long period [19–21] and was grouped as inflammatory and non-inflammatory enthesopathy. Few authors had considered OPLL as enthesopathy however. The results of this study have reminded us that OPLL might have some common pathogenesis with DISH or ankylosing spondylitis. It would be helpful to find out the real mechanism of OPLL.

Lateral plain film and axial CT scans [7] were always used to assess the size and morphology of OPLL, but multi-detector CT with MPR was a much more precise method to observe and measure OPLL [23, 24], as it provides meticulous information of OPLL plaque, and could tell the relationship between the plaque and the vertebral body.

There are two main limitations in this study. The first one is lack of long-term follow-up MPR images to support the assumption of the “broken sign”, which is important to the theory. The reason for this is that OPLL usually develops slowly, and MPR techniques have been available for less than six years. The second reason is lack of support from direct histological evidence, because it is always difficult to get en bloc specimen of ossified plaque with

the posterior wall of the vertebral body in surgery. Thus, further studies are recommended, which should include the longitudinal MPR study and direct histological study.

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