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Spinal intradural capillary haemangioma: a review

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Abstract Capillary haemangioma is a benign tumour frequently encountered in the skin and other soft tissues. Histologically, these vascular lesions are characterised by nodules of capillary-sized vessels lined by flattened endothelium, each of which is subserved by a feeding vessel. Capillary haemangioma of the central and peripheral nervous system is extremely rare. Less than 20 of these lesions have been described as occurring within the confines of the spinal dura mater, in close relation to the conus medullaris and nerve roots of the cauda equina. The presenting symptoms are similar to those of more common intradural tumours at the conus-cauda region. Magnetic resonance imaging is the imaging modality of choice, and homogeneous enhancement following administration of Gd-DTPA is a useful clue to

the diagnosis. Complete resection is the treatment of choice, and during surgery the vascular tumour is usually found encapsulated and sharply bordered from the surrounding parenchyma of the spinal cord and affected nerve roots. In the present account we give an overview of the clinical features, neuroradiological findings, therapeutic options and histopathological differential diagnostic aspects of spinal intradural capillary haemangioma. In general, vascular lesions of this entity are preoperatively misdiagnosed as neoplasms, and a higher level of clinical and radiological suspicion may avoid surgical overtreatment of these benign tumours.

Keywords Capillary haemangioma · Spinal cord · Vascular malformation · Spinal surgery · Review

Introduction

Spinal cord tumours account for about 15% of all central nervous system (CNS) neoplasms, with 10% of these arising at the level of the conus medullaris and cauda equina [2, 37, 43]. Vascular lesions comprise about 6–7% of all spinal intradural tumours [7, 19, 29, 37]. Spinal vascular tumours may be classified as capillary teleangiectasias, cavernous angiomas, arteriovenous malformations or venous malformations [43]. Cavernous angiomas of the CNS clearly favour the cerebral hemispheres [12, 20], but may occur anywhere in the neuroaxis and account for 5–12%

of all vascular space-occupying masses of the spine [7, 8, 19]. Histologically, cavernous angiomas are defined as vascular malformations comprised of closely packed, large dilated vascular channels without interposed neural tissue [20, 19, 31, 38, 43]. Spinal intradural cavernous angiomas commonly present with intramedullary spread of growth [1, 4, 5, 7, 8, 31, 54]. In contrast, intradural extramedullary location of cavernous angioma is only sporadically seen, most frequently at the level of the conus medullaris and cauda equina [3, 6, 9, 17, 31, 35, 36, 49].

Capillary haemangioma is a benign vascular lesion, most often found in the skin and other soft tissues of children [11] and occasionally invading the nervous system in

a metameric pattern of distribution [26]. Unlike cavernous angioma, this entity is histologically characterised by a lobular architecture, with each lobule separated by septa of fibrous connective tissue and consisting of a myriad of small and very small capillaries lined by endothelial cells [11]. Nevertheless, specimens of capillary haemangioma have been documented that exhibited a more [16] or less [40] cavernous component, indicating that transitional forms exist as well.

Neurological manifestation of capillary haemangioma is very rarely seen, and has been mainly reported to involve the peripheral nervous system. Involvement of peripheral nerves had been described for digital [24], median [23, 44], cubital [22], superficial peroneal [51] and sciatic nerves [34]. The occurrence of capillary haemangioma within the confines of the spinal dura mater is exceedingly rare. Spinal intradural capillary haemangioma usually presents at the surface of the distal spinal cord [42, 46], close to the conus medullaris or attached to nerve roots of the cauda equina [15, 18, 25, 30, 41, 40, 53]. The purpose of this study was to assess the clinical presentation, imaging features, therapeutic options and differential diagnosis, with particular emphasis on histopathological considerations, of spinal intradural capillary haemangioma.

Pathogenesis

The neuro-epithelium, ontogenetically giving rise to the distal spinal cord, is of mesodermal origin. Frequently, tumours at the level of the conus medullaris and cauda equina contain mesodermal elements. The occurrence of vascular lesions involving the conus medullaris and cauda roots in a metameric distribution has occasionally been recognised. Mawk et al. reported a capillary haemangioma that was occupying the parenchyma of the conus medullaris, the subdural and epidural space, the deep soft tissues of the back and the skin overlying these regions in a 7-month-old boy [26]. The tumour contained adipose and skeletal muscle cells and a prominent component of haemangiomatous stroma. The authors suggested that the lesion evolved during the early somitic differentiation, at the time when angioblastic differentiation starts (days 21–24 of embryogenesis). The tumour was thought to result from impaired movement and differentiation of primitive mesoderm from the embryonic mesodermal plate.

Russel and Rubinstein defined vascular tumours of the conus-cauda region as hamartomas, which implies that these lesions are of congenital origin [43]. The familiar occurrence of cavernous angiomas, following an autosomal dominant pattern of inheritance, is well documented and favours this assumption [43]. Another early school of thought claimed the origin of growth from vascular structures within the epineurium of the nerve roots affected during individual ontogenesis [18, 44].

In pathological terms, a hamartoma is not a true neoplasm, as it grows on the basis of hypertrophy and not due to cellular anaplasia. Histologically, mild to moderate mitotic activity had been described to occur in capillary haemangioma [11, 40, 41, 42]. The fact that capillary haemangioma is usually found well demarcated from the surrounding parenchyma by a connective tissue capsule emphasises the benign nature of the lesion, despite the lack of precise understanding about the details of its development and growth.

Spinal intradural capillary haemangioma has a slowly progressive growth potential. However, any intradural space-occupying lesion within the spinal channel develops a mass effect over a certain period of time, possibly resulting in serious neurological deterioration. Thus, thorough clinical and imaging investigation is warranted.

Clinical presentation

Age and sex distribution

Roncaroli et al. reported the mean age at presentation in ten cases of spinal nerve root haemangiomas (nine capillary and one haemangioendothelioma) to be 52 years, ranging from 40 to 62 years [40]. Within the other documented cases of spinal intradural capillary haemangioma arising in close relation to nerve roots of the cauda equina, the age at onset of clinical symptoms ranged from 41 to 74 years, with a mean of 57 years [15, 18, 25, 30, 41, 53]. The oldest patient reported was a 74-year-old man, who presented with a 9-months history of progressive painless weakness of both legs due to multiple capillary haemangiomatosis at the level of the cauda equina [41].

Roncaroli et al. documented intradural capillary haemangiomas of the cauda equina in six men and four women (with one further case of haemangioendothelioma in a patient whose gender was not reported) [40]. The sex distribution among the other reported cases of intradural capillary haemangiomas of the cauda equina is: three men [15, 25, 41] and three women [18, 30, 53]. Thus, intradural capillary haemangioma of the cauda equina appears to occur with equal frequency in men and women.

In the series of four intradural extramedullary capillary haemangiomas of the distal spinal cord reported by Roncaroli et al., the age at presentation ranged from 42 to 64 years, with a mean of 52 years [42]. The series comprised three male and one female patient [42]. Shin et al. documented an intradural extramedullary capillary haemangioma compressing the dorsal aspect of the lower thoracic spinal cord in a 66-year-old woman [46]. Hida et al. described the case of a 50-year-old man suffering from an intramedullary disseminated vascular lesion in the cervical cord [16]. The lesion was designated as capillary haemangioma, but contained teleangiectatic vessels and featured spinal cord tissue between blood vessels.

Table 1 Capillary haemangioma affecting nerve roots of the cauda equina. A summary of previously reported cases (*L* lumbalgia, *LS* lumbosciatalgia, *SD* sensory deficits, *ATR* Achilles tendon reflex, *QR* quadriceps reflex, *L'S* Laségue's sign, *HYPALG* hypalgesia, *HYPAES* hypaesthesia, *PARA* paraparesis, *Cap Haem* capillary haemangioma, *Int Neu Cap Haem* intraneural capillary haeman-

gioma, *Haemangendo* haemangioendothelioma, *MRI* magnetic resonance imaging, *CT* computed tomography, *LE* laminectomy, *compl res* complete resection, *incompl res* incomplete resection; *tib ant* tibialis anterior muscle, *gastrocn* gastrocnemius muscle, *m/yfs* months/years followingsurgery)

Author, year	Sex; age (years)	Clinical presentation	Imaging modalities	Level	Histology	Surgery	Outcome, follow-up
Hanakita et al. 1991 [15]	M; 58	L and left-sided LS; SD of the left L5 and bilateral S1 dermatomes	Myelography, spinal angiography, MRI	L1/L2	Cap Haem	LE T12-L2; compl res	?
Mastronardi et al. 1997 [25]	M; 41	Intermittent L and left-sided LS; diminished left ATR; L'S bilaterally positive	CT, myelography, MRI	L5	Int Neu Cap Haem	LE L5; compl res	No neurological deficits, 1 mfs
Zander et al. 1998 [53]	F; 51	L and right-sided LS; weakness of leg dorsiflexion; no sensory deficit	Myelography, CT, MRI	L4/L5	Cap Haem	LE L4-L5; compl res	?
Holtzman et al. 1999 [18]	F; 56	L and right-sided LS; HYPALG in the right S1 dermatome; diminished right ATR	MRI	L4	Cap Haem	LE L3-L5; compl res	Residual paresis of the right gastrocn, 6 mfs
Roncaroli et al. 1999 [40]	6M and 4F; 40–62	LS (70%); uni- and bilateral paraparesis (60%); nocturnal L (20%); L'S (30%); HYPAES (20%); hyperreflexia (20%); bowel/bladder dysfunction (10%); no deficits (40%)	CT, MRI	8 at the level of the cauda equina, 1 at T5 and 1 at the level of T1 nerve roots	9 Cap Haem and 1 Haemangendo	LE in all cases at different levels; 8 compl res, 1 incompl res	All patients were free of pain; residual paresis in 3 patients; persistent HYPAES in 2 patients; new HYPAES in 1 patient; follow-up period ranged from 2 mfs to 26 yfs
Nowak et al. 2000 [30]	F; 63	Intermittent L; HYPAES and activity-related LS on the ventral aspect of the left thigh	MRI	T12/L1	Int Neu Cap Haem	LE T12; compl res	Residual paresis of the left tib ant, 14 mfs
Roncaroli et al. 2000 [41]	M; 74	Progressive painless PARA; urinary frequency; patchy HYPALG in both distal legs; diminished left QR and absent right QR	MRI	Multiple lesions at L2/L3	Cap Haem	LE L2-L3; two compl res	No change of neurological deficits, 12 mfs

Neurological signs and symptoms

In general, clinical presentation of spinal intradural extramedullary capillary haemangioma does not differ from other intradural mass lesions of the conus-cauda region. Points of distinction between the clinical presentation of patients with spinal intradural extramedullary capillary haemangioma and those with other neoplasms in this location are the lack of severe neurological deficits, which usually develop over a several months period [15, 18, 25, 30, 40, 41, 42, 46, 53] and the non-infiltrative nature of the lesions. Whereas capillary haemangioma is associated with slowly progressive worsening of neurological deficits, cavernous angioma may present with sudden onset associated with bleeding [3, 27, 49].

Table 1 summarises the clinical data of intradural capillary haemangiomas at the level of the cauda equina reported in the current literature. Intermittent, progressive and finally persistent low back and/or uni- and bilateral lumbosciatic pain is probably the most frequent (70–80%) clinical symptom of capillary haemangioma occurring in close relation to spinal nerve roots [15, 18, 25, 30, 40, 53]. Sensory deficits (20–70%) [15, 18, 30, 40, 41], motor deficits (30–60%) [40, 41, 53] and sphincter dysfunction (10–15%) [40, 41] according to the nerve root(s) affected are frequently present.

Characteristic symptoms in cases of intradural extramedullary capillary haemangioma of the lower spinal cord are lumbalgia and lumbosciatalgia (in all cases) motor deficits (in all cases) and sensory deficits (30%) [42,

46]. When capillary haemangioma is partially [46] or completely [16] sited intramedullary or superficially attached to the spinal cord [42, 46], mostly around the level of the conus medullaris, progressive weakness, a sensory level and upper motor neuron signs may occur. Sexual and sphincter dysfunction, eventually combined with saddle anaesthesia, are further symptoms to be encountered.

Radiographic findings

Whereas formerly, myelography, often combined with a computed tomography (CT) scan, was the imaging modality widely performed to detect spinal intradural vascular lesions [17, 31, 35, 48, 53], magnetic resonance imaging (MRI) is the diagnostic procedure of choice today [8, 9, 15, 18, 25, 30, 40, 41, 42, 46, 48, 53]. A surrounding hypointense haemosiderin ring on T2-weighted images was shown to be typical for cerebral cavernous angiomas [39], but was less commonly found in intramedullary cavernous angiomas [4, 48]. A tendency for signal intensity to decrease seems to be a useful hint to strengthen the diagnosis on follow-up MRI studies [48]. Due to recurrent incidence of bleeding, MRI features of intramedullary cavernous angiomas include heterogeneous high and low signal intensity [9, 48].

In the case of capillary haemangioma, these particular MRI findings are usually absent [15, 18, 25, 30, 40, 42, 46, 53]. Spinal intradural capillary haemangioma appears isointense relative to spinal cord on T1-weighted, and isointense or slightly hyperintense on T2-weighted, images [15, 25, 30, 46]. In four cases the lesion was reported to be slightly

hyperintense on T1-weighted images [15, 25, 30, 53], as illustrated in Fig. 1. In general, capillary haemangioma shows homogeneous enhancement following Gd-DTPA administration [15, 18, 25, 30, 40, 42, 46] (Fig. 1). Selective spinal angiography may give additional hints for pre-operative diagnosis of an intradural vascular tumour [15].

It is indeed impossible to differentiate spinal intradural capillary haemangioma from other common intradural extramedullary tumours of the spine by means of MRI. In particular, meningioma, neurofibroma and schwannoma provide similar or even the same MRI characteristics. In a number of reported cases, schwannoma was the preliminary diagnosis, based on the findings obtained by MRI [25, 30, 40].

Surgical intervention and outcome

The surgical removal of spinal intradural tumours was not successfully achieved until the epoch-making report of Gowers and Horsley in 1888 [13]. However, uniformly high morbidity and an operative mortality rate of nearly 50% resulted for patients treated surgically until 1918 [2].

Surgical procedure

Complete surgical removal is definitely the treatment of choice for spinal intradural capillary haemangioma. Depending on the vertebral level of the lesion, a one- or two-level laminectomy was performed in all cases [15, 16, 18, 25, 30, 40, 41, 42, 46, 53]. Access to the intradural space

Fig. 1 Sagittal T1-weighted magnetic resonance (MR) images of the thorocolumbar level of the spine before (*left*) and following (*right*) Gd-DTPA administration. The capillary haemangioma appears slightly hyperintense and shows homogeneous enhancement after Gd-DTPA injection. Enlarged radicular vessels are accompanying the nerve roots cranially and caudally to the lesion [30]

was obtained by a midline durotomy and an operating microscope was commonly used to facilitate total tumour resection [30, 40, 41, 42]. Because of the excessive vascularity of capillary haemangioma, piece to piece resection should be avoided, as bleeding resulting in incomplete resection might occur [46]. Most tumours were removed en bloc [18, 25, 30, 40, 41, 42].

The role of radiation therapy has not yet been investigated in the therapy of spinal capillary haemangioma. Selective spinal angiography has shown to be sufficient to demonstrate the tumour's intense vascularity and feeding vessel(s) [15], but embolisation methods were not performed in any of the reported cases. If complete tumour resection is not achieved, regular MRI controls are warranted.

Surgical outcome

In all documented cases, progression of neurological symptoms was stopped and definite histological diagnosis was established [15, 16, 18, 25, 30, 40, 41, 42, 46, 53]. In the majority of cases, preoperative pain was considerably relieved [18, 25, 30, 40, 42, 46]. Radicular symptoms due to spinal nerve root(s) involvement recovered quite well following surgical intervention, as the capsulated tumour was usually found to be attached to the epineurium of the nerve trunk affected, which facilitated complete resection [18, 40, 53]. Total surgical excision of intraneural capillary haemangioma growing within the sheaths of a spinal nerve trunk, without sacrifice of the nerve fibres involved, is generally possible [25]. However, neurological deficits may result due to partial nerve root dissection [30, 40, 41].

Roncaroli et al. reported the surgical outcome of intradural capillary haemangioma found on the surface of the spinal cord to be comparable to other spinal cord tumours. In particular, patients experienced a slight worsening of preoperative motor and sensory deficits immediately following surgical manipulation [42]. Presumably, this is due to transient oedematous transformation of spinal cord parenchyma. Motor and sensory deficits commonly resolved or substantially improved over a few months after surgery, but sphincter dysfunctions were less likely to improve postoperatively [42, 46].

Histological examination and differential diagnosis

Typical appearance of capillary haemangioma

On gross inspection, spinal intradural capillary haemangiomas appeared as "reddish" [15, 46], "red-greyish" [25, 30], "blueberry-coloured" [20, 53] or "red-blue" [40] tumours of "soft" [25, 42], "moderately hard" [15] or "rubbery" [18, 30] consistency. Figure 2 illustrates the gross appearance of capillary haemangioma as a well-circumscribed nodular vascular lesion [30].

Roncaroli et al. reported ten cases of haemangiomas associated with spinal nerve roots (including one haemangioendothelioma) [40]. The lesions were "situated within the subarachnoid space," and enlarged radicular vessels often accompanied the nerve roots (see Fig. 1). The authors emphasised the varying histological convenience of vascular tumour growth and the neural tissue of affected nerve roots. In three instances, the capsulated tumour was

Fig. 2 Serial section of the tumour (immunohistochemical analysis with the Ki 67 antibody $\times 2.5$). The Ki 67 antibody is reacting with a nuclear protein, expressed during the proliferative phases of the mitotic cell cycle. The section demonstrates an encapsulated nodular lesion seated within the sheaths of a spinal nerve trunk

Fig.3 Histopathological photomicrograph of capillary haemangioma (haematoxylin & eosin staining $\times 6.5$). The tumour specimen consists of a myriad of tightly packed well-formed capillaries lined by endothelial cells. A few cavernous formations are occasionally found within the fields of innumerable clustered capillaries. The nerve trunk of the cauda equina affected by the intraneural growth of the tumour is partially demonstrated in the upper part

Fig.4 Immunohistopathological photomicrograph of capillary haemangioma (CD 34 immunostaining $\times 250$). The endothelial cells lining the capillary lumen are stained red by the CD 34 antibody [30]

adjacent to the epineurium, in six cases several nerve fascicles were involved and displaced by the tumour, and in one case the tumour showed an endoneurial spread of growth [40]. Superficial attachment of the capillary haemangioma to one or several nerve roots of the cauda equina was reported in four cases [15, 18, 41, 53] and intraneural growth within the boundaries of a spinal nerve trunk was found in two additional cases [25, 30].

Roncaroli et al. summarised four cases of capillary haemangioma, presenting at the surface of the spinal cord and conus medullaris, each of which was found to be well demarcated from the spinal cord parenchyma [42]. Shin et al. described a well-circumscribed intradural capillary haemangioma broadly adherent to the thoracic spinal cord with an intramedullary component [46]. Hida et al. reported a totally intramedullary vascular lesion of the cer-

vical cord [16]. The tumour was found to grow disseminated within the spinal cord, and histological examination featured capillary-sized vessels embedded in oedematous, partially necrotic cord parenchyma. It was argued that this case does not fulfil the diagnostic criteria of capillary haemangioma, mainly based on its diffuse growth, lack of lobularity and coexistence of capillary and teleangiectatic vessels [42].

Microscopically, capillary haemangioma features a lobular architecture, with the lobules being composed of tightly packed capillary-sized vessels lined by a single layer of cytologically benign endothelial cells [11, 15, 18, 25, 38, 40, 41, 42]. The lobules are separated by fibrous tissue septa and fed by thick-walled feeding arteries. Some authors focussed their histological description on the encapsulated solid tumour mass, consisting of a myriad of small capillary-sized vessels not considering its lobular architecture [30, 46, 53]. Figure 3 and Fig. 4 illustrate the characteristic histological features of capillary haemangioma [30].

Differential diagnostic considerations

Differential diagnosis from the histopathological point of view should include *arteriovenous malformation* and *capillary teleangiectasia* [21]. Both vascular malformations invariably feature a racemose histological architecture, with isles of parenchyma between the vascular channels. These tumours lack the distinct demarcation from the surrounding spinal cord parenchyma. *Cavernous angiomas* are comprised of dilated hyaline vessels arranged in diffuse patterns with inflammatory cells scattered throughout the stroma. Frequently, thrombosis and perivascular haemosiderin deposition due to (recurrent) bleeding events are found [4, 5, 21, 38].

Haemangioendothelioma may be classified into an epithelioid and a spindle-cell dominant type. It features cellular anomalies and an increasing number of cell mitoses, leading some authors to suggest it is a vascular tumour of intermediate malignancy [10, 32, 38, 40]. However, others regard haemangioendothelioma to be a benign variant of capillary haemangioma [33]. Pericellular deposition of reticulin fibres and collagen IV, as well as uniform spindle cells arranged around a central capillary, are the characteristic findings in haemangiopericytoma. *Haemangiopericytoma* must be considered a potentially malignant lesion [38, 45].

Angiomatous meningioma contains an innumerable number of vessels, and may cause diagnostic difficulties. In these cases, meningotheial cell nests are seated within the vascular channels, and may be demonstrated by immunostains for epithelial membrane antigen.

A *vascular dominant capillary haemangioblastoma* may feature a lobular architecture with feeding vessels and a compact growth [47]. Unlike capillary haemangioma,

haemangioblastoma contains foamy stromal cells, and is not bordered by a fibrous pseudocapsule [50, 52]. Stromal cells secrete endothelial growth factor, and thus play an important role in uncontrolled endothelial cell proliferation [28]. Immunohistochemical stainings are a useful clue in the diagnosis of haemangioblastoma, as stromal cells are reactive for neuron-specific enolase and S-100 protein [38].

Discussion

Pagni et al. reviewed intradural cavernous angiomas of the spine documented in the literature [31]. They concluded that intradural extramedullary cavernous angiomas are the most rare, with only ten cases reported between 1903 [14] and 1990 [31]. In the last 10 years, a few additional cases were published [3, 6, 9, 35, 36, 48]. Intradural extramedullary cavernomas are most common in males (3:1), located at the thoraco-lumbar level and cluster in the third to fifth decades of life [1, 3, 9, 17, 31, 35, 48]. In contrast, intramedullary spinal cord cavernous angiomas are about three times as frequent, and mainly affect females presenting in the second to fourth decades of life [4, 5, 7, 31, 54]. Intramedullary cavernous angiomas have a predilection for the cervical and thoracic spinal cord [4, 7, 54].

Whereas cavernous angiomas consist of diffusely arranged large dilated vascular channels, the unique characteristic of capillary haemangioma is a capsulated nodular lesion composed of capillary-sized vascular channels, which are tightly packed into nodules separated by fibrous septa, and each of which is nourished by a single feeding vessel [11, 42]. Capillary haemangiomas are of benign nature, with slowly progressive growth potential.

Not only histologically, capillary haemangioma can be distinguished from cavernous angioma. Patients with spinal intradural capillary haemangioma are commonly older, presenting in their fifth to sixth decades of life [15, 18, 25, 30, 40, 42, 46, 53]. There is no obvious sex predilection. Clinically, capillary haemangioma is associated with slowly progressive worsening of symptoms, whereas cavernomas often present with acute symptoms due to bleeding. MRI features of capillary haemangioma include iso- or hyperintensity on T1-weighted images and uniform intense enhancement after Gd-DTPA administration. Heterogeneous high and low signal intensity, consistent with recurrent bleeding events, as found in spinal intradural cavernous angioma, is missing in capillary haemangioma.

The surgical goal should be total excision of the lesion. Tumour recurrence had not been reported and is very unlikely. In most instances pain was considerably relieved, and sensory-motor deficits were reversed. Surgical standard procedures consisted of a one- or two-level laminectomy, and were frequently guided by the operating microscope. On operation, the tumour was found well demar-

cated from the spinal cord parenchyma [42, 46], attached to one or several nerve roots of the cauda equina [15, 18, 53] or growing within the sheaths of a spinal nerve trunk [25, 30, 40]. These lesions cause challenging diagnostic problems, because radiologically, intraoperatively and histologically they may mimic other tumours. Knowledge

about their existence is important, as they are benign and potentially curable lesions.

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