EDITORIAL

FROM THE LABORATORY TO THE OPERATING ROOM. IMPORTANCE OF SURGICAL ANATOMY AT THE HISTOLOGICAL SCALE IN NEUROSURGERY.

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INTRODUCTION

Most if not all advances in surgery are built on research works, feeded by basic sciences, from biology to engineering, passing through physics, chemistry, genetics etc. But because surgery is primarily "Applied anatomy", there is no doubt that surgeons should devote a large amount of time to acquire anatomical knowledge and improve skills.

The quest for a solid practical background should not be limited only to morphology, i.e. gross anatomy, even the one observed using microsurgical and endoscopic techniques. Studies should go further, that is at the histological level. As a matter of fact, what we like to name "Histological surgical anatomy" is of paramount importance to understand the histogenesis and the fine structure of the organ and tissue the surgeon has to deal with.

Along the 40-year experience as a neurosurgeon of the senior author with around 25.000 operations performed at all levels of the nervous system from brain to peripheral and cranial nerves, surgery has strongly benefited from a close collaboration with the Research University Laboratories especially of Histological sciences.

Those works contributed to change some basic concepts and therefore surgical objectives. This in turn leads to changes in surgical approaches and creates new surgical operations. This was especially true for surgery performed on the Dorsal Root Entry Zone now a target for some well-defined pain syndromes.

This editorial will provide some examples of this fruitful cooperation with the aim of developing or improving surgery.

Are intracranial (convexity) meningiomas fully cleavable tumours?

Most convexity meningiomas are reputed "tumors easy to remove". However, in spite of a careful dissection under magnification of the operative microscope, resection may lead to some degree of ischemic infarction at the underlying tumor bed which for a a long time was poorly understood, and rises the following dilemma. Attempt at total removal may create new deficit, whereas leaving a remnant in place may increase the risk of recurrence (Alvernia, Dang, & Sindou, 2011). What might be the reasons for that?

Going back to histogenesis, meningiomas arise from the arachnoid-leptomeningeal (and not the dural) layer of the meninges. Starting from this essential histological feature, it becomes clear that vascularization should come not only from the dural arteries (Alaywan & Sindou, 1993; Sindou & Alaywan, 1994) on one side but also from the cortico-pial arterioles on the cerebral side. This can be observed during the microsurgical dissection and can be proven by histopathological examination. The so-called tumor capsule is actually formed by the piamater itself and thus avulsed at resection, which may lead to focal neurological deficits when the tumour is located in "eloquent" areas. Attempt at complete tumour removal should take these histological features into account (Alvernia & Sindou, 2004; Sindou & Alaywan, 1998), and be prudently performed.

The Cavernous Sinus: a no man's land surgical region?

The cavernous sinus has been considered for a long period of time a surgical no mans' land. Reasons were its deep situation and the important contained neurovascular structures.

Histogenetic and histological studies have shown that the cavernous sinus is neither a venous dural sinus nor of cavernous type, but simply a parasellar space between medially, i.e. on the sphenoidal and pituitary side, an osteoperiosteal wall and laterally, i.e. the mesiotemporal side, a dural wall, a space in continuity with the orbit through the superior orbital fissure (SOF).

In addition, histologic studies could demonstrate that its laterally situated dural wall is constituted by two layers giving pass to the third, fourth and fifth cranial nerves (the latter one with a wide meningeal cave: the Meckel cave), pass from an intradural to an extradural location to enter the orbit through the SOF. The sixth nerve escapes this configuration as it transits through the parasellar lodge before entering the SOF.

Studies also showed that this inter-osteoperiosteal-dural lodge contains an abundant venous plexus, which inter-connects the neighbouring skull base venous systems, and crossed by the internal carotid artery, which comes from an extracranial-extradural location (through the proximal dural ring at the foramen lacerum) to enter an intradural location (through the distal dural ring adjacent to the clinoid process).

This revisited anatomical-histogenetic conception of the cavernous sinus led to establishing new bases for more appropriate and safer surgery to this "dangerous" skull base region (Sindou 1995).

The Spinal Cord and its dorsal median sulcus

Intramedullary tumours, especially ependymomas, are classically approached by opening the dorsal medial sulcus (DMS). The DMS, although narrow, is generally considered by most surgeons as a true detectable sulcus on the posterior surface of the cord.

Because practice showed that DMS opening even with microsurgical techniques is not easy and may lead to some degree of dorsal column deficit, we took the decision to launch an anatomical study at the histological scale for a better understanding of the DMSs' real constitution (Jacquesson, Streichenberger, Sindou, Mertens, & Simon, 2014). Study showed that the DMS was not a sulcus but a septum which appears as a thin blade of capillary caring collagen, this septum extending from the adjacent pia-mater and tightly separating the two dorsal columns. Importantly, no arachnoid was found, as well as no true space between the dorsal columns.

From these histological findings it was concluded that penetration into the spinal cord has to follow the dorsal median septum (on the more affected side) as closely as possible to minimize damage to the adjacent dorsal column(s), damage that however will inevitably occur to some degree since no true space exists between the columns.

The Spinal Dorsal Root Entry Zone as a Target for Pain Surgery

The "gate control" theory published in 1965 by Melzach and Wall in the Journal "Science" brought neurosurgeons' attention to the dorsal horn as an important region for the control of pain. The theory put in light the inhibitory role of the primary afferent sensory neurons, that ascend into the dorsal columns and, by their recurrent inhibitory collaterals to the dorsal horn, close the gate to the nociceptive inputs that go up to the supraspinal structures involved in the pain sensation. This theory opened the way to the presently well-known methods of neurostimulation for pain control that are effective in many peripheral neuropathic syndromes. Soon after, in the seventies, we hypothesized that a selective destruction of the excitatory structures of the dorsal horn could be effective in some pain syndromes, especially the ones generated by a hyperactivity of the dorsal horn circuits and neurons.

First step was to check in the Histology lab that the nociceptive fibers and the excitatory structures were topographically segregated from the inhibitory pathways at the Dorsal Root Entry Zone (DREZ) (Sindou, Fischer, Goutelle, & Mansuy, 1974). This was confirmed by the studies of MD Thesis (Sindou 1974) that were published in the Journal of Comparative Neurology (Sindou, Quoex, & Baleydier, 1974).

Next step was to demonstrate the electrophysiological hyperactivity of those structures, especially in the so-called deafferentation pain syndromes, like plexus avulsion or segmental spinal cord injuries. Demonstration was achieved using microelectrode recordings in animal experiments (Guenot, Bullier, & Sindou, 2002) and on the occasion of patients surgeries (Guenot et al., 1999; Guenot et al., 2003).

Also microdialysis studies of the neurotransmitters in the dorsal horn in patients operated on for pain showed that excitatory neurotransmitters were increased and inhibitory ones decreased (Mertens et al., 2001).

After pilot studies indications were codified and popularised through a large number of publications and book chapters (Aichaoui, Mertens, & Sindou, 2011; Sindou, 1995; Sindou, Mertens, & Wael, 2001; Sindou et al. 2005; Sindou 2015).

Peripheral nerves and their surgical repair

The way nerve fibres regenerate after surgical repair – suturing or grafting – has practical implications especially to understand sensory and pain phenomena in the recovery period.

Histological studies in animal experiments (Gloppe, Sindou, Comtet, Fischer and Jeannerod, 1980) show that regrowing of fibres starts by the sprouting phenomenon, one proximal fibre giving rise to a number (often many) of fine non-myelinated fibres of the type C fibres of the Erlanger and Gasser classification. These newly regenerating fibres when attaining the periphery will develop free terminals in the peripheral tissues and behave similar to pain fibres. Then most of them will degenerate excepted the ones that (likely) reach distally the muscular end-plates or the peripheral sensory receptors and that will then become myelinated fibres and contribute to recovery of neurologic function.

It is a common clinical observation that until recovery occurs patients frequently complain of painful dysesthesias and allodynia. These pains can be explained by the at least temporary predominance of C fibres in the peripherally regenerating nerve portion. Thus this histological insight in mechanisms of sensory phenomena helps for an appropriate management of the pain after peripheral nerve repair (M. Sindou & Gloppe, 1982).

Cranial nerves and their hyperactive syndromes

There is now evidence that most of the so called "idiopathic hyperactive syndromes" of the cranial nerves (CN) arising from brain-stem in the cerebello-pontine angle are related to neuro-vascular conflicts (NVC). It is also classically admitted that the majority are located in the root entry (for the sensory CN) or exit (for the motor CN) zone (REZ). This zone corresponds to the central portion of the root and is considered more excitable than the more peripheral portion, characterized by its schwannian structure.

To comfort this hypothesis, we launched an anatomical-histological study in cadavers, of the trigeminal, facial, glossopharyngeal and vagus nerves (Guclu et al., 2011) and also of the cochleo-vestibular CN complex (Guclu et al., 2012). Length and volume of the central myelin portion of the roots were measured and compared in between the various CN studied. Study showed that length and volume had positive correlations with incidence in the general population, of trigeminal neuralgia, hemifacial spasm, vaso-glossopharyngeal neuralgia, and also tinnitus and vertigo for the eight nerve complex.

Although far from all NVCs are located at the REZ, these data contribute to the validation of the role of a vascular compression at the central myelin portion in the genesis of hyperactive cranial nerve syndromes and this influences surgical technique (Sindou, Amrani, & Mertens, 1990; Sindou, Howeidy, & Acevedo, 2002).

Further studies using high resolution MRI with DTI techniques are in progress to help proving and understanding further the mechanisms of alteration of the root at the tissue level (demyelination, decrease in the fraction of anisotropy, increase in the apparent coefficient of diffusion, etc…). These histological alterations, harvested from imaging, appear to be correlated with outcome through prospective statistical studies (Brînzeu, Drogba, & Sindou, 2018; Leal et al., 2014, 2011)

CONCLUSION

These few examples, taken from neurosurgical experience, show that anatomical research at the histological scale – what can be called "Histological Anatomy" – is crucial for the understating of the fine structure of the nervous system and its pathology. Such knowledge is key to performing appropriate surgery and to improving Safety and Effectiveness of surgical interventions.

Therefore we strongly recommend that neurosurgeons – especially those in training – develop tight links with anatomical/histological Laboratories and participate to Research programs dedicated to Clinical Medicine and Surgery.

Of course Anatomy and Histology are not the only fields that the surgeons have to visit. Anatomical-histological studies can be combined with biological and neurophysiological investigations in order to complete the basic skills of the surgeon and open alternative avenues for surgery design and improvement.

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