NEURODIAGNOSIS: A LOOK TO THE PAST AND CHANGING TRENDS OF THE PRESENT

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Abstract:
Perhaps of all the organ systems the central nervous system (CNS) is the most complex and difficult to understand. Physicians have been struggling from the dawn of the medical history to grasp the fundamentals of the CNS and its disease process. Time and again relentless trials of new methods have emerged. The experience gained over the decades along with the improvement in equipment and other pertinent technology facilitate the diagnosis and understanding of this complex system. It has been much simplified in modern days. What medium has not been tried? X-ray, heat, sound and magnet. Each of these approaches surpassed the other yielding further information. Neurodiagnosis has traveled a long way from the simple and crude skull x-rays to the high resolution brain images and it's chemical spectral analysis in vivo.

Key Words: Neurodiagnosis, Radiology - Neuroradiology, X-rays, Computed Tomography of Brain, Magnetic Resonance of Brain.

It is very interesting to stand back and recall those early days of neurodiagnosis. Over several decades there has been much change.

Since the discovery of an invisible ray called x-ray by Wilhelm Conrad Roentgen on November 8, 1895, its use has been continuous.

As early as 1896, Stenbeck, a Swedish physician, obtained a lateral and frontal view of the skull to localize a bullet and in surgery the bullet was removed from the same site of radiolocalization. Perhaps this was the earliest use of x-ray on a human being.

In 1899, Church and Oppenheim demonstrated tumor by skull radiograph. In those days a single skull exposure took about thirty minutes with interval cooling time of one minute.

In 1902, Pfahler succeeded in reducing the exposure time to four minutes with fairly good radiograph of the skull.

Various projections and further detail work was done by Schuller who published a treatise by the end of the nineteenth century.

In 1902, Beclere, in Paris, demonstrated a comparison of normal and acromegalic skull.

Thus, in the first decade of the Twentieth Century, knowledge had been acquired regarding the most important profections for different anatomic structure in the skull (Fig. 1).

At the beginning of the second decade of the Twentieth Century various pathological processes altering the skull such as pituitary and acoustic tumors were diagnosed by simple observation of their location, which were proven at necropsy.

Heuer and Dandy in 1916 reported that only 15 out of 100 skulls were identified as abnormal which correlated well with necropsy.

The birth of neuroradiology is not considered to be true until some part of the brain or intra cranial structures could be visualized. Some form of contrast material was necessary but none was available in those days.

In 1912, gas in the ventricular system was demonstrated by W.H. Stewart on a head injury patient. In the operation, no change in cerebro spinal fluid (CSF) or any abnormality was noted suggesting that the gas was air. This was called pneumatocele.

William as early as 1901, had described various radiological procedures based on air injection but air as a contrast agent was not suggested until 1918.

In 1919, W.E. Dandy (1886-1946) published a paper on "Ventriculography" following the injection of air into the cerebral ventricles (2). This could be considered the birth of neuroradiology. Without knowledge of Dandy, Adolf Bingel (1879-1963) performed ventriculography as well as encephalography. He injected air into the lumbar canal and observed the air rising into the cerebral surfaces.

The first positive contrast material used in neurodiagnosis was iodiosed oil (Lipiodol) introduced by Sicard and Forresteir (1922).

Balado (1928) first used positive contrast material (Lipiodol) in the cerebal ventricles. Due to nonabsorbable oil medium and irritant, it was abandoned.

In the early 1940's, a mixture of ethyl esters of isomeric iodophenyl undecyclenic acid (called pantopaque) was invented. It was, being less droplet forming and irritant, considered to be suitable for neuroradiodiagnosis. During those days the 4th ventricle and Internal auditory canal was studied by this contrast media. Pneumoencephalography has been

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popular since that time. The late 1960's and early 1970's are considered to be the golden era of pneumoencephalography (PEG). Detailed works using fine polytomography were performed, but its use sharply declined to the point of academic interest in the late 1970's.

MYELOGRAPHY

In 1922 Siccard and Forrestier introduced lipiodol. In 1940 pantopaque was available for the study of the spinal canal and the spinal cord. After Dandy and Gingel introduced air in the lumbar spinal canal, lumbar myelogram came into light. Prior to the use of positive contrast material, air (negative contrast) was popular in the European countries. In 1925, Dandy described thirty-six cases of spinal canal tumor localized with air which were all proven surgically except two. In the same series, he described the use of lipiodol and advocated its use even though it was an irritant. He wrote further "its employment makes the diagnosis and localization almost foolproof and doubtless one can exclude spinal cord tumors with equal certainty."

During 1936, air myelogram became popular. This was an excellent negative contrast material which could outline the cord and detect its shape, size and change in appearance according to the position of the patient.

In the early 1930's, Thoratrast was considered an ideal medium, but did not gain much ground due to its high radioactivity.

A constant search for a suitable contrast medium was in order. Some people tried water soluble triiodionated meglumine iothalamate (Conray), but it was very irritating and its use was discarded.

For thirty years pantopaque myelography dominated the scene in the United States whereas the practice of a gas and water soluble medium was confined to a few centers. In Europe, this situation was different. In Sweden, air myelography and water soluble contrast monoiodinated compound (Aberdil) have been used for several years while pantopaque was almost banned.

In 1968, Almen theorized that a non-ionizing material would substantially cut osmolality without reducing iodine content. By the mid 1970's Almen's theory became fact. The first non-ionic contrast medium was introduced in the United States in 1978 and revolutionized neurodiagnosis of the brain and spinal cord.

During the late 1970's and early 1980's, the water soluble contrast agent "metrizamide" became popular due to its easy use, no need to withdraw, better outlining of the spinal cord and roots. The only objection has been that this agent is an irritant to the CNS especially if a large amount is dumped into the ventricular system. It can be epileptogenic and can give trasient neurological deficit, but these complications are not seen on every patient. With careful study and post-study management, complications are minimal.

During the same period myelocisternography became popular and several excellent papers were published delineating the posterior fossa structures.

There was also demand for a less toxic and non-irritant contrast agent. A new compound "iohexol" is on the way which is supposed to be almost isotonic and least irritating of all.

ISOTOPE BRAIN SCANNING

In 1950, isotope brain scan was used utilizing ^{131}I tagged sodium diiodofluorescein. The radioactivity in the brain was detected by Geiger-Muller Counter. In the late 1950's and early 1960's, the most commonly used isotope was gamma emitter iodine tagged human serum ablumin. Various other agents were also used. Introduction of Technicuim 99 revolutionized the practice of isotope imaging. This isotope, with six hours half life and suitable energy (140 kev) for gamma camera is almost an ideal agent. Also there was availablity of slow-lived agents ^{113m}Indium, ^{133}Xenon, ^{85}Krypton by the turn of 1980. Only static brain scan was possible with the old and slow rectilinear scanner but with the advent of the computerized gamma camera, dynamic scanning became popular. The isotope scan is sensitive but rather non-specific.

ANGIOGRAPHY

Argentinian Radiologist Henseo (1919) was probably the first to opacify the blood vessels in human beings. Potassium or Sodium Iodide, an antisyphilitic agent when injected into the vein becomes opaque under x-ray. He offered to outline the pulmonary vein and arteries in a hospitalized patient.

In 1923, Osborne noted that urine become radio-opaque in the bladder of a syphilitic patient being treated with oral and intravenous sodium iodide leading to the discovery by Osborne, Sutherland, Scholl, and Roundtree that iodine makes urine opaque to x-rays.

In 1925, Binz and Rath made iodine less toxic by synthesizing an iodinated phyidine compound.

In 1929, Thomix, a Portugese Neurologist is credited with being first to visualize the human cerebral blood vessels. He investigated various agents and found that 25, sodium iodide was the least toxic. Later in 1931, Moniz changed to thoratrast (colloidal thorazine dioxide) which in his view, could be used without risk. In those days the carotid artery was exposed by cut down method.

In 1932-33, Lous and Jacobi published a monogram of comparative encephalography and angiography.

In 1936, Loman and Myerpon reported the percutaneous puncture of the carotid artery. Also Shimidzu, without knowledge of others, reported the cases of percutanious angiography. Thus they are credited for this methodology.(1, 3)

In 1940 rapid serial angiography came into use.

In 1951, when Radner was trying to introduce a catheter into the thoracic aorta via radial artery, it accidentally slipped into the vertebral artery. Thus, the possibility of vertebral artery catherization was thought of.

In 1956 Lindgren described subclavian and vertebral artery catheterization.

In the early 1960's percutaneous puncture of the carotid and brachial arteries was popular. During those days there was remarkable inclination toward arteriography.

Between 1960 and 1975 there was tremendous advancement in cerebral arteriography. Technical advancement such as biplane serial exposure, high quality film-screen combination, small focal spot, substraction and magnification provided a fine detail of the intracranial vasculatures. Various catheters were invented and superselective catheterization was possible. Major advancement took place during this time and this was considered to be the golden era of neurovascular radiology. Until now this diagnostic modality is considered to be a gold standard of neurodiagnosis.

COMPUTED TOMOGRAPHY IN NEURODIAGNOSIS

Computed Tomography (CT) was first developed in late 1968 by Godfrey Hounsfield at Central Research Laboratory of EMI Limited. In 1972, he introduced a prototype for clinical study of the brain.

Exercises in the reconstruction of images from individual data points has been of interest in mathematics and physics for many years. Radon (1917) Bracewell (1956) Oldendorf (1961) Kuhl (1963) and Cormack (1963) are credited for the early conception of CT. During 1963 and 1964, Cormack published reports on reconstruction imaging, but no one paid attention. Godfrey Hounsfield at EMI independently developed a practical system for radiological studies. Early images were produced from an Americium isotope source and a primitive tool. Initial image production took nine days of scanning and 2½ hours of processing for a single image. Upon switching to the x-ray, the time was reduced to nine hours. The initial commercial EMI unit (Mark X) was only used for head scanning and took 4½ minutes to produce an image. The year 1974-1975 was both controversial and revolutionary. The clinical use of CT began to be popular. Also, several manufacturing companies began to focus in this area. By the end of the 1970's, high resolution dynamic scanners began to proliferate. Today CT has become an essential tool of every community of medical practice. Detailed imaging of the minute structure of the body and the ability to diagnosis in early stages of disease has benefited mankind as a whole. As a result, we have from first generation CT scanner to fourth generation scanner with the capability of dynamic multiplanner scanner.

NEURODIANGNOSIS - PRESENT AND FUTURE TRENDS

DIGITAL SUBTRACTION ANGIOGRAPHY (DSA)

Since the advent of high resolution, fast CT scanner, the role of pneumo encephalogram has diminished to non-existence. Also the role of arteriography and myelography has diminished. In those centers where neuroradiology and neurosurgery services are not available, arteriograms are not performed. Most of the patients are managed with the help of CT scan.

With further advancement in technology, there is a trend to replace arteriography by digital subtraction angiography. DSA, as it is called has not been successful in the production of satisfactory images capable of replacing arteriography. In addition to poor spatial and temporal resolution of DSA, it is not cost effective and does not reduce the radiation exposure to the patient. Even though several medical facilities claim the DSA to be adequate for their daily diagnosis, it is inadequate in the sense of superior quality, detail and ability to image minute intracranial blood vessels. One of the main draw backs of DSA is the requirement of a good quality mask otherwise it gives many artifacts. There are several Neurosurgeons who are reluctant to operate on data from the DSA alone. Its role appears to be limited to the extracranial arteries e.g. the caratid, vertegral, etc. Moreover, for detail visualization of these vessels, arterial DSA is desirable.

ULTRASOUND IN NEURODIAGNOSIS

Leaving behind the old memory of amplitude (A-mode), analysis of midline shift (echoencephalography) of the skull content, we enter a new era of high resolution, multidimensional grey scale, automatised high frequency ultrasound. Even though the skull is a limiting factor in adults, ultrasound use in pediatric ages, especially in peri- and neonates is very beneficial. Without subjecting the unborn, newborn, and toddler to the effect of ionization radiation, we can evaluate the status of the brain. Any obstruction, hydrocephalus, hydrencephalus, hemorrhage, mass or congenital abnormality are precisely determined. It requires knowledge in scanning technique and of the scanned area. Therefore, its use is personnel dependent otherwise it is highly dependable and accurate. In older people, the examination of extracranial blood vessels, spectral analysis and qualitative measurement of the arterial luminal blood passage and degree of stenosis are evaluated by the Doppler system. Even though the place of ultrasound in neurodiagnosis is limited, it has its role which cannot be denied.

POSITION EMISSION, TOMOGRAPHY (PET) SINGLE PHOTON EMMISION COMPUTED TOMOGRAPHY (SPECT)

The PET and SPECT isotope imaging modalities appear to play a secondary role especially in neuro-diagnosis. Putting aside the older isotope brain scan, we venture toward the more comparatively realistic scanner. In his regard PET and SPECT are not to be omitted.

SPECT provides three dimensional quantification of physiologic processes, improvement in spatial resolution and thus better images. One attraction of this system is its ability to utilize conventional, readily available nuclide (^{99m}Tc, ^{123}I) suitable for external detection by a rotating camera head. SPECT produces tomographic images of the brain and gives information about metabolic, functional and physiological status. While this technique is sensitive, it does lack specificity and requires correlation with other imagine modalities.

The PET system has the unique ability to reveal metabolism on a qualitative basis. It has high detection efficiency and spatial resolution due to inherent tomographic nature. PET imaging is the most expensive of all diagnostic tools, time consuming and the least practical, so its clinical utility is not popular.

NUCLEAR MAGNETIC RESONANCE IMAGING (NMRI)

As the CT scanner reaches the fourth generation and is somehow leveling off, many scientists and manufacturers are devoting their time and money to the development of magnetic resonance imaging. Even though the magnet and its use has been known to the scientist for a long time, its use in human beings is new. In the beginning, it appeared that the manufacturers devoted most of their time and money on CT scanners, but now their attention is directed to NMRI. As we recall, the beginning of the CT scanner was rocky. Several technical difficulties, inadequacies and lack of widespread knowledge were prevalent. Within the decade this diagnostic modality has played a main role and revolutionized the whole concept of imaging. NMRI also has to come a long way in order to be popular, useful, and cost effective. In the early stages, the images were rather crude, producing thick sections and the scanning time required is excessively long. If these problems are corrected, NMRI will have a dual role as an imager and chemical metabolic analyser. With a high field of magnetism (2 Tisla or greater) multiplanner images utilizing various modes and chemical spectrao analysis will be a reality. In the near future, we will not only detect early changes by images, but also chemical shifts and changes in the metabolic phenomenon. If ischemia of the brain or occlusion of the small blood vessels could be detected as soon as they occur, then therapy could be instituted immediately. Thus, there would be a higher chance of cure or at least effective management.

In light of recent developments it is essential to look closely at the status of NMRI and its basic principle. As new technology comes to use, we have to train ourselves and adapt to it.

The study of matter and energy and their interaction has occupied mankind's mind for a long time. The resource is there, but how to harness it and utilize it for the benefit of human beings has always been the big question. The existence of "nuclear spins," the heart of the NMRI was known long before the first NMRI experiment reported by Felix Block and coworkers at Stanford University and independently by Edward Percell's group at Harvard in 1946. In 1967 Jasper Jackson produced the first NMRI signal from a live animal. In 1971 Danadian then showed the NMRI might be useful to diagnose cancer based on the observation that diseased tissue exhibits prolonged relaxation time. In 1972 the first two dimensional proton NMRI image of a water sample was obtained by Paul Lauterbur of State University of New York at Stony Brook. Prior to that, Girard has investigated one dimensional distribution of NMR signal. It utilizes magnetic field rather than the radiation to produce the image of the body. The principle of the NMRI is based on the magnetic property of atomic nuclei which in an applied static magnetic field align themselves in the direction of the field. These nuclei process at resonant frequency determined by the strength of the applied field.

The NMRI signal depends upon the hydrogen density distribution in the body, T_1 and T_2 relaxation parameters and the speed through the volume being scanned. In the intensity image, when using a grey scale on which white indicates high intensity, we find that fat is white, soft tissue, grey; muscle, a dark grey; bone, dark grey and black; air, black due to the virtual absence of H_2. Blood vessels with running blood appear black, but clots in the blood appear grey. Many tumors appear lighter than the surrounding tissue because of their long T_1, T_2 relaxation time. Differentiation of white and grey matter can be clear when its relaxation parameters are taken into account.

The images produced by this magnetic system are not fool proof. They can be very misleading because there are several parameters and modes of imaging, e.g. Inversion Recovery (IR), T_1, T_2 and proton density, 2D spin echo (SE) 3D spin echo, to name a few. (4)

Utilizing various parameters such as spin echo technique, the cerebral vascular flow pattern and veins and arteries can be distinguished. Arterial abnormalities and quantification of blood flow can be determined. Thin slice high resolution brain image, quantification of the cerebral blood flow, very early changes in disease process, and chemical analysis in vivo will be the future utility of the magnetic resonance system.

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