The Thalamic Syndrome and its Mechanism

Report of Two Cases, One Due to Arteriovenous Malformation in the Thalamus

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The thalamic syndrome was defined in 1906 by Dejerine and Roussy who original description has been little improved upon. Confusion still surrounds the true nature of many of the disorders that have since been labeled "thalamic syndrome." As originally described, it possessed the following features: 1) continuous pain on one side of the body commonly referred to as aching, boring, gnawing, burning, icy, or crushing; 2) paroxysms of hypersensitivity to sensory stimulation, sometimes of sufficient severity to prevent adequate sensory examination; 3) elevation of the sensory threshold, generally slight in degree and selective of certain sensory modalities; 4) referral of pain over a wide area which may not include the location of the actual stimulus; 5) evocation by touch, pain, heat, and cold of similar diffuse highly disagreeable sensations more unpleasant and less definable than the effect of the same stimulus to an unaffected area; 6) a distinct lag between the time of application of a stimulus and its appreciation; 7) pain which may far outlast the stimulus which evoked it; 8) lack of association with severe motor deficit, so much so that the presence of severe paresis argues against the painful state being of thalamic origin.

Consideration of the physiology of sensation is essential in understanding the disturbances present in patients with thalamic and other central pains. Head et al. in 1905 first postulated that the afferent system incorporated double qualities to which he applied the terms protopathic and epicritic. These terms have lost popularity in the recent literature but the concept of two types of pain remains. In 1915 Ranson suggested that "protopathic" or what we now call "slow pain" sensibility was transmitted in peripheral nerves by fine unmedullated fibers. In 1930 Erlanger and Gasser studied peripheral nerve transmission by action potential measurements and classified them by fiber size and rate of transmission; the large medullated fibers served as conductors of highest velocity impulses, small medullated fibers had an intermediate conduction rate, and the unmedullated fibers conducted at the slowest rate. Also the threshold of response varied inversely with the fiber diameter.

Attempts have been made to relate the different modalities of sensation to specific types of fibers. Most experimenters have attempted to block certain sized fibers differentially and then determine which sensory modalities have been impaired and which remain intact. Studies of neuronal asphyxia clarified the roles of the types of fibers transmitting various sensations, for it was found, after applying an atraumatic clamp to a nerve or a pressure cuff to an extremity, that the modalities of "fast pain" and temperature discrimination were lost early whereas "slow pain" transmission persisted. During the persistence of slow pain the response to stimulus was exaggerated and the pain had many of the features of thalamic pain. Kendall performed an illuminating experiment upon himself by running water at 35°C over his elbow for one hour after which he tested sensation in the distribution of the ulnar nerve to his hand. He found complete loss of thermal discrimination in the affected area where both hot and cold stimuli were appreciated as heat having an intense, unpleasant, burning quality after approximately one second's delay in perception of the stimulus. It thus appeared that the rapidly appreciated sensations could be divorced from the slow ones, resulting in thalamic-like pain from a subthalamic, even peripheral, level. Studies of cocainized nerves in which the chemical tends to block the more slowly transmitting fibers first and the rapidly transmitting ones last, have yielded more variable results.

The various fibers which subserve pain

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sensation are intermingled in the peripheral nerves and the spinothalamic tract of the spinal cord. The larger medullated components then course superficially in the mesencephalon to the ventral posterolateral (VPL) nucleus of the thalamus. Of great interest are the separate courses taken by the fine unmedullated pain fibers to the reticular formation, central grey, nucleus intercollicularis and deep strata of the superior colliculus and then to the thalamic nuclei parafascicularis, paracentralis, and centralis lateralis. During axon degeneration studies in humans, Bowsher has found, in postchordotomy subjects, distribution to the ipsilateral lateral reticular nucleus of the medulla and bilaterally to the VPL nucleus and the medial reticular substance of the medulla. Degeneration to the VPL nucleus was seen by Biemond in a case of softening involving the secondary sensory area of the parietal cortex. This patient had a severe painful state of the contralateral half of his body with hemihypaesthesia, though all other modalities of sensation were intact. The study of patients subjected to stereotactic thalamotomy for relief of pain sheds some light on the physiology of the thalamus and the perception of pain. Mark et al. found their eleven patients treated for pain of advanced cancer fell into two groups. After surgery, the patients of one group experienced no relief of the pain of the disease. The pains of the malignant diseases could no longer be localized but the patients were no more comfortable than they had been prior to thalamotomy. The lesions producing these results were primarily in the VPL and ventral posteromedial (VPM) nuclei. The patients in the second group were relieved of pain and had minimal or no sensory deficits. The lesions producing this effect were found primarily in the parafascicular and intralaminar nuclei. The study of thalamic lesions produced by Hécaen et al. in attempts to alleviate thalamic pains is similarly instructive. Four of 5 patients in whom lesions were made in the medial thalamus were pain-free for periods up to several months. One of these 4 patients experienced paresthesias at 5 months, but had no pain. The 5th patient had recurrence of moderate pain after 2 1/2 months but no further worsening occurred in the next 8 months. Two other patients having lesions in nucleus VPL experienced considerable sensory deficit without satisfactory relief of pain.

Pertinent also is the result achieved by Logue with a small lesion in the centrum medianum. His patient suffered from recurrent pain in the left leg after bilateral thoracic chordotomy for spinal malignancy. Complete relief followed the creation of such a thalamic lesion and it endured for the patient’s remaining 8 months of life. No sensory deficit was produced by this operation. The patient’s course strongly suggested that the permanent relief of pain resulted from the thalamic lesion and not from the compression of the cauda equina by the malignant process at L-3. At post mortem the 4 mm. lesion was primarily in the centrum medianum with but slight extension into nucleus parafascicularis.

Dejerine and Roussy believed that the lesion responsible for the thalamic syndrome resulted from occlusion of the thalamogeniculate artery. Others have found the classical thalamic syndrome sequential to softening of the posterolateral thalamus alone. In the majority of cases the disturbances appear to have been produced by hypertension or arteriosclerosis that resulted in infarcts or hemorrhages in the thalamus; other etiologies are embolism, diabetic arteritis, intracranial aneurysms, and arteriovenous malformation. However, pain having many if not all of the features described by Dejerine and Roussy has resulted from a variety of pathological lesions in several sites including the peripheral nerves, the spinal cord, the medulla, and the mid-brain. Even lesions of the cortex not involving the thalamus seem to have produced the thalamic syndrome.

Neoplasms only rarely produce the thalamic syndrome. The brains of 6 patients who died of thalamic tumor were examined by Smyth and Stern by a technique which allowed determination of the intimate distribution of the tumor and they were able to distinguish areas entirely replaced from areas merely infiltrated by tumor. Dividing the cases in two groups, based upon whether tumor origin was in the medial or the lateral portion of the thalamus, they found the clinical manifestations varied significantly with the pathological grouping. Those in