PAPILLOEDEMA

SIMON BEHRMAN, B.Sc. (Lond.), F.R.C.P.

*Physician, Moorfields Eye Hospital;
Neurologist, South-East and North-East Metropolitan Regional Hospital Boards.*

History

Herman von Helmholtz—unique among scientists in modern times in occupying successively chairs in physics and physiology—published details of his “Augenspiegel” in 1851, and von Graefe was among the first to apply ophthalmoscopy to ophthalmology. In 1860 was published his paper in which he described four cases illustrating the relationship “optic neuritis and sarcomatous brain tumour”.

Definition

Papilloedema is passive oedema of the optic disc without inflammatory changes, and often without disturbance of vision.

The oedema remains circumscribed to the relatively loose tissue of the nerve head, since Müller’s fibres, which constitute the main framework of the retina, impart an exceptional degree of compactness to the retina. They effect this by transversing all the layers of the retina from the external to the internal limiting membranes and giving off fibrillar extensions at intervals. The laxity of the nerve head is not only due to absence of fibres of Müller but also to the attention of the astrocytes at the papilla where they become “spider cells” which unlike typical astrocytes have no attachment to capillary vessels.

Pathology

In the early stages microscopic sections reveal little that cannot be recognized by the ophthalmoscope. The swollen optic disc not only protrudes forward, against the vitreous, but it bulges also laterally throwing the retina immediately surrounding the disc into small folds. With higher magnification tissue fluid can be seen enmeshed in the nerve fibres, thus loosening the tissue elements of the nerve head. The centrally situated nerve bundles are displaced forwards and inwards. In consequence the dimensions of the physiological pit become greatly reduced. However, a congenital dense band of connective tissue tethering the central vessels to the lamina cribrosa may cause the pit to be preserved even in the advanced stages of papilloedema.

In young subjects oedema, when severe, can occasionally be seen to spread in the form of small vesicles from the disc margin, and to follow the nerve fibres converging upon the macula, thus giving rise to the appearance of the macular fan, with the apex at the macula. Macular “fan” is not to be confused with an incomplete macular “star” the pathology of which is entirely different. The central vessels sweep over the swollen optic disc, and this abrupt change of direction at the periphery, and consequent loss of light reflex of the vessels in this position, accounts for an important ophthalmoscopic sign of papilloedema. The capillaries of the nerve head are dilated. This as also the resulting disturbance of micro-circulation, can well be demonstrated by means of fluorescein fundus photography.

The first degenerative changes, which appear after an interval, consist of localised swellings of the individual slender naked nerve axons which at the disc are 1.5 μ in diameter. These varicosities enlarge, becoming spindle-shaped or globular in form. At first continuity between this swelling and the nerve fibre can be demonstrated at both ends. Later, connections with the original nerve fibre become invisible, and the bulbous swelling comes to resemble a cell body, an illusion which is fostered by the staining characteristics which differentiate a highly refractile central pseudo-nucleus and pseudocyttoplasm. The swellings have, therefore, been called “cytoid bodies”, and are in all essentials similar to cytoid bodies found in clusters in the nerve fibre layer of the retina in the cotton wool spots. *Pari passu* with these changes there occurs glial proliferation which leads to shrinkage of the disc and obliteration of capillaries. Eventually this process brings about the characteristic changes seen in optic atrophy.

Diagnosis

In the great majority of cases there should be little difficulty in deciding whether optic-disc oedema is present or not. Early papilloedema or long-standing low-grade papilloedema with minimal mushrooming, and excess, or neuro-

glial tissue at the optic disc may, however, tax the judgement of the most experienced. Conditions which at various times have been grouped under "pseudopapilloedema" are particularly liable to simulate these latter cases, viz those with minimal elevation of the disc, with or without excessive gliosis. Among them are those in which there is heaping up of the nerve fibres at the optic disc caused by a congenital narrowing of the scleral canal. This condition, which is said to be more common with hypermetropia may simulate low grade papilloedema very closely (Lambert and McDonald, 1930). Swelling of the papilla may also be due to the deposition in its depth of a cryptogenic hyaline material which the early German ophthalmologists described as "drusige Ablagerungen" and which despite much opposition has retained, to this day, the name of drusen. Drusen is distributed irregularly, in microscopic depots, within the substance of the disc, anterior to the lamina cribrosa but rarely reaching the vitreous surface. This material, which is basophilic and acellular, is liable to become calcified. Varying degrees of disturbance of vision, presumably due to involvement of nerve fibres, have been reported in such cases (Chambers and Walsh, 1955).

Symptoms

Papilloedema in the early stages is entirely symptomless. Severe papilloedema is occasionally associated with brief attacks of blurring or loss of vision. Very rarely the disturbance of vision affects one eye only. With onset of degenerative changes at the nerve head, there occurs progressive deterioration of vision.

The conditions under which papilloedema is encountered can be listed as follows:—

1. Disorders associated with generalized brain swelling.
2. Disorders associated with elevation of intracranial pressure.
3. Diseases involving the anterior segment of the optic nerve.
4. Reduction of intra-ocular pressure.

1. Disorders associated with generalized swelling (intumescence) of the brain.

From the point of view of pathology of oedema, the brain differs from other tissues of the body, in two respects:

a. Whereas following such procedures as water intoxication in pitressin-treated animals, or intraperitoneal injections of saline, there is great increase in body weight, the brains of the animals so treated show neither change in the water content nor in the microscopic appearance.

b. In contrast to most other tissues, the electron micrographs of brain tissue reveal only 200°A distance between closely packed cells and processes and little extracellular space. Calculations based on standard sized cellular elements indicate that this space amounts to approximately 5% of brain volume.

This figure is in agreement with estimations on the accumulation in the brain of such "indicators" of the extracellular space of the CNS as ^{35}S sodium sulphate.

The electron microscope has revealed that experimentally produced oedema in cerebral cortex is an intracellular phenomenon consisting of massive swelling of glial cells. The major site of gross brain swelling is, however, the white matter. The ultrastructural changes here vary with the experimental method of producing oedema. In the oedema in rats intoxicated by tri-ethyl tin, the swelling was found to be due to fluid containing vacuoles or "blisters" formed by splitting of myelin lamellæ. On the other hand, enlarged spaces, which are regarded as extracellular, are seen in a variety of white matter oedema. It is uncertain whether in part they are produced by fracture of glial membranes. It is clear from the foregoing that though generalised "swelling" (intumescence) is a common pathological event, and can be readily produced by various means experimentally (anoxia, ischaemia, trauma) the precise pathological mechanism of this phenomenon is little understood. It occurs in a variety of conditions, all of which, at the more advanced stage, are associated with papilloedema. Among them are pseudotumour cerebri (Dandy, 1937); malignant hypertension (Byrom, 1954); tetany (Grant, 1953); respiratory deficiency with hypercapnia (Miller, Bader and Bader, 1962); intoxications with lead and tin compounds (Popoff, Weinberg and Feizin, 1963; Magee, Stoner and Barnes, 1957); Addison's disease (Jefferson, 1956); interruption of corticosteroid therapy (Benson and MacKeith, 1961); and vitamin A intoxication (Morrice, Havener and Kapetansy, 1960).

2. Disorders associated with elevation of intracranial pressure.

It is commonly agreed that there is no direct or linear relationship between elevation of intracranial pressure and papilloedema. This has been borne out by numerous experiments on monkeys, and by clinical records in which exceptionally high intracranial pressure were noted in the absence of papilloedema. It is clear that at least one factor other than elevation of intracranial pressure is required. Generalized brain swelling (intumescence) already described

would appear to be this factor. Perret and Kernohan studied the histopathological changes of the brain caused by intracranial tumours (Perret and Kernohan, 1943). They reported cases in which the "entire" white matter of both hemisphere of a tumour-bearing brain was "alveolar or sieve-like" in appearance, and this they attributed to "œdema". "We found a relatively small glioblastoma multiforme growing in the medulla oblongata. This tumour had produced slight internal hydrocephalus, and was accompanied by very severe œdema of both cerebral hemispheres. In this case the hydrocephalus was slight and had not prevented the brain from becoming œdematous".

It must be emphasized that, under consideration here, is the *generalized* intumescence of the brain, and not the "swelling" or "œdema" constantly seen around and in the vicinity of, a brain tumour. Machesini examined 120 brains and noted a definite relationship between swelling of the brain and papillœdema. (1934).

Raised intracranial pressure is commonly due to intracranial neoplasms or to the obstruction of the channels of spinal fluid flow in a number of well known critical anatomical positions by a variety of pathological conditions, congenital and acquired. These need not be considered here. Another important cause of elevation of intracranial pressure is interruption of the drainage of the dominant dural sinus. Pennybacker (1943) has described a small series of such cases. Among the pathological conditions were the following: — tumour of thymus compressing the innominate vein, and causing retrograde thrombosis of the left internal jugular vein and left transverse sinus; a small penetrating wound in the region of right lateral sinus. More recently papillœdema was described following unilateral radical dissection of lymph glands on one side of the neck (Marr and Chambers, 1959).

It is well known that an infective process in the vicinity of an intracranial venous sinus, such as mastoiditis, by causing thrombosis, may engender the syndrome of "otitic hydrocephalus" Greenfield when describing the autopsy findings in one such case, was at pains to emphasise the degree of brain swelling in the absence of my dilation of the ventricles (Greenfield, 1936).

3. *Diseases involving the anterior segment of the optic nerve.*

These diseases when associated with papillœdema, are said to exhibit the syndrome of "papillitis". Papillitis should, of course, signify a morbid condition in which the optic nervehead is the seat of inflammation. Used in this sense,

this terminology is inappropriate in demyelinating diseases, since the site of the inflammatory process must be *retrobulbar*, as myelination ceases a short distance behind the lamina cribrosa. Yet swelling of the disc can be very considerable in these diseases and can mimic ophthalmoscopically severe papillœdema in every respect. Furthermore, these changes at the disc are capable of such rapid resolution as to render an inflammatory process unlikely. It must be concluded, therefore, that the swelling of the nervehead is due to œdema as the ophthalmoscopic appearance suggests. Thus, the inflammatory process within the nerve seems, under certain conditions, to engender œdema of the nervehead. Concerning one such condition there is a wide measure of agreement, viz. for swelling of the disc to occur the plaque of demyelination must be situated in the most anterior segment of the medullated part of the optic nerve. Clearly the topography of the lesion is of paramount importance.

Ischaemic lesions in this region of the optic nerve, as is known to occur in giant cell arteritis, can give rise to a similar temporary "papillitis". The lesion of the optic nerve also accounts for the temporary or permanent disturbance of vision seen in these cases. Orbital space-occupying lesions by involving this segment of the nerve, are occasionally associated with papillœdema, before severe degree of optic atrophy sets in.

Rapid failure of vision is occasionally encountered in association with swelling of the optic disc ("papillitis") and the simultaneous or delayed appearance of keratic precipitates on the posterior surface of the cornea.

In these rare cases affections of anterior segment of the uveal tract are associated with optic nerve lesion (Fry, 1938).

4. *Reduction of intraocular pressure.*

Any condition liable to bring about a sudden lowering of the intra-ocular pressure (such as perforation of the globe following cautery puncture, or a trephine operation) may be followed by papillœdema.

Pathogenesis of Papillœdema

Von Graefe in his original paper attributed the optic disc œdema occurring in association with brain tumours, to pressure on the cavernous sinus. Subsequent observations that thrombosis of the cavernous sinus could occur without coincidental papillœdema, disproved this theory. By the same token cases of central retinal venous obstruction without associated papillœdema, should be regarded as providing

evidence which would render untenable any theory of the pathogenesis of papilloedema based on obstruction of the central retinal vein. Reference to such cases can be found in Paton and Holmes' classic paper on papilloedema (1911).

Any theory of the pathogenesis of papilloedema must take account of such cases, as also of all the four conditions—already considered—which favour the development of papilloedema.

The perivascular space surrounding the central retinal vessels within the optic nerve has been traced to the perineural subarachnoid space, where it is enclosed in the "arachnoid tube". (Singh and Dass, 1960). Behr has repeatedly emphasized the absence of any demonstrable union between the adventitia of the central retinal artery and the dura where the artery traverses obliquely the dural sheath (1935). These morphological details serve to establish the basis for the existence of a channel between the retina and the orbit. Because of the known pressure gradient it can be concluded that the

flow in this channel must be in a retrobulbar direction. Based on these morphological and barological considerations, Behrman has put forward recently a theory of the pathogenesis of papilloedema (1964, a and b).

This theory can be summarized as follows:

1. The stasis oedema of the most lax region of the fundus oculi constitutes papilloedema.
2. The stasis oedema of the papilla occurs when there is choking of the perivascular space enveloping the central retinal vessels within the optic nerve, or when the intraocular tension is inadequate to maintain the flow within this channel.
3. The principal cause of choking of this fluid channel is intumescence of the channel-bearing segment of the optic nerve. Such intumescence may be due to a localized lesion or part and parcel of a generalized encephalon intumescence. Such affection of the optic nerve was observed by Glew (1960) among monkeys in which raised intracranial pressure was produced by means of an inflated balloon placed in the subdural space.

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