THE DIFFERENTIAL DIAGNOSIS OF URÆMIA AND MENINGITIS, WITH REPORT OF OBSCURE CASES.

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Uræmia is usually readily differentiated from organic cerebral disease, yet confusion may occur in atypical cases. Leube's chief rule in the diagnosis of uræmia is formulated as follows: In patients with nephritis uræmic intoxication is to be assumed as the cause for nervous symptoms only when other causes can be excluded. This method of diagnosis by exclusion has served Leube well, and he considers the method important, since in the course of renal disease occasional organic nervous lesions, such as hemorrhage and meningitis, may simulate uræmia. The clinical diagnosis in such cases is often made only with a certain degree of probability.

Pre-eminent importance attaches to the presence of albumin and casts, and to the amount of urine. With typical nephritic findings in the urine the diagnosis of uræmia is usually easy. Exceptions exist in that nephritis may be unattended by albuminuria, casts may be permanently absent (Ackermann), and uræmia may intervene when the amount of urine and urea is normal (Christison). I have had under observation for over a year a case of chronic parenchymatous nephritis in which every variety of cast—epithelial, granular, and hyaline—is constantly present, while albumin is absent for months consecutively. Liebermeister instances a case in which immediately before a uramic seizure both urine and urea were increased twofold. To offset this case, Biermer reports an instance of anuria for 222 hours before uræmia appeared. Albumin alone is no proof of uræmia, as it may occur in nervous lesions; e.g., meningitis, hemorrhage, epilepsy, tetanus, etc. According to Fleischer, uræmia being due to cerebral anæmia, we must guard against confusion with cerebral anæmia of other origin, since lowered arterial pressure may induce both cerebral anæmia and albuminous urine. Such albuminuria is transitory and unaccompanied by casts.

When conspicuous cardio-vascular symptoms attend nephritis they become valuable diagnostic adjuvants, worthy of considerable, but not implicit, confidence. Case III. exemplifies this point (latent meningitis with albuminous urine and cardio-vascular alteration, v. i.). Cardiac hypertrophy predisposes to apoplexy, hemorrhages, and inflammations in various viscera, especially in the retina. Cortical irritation increases arterial tension. Moderate arterial tension increases the cardiac force, while excessive tension decreases it. Redundant toxins paralyze the
vasomotor system and the heart's strength flags by the absence of that
difference in arterial tension imperative for the maintenance of the
circulation, hence the multiplicity of cardiac conditions conceivable in
uræmia. The pulse is slow, 40 to 60, before a uræmic attack (Thomas,
Rosenstein, and Wagner), and later, after a convulsion, it is usually
rapid. Early in meningoïd the pulse is slow; later it is frequent.

Most important are the ophthalmoscopic findings, for retinitis albu-
minurica is rarely absent in chronic nephritis, leading to uræmia (Leube),
and in acute uræmia the abundant albumin, casts, and edema are suffi-
ciently suggestive. In meningoïd the pupils are mostly narrow and in
uræmia dilated, yet uræmic myosis is observed.

Leube does not hesitate to admit that in certain cases the diagnosis of
meningoïd is for him more difficult than of any other cerebral lesion,
because the complexus of symptoms varies and certain signs of menin-
gitis occur in other intracranial diseases. Uræmia and meningoïd have
many symptoms in common—dellirium, headache, vertigo, coma, convul-
sions, irregular breathing, and vomiting. Confusion is especially prob-
able when the convulsions are localized in a few muscles, in which partial
contractures, focal paralyses, and temperature appear. In such combina-
tions the most experienced diagnostician may err. Meningitis and
uræmia may coexist, yet meningitis is the least frequent of all the forms
of serositis to which the uræmic patient is exposed. Broadly speak-
ing, circumscript convulsions and paralyses speak strongly for anato-
mal changes in the central nervous system, especially when constant,
although such alterations occur rarely in uræmia. In uræmia they are
chiefly fugitive. Literally I know of no focal nor general symptom or
sign observed in meningoïd which has not been recorded, singly or
combined, in uræmia.

A synopsis of anomalous cases observed by others, with several of my
own, seems in place because of meagre mention of the subject in litera-
ture. Jolly and Guinon admit possible errors between uræmia and
meningoïd. Desnos reports a case in which the patient during sound
sleep was suddenly seized with dyspnoea, coma, and vomiting, and the urine
showed much albumin. On autopsy the kidneys were normal, but there
was a hemorrhage the size of a nut in the pons Varolii, breaking into
the fourth ventricle. Rosenstein remarks that diagnosis is nearly impos-
sible when motor and sensory symptoms occur synchronously with
nephritis, which are due, however, not to urinary retention, but to a
palpable disease—e.g., meningoïd. He cites a case: Urine 1009, much
albumin, red and white blood-cells, casts, fat-granules; headache; dilated
heart; coma; temperature 39.4°C; wide pupils; no paralysis; slight
twitchings of nurns; autopsy disclosed nephritis plus suppurative nasal
meningoïd. Murchison has described cases of uræmia closely resembling
meningoïd, presenting rigid neck, convulsions, and coma; but Gowers
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remarks that the temperature is normal in uremia, v. i. Rosenstein's experience includes a case of uremia with edema, but without urinary findings, presenting a typhoid appearance; the post-mortem disclosed nephritis.

Stenhouse Kirkes drew attention to the fact that not all cerebral symptoms in nephritis are functional, but that some are of organic origin—e.g., apoplexy. Thus uncomplicated aphasia was found due to hemorrhage in Broca's convolution.

In meningitis the breathing is frequently sighing, irregular, and of the Cheyne-Stokes type. In uremia, asthmatic attacks, angina pectoris vasomotoria, a laryngeal croup type, Cheyne-Stokes breathing, and cyanosis are recorded.

The subject of temperature in uremia is a mooted point. Many maintain it is reduced (Kien, Roberts, Hirtz, Billroth, Thaon, Hutchinson, Bourneville, Budin, Hanot, Lecombe, Behier, Lionville). Netter observed the temperature fall as low as 30° C. Others note a rise (Tarmier, Torday, Hippolite, Chauffard, Tenneson, Chantemesse). Lépine found that the temperature may rise without convulsions or inflammation, explicable by vasomotor irritation and decreased heat-elimination. Landois produced a rise of temperature by irritation of the cerebral cortex, caused by vaso-constriction. Unusually low temperature is found where vasomotor paralysis exists and effete products accumulate in the system. Strümpell observed not uncommonly a temperature rising to 39° C, irregular in type, rarely reaching 41.5°, and often associated with chills, vertigo, sweating, headache, and tinnitus aurium. Rosenstein expects low temperature only in subjects depleted by diarrhea and vomiting. Bartels, Guyot, d'A. Robert, Dumont, and others confirm Rosenstein's position, although most authorities oppose his views.

The most concise general statement regarding uremic nervous phenomena asserts: 1. That paralysis affects especially the sensorium, to a less degree the special senses, and rarely motility; 2. That irritation seldom selects the sensorium (e.g., delirium); it mostly engages the motor paths (convulsions), and never implicates the special senses.

Uremic convulsions are tonic or clonic. Described usually as general, they may by unusual localization resemble focal symptoms. Thus Rosenstein, Strümpell, and Bartels have found convulsions on half the body, one-half the tongue, and in the left arm and leg, with deviation of the head to the left. They have occurred with convergent strabismus, facial spasm like tic convulsive (Lasègue and G. Sée), delirium, etc. Convulsions have simulated epilepsy and Jacksonian epilepsy. Nystagmus, localized tremblings, and twitchings are recorded. Twitchings are easily overlooked before and after coma (Traube). Grinding of the teeth, frequently observed in meningitis, also occurs in uremia (Strümpell and Bourdillat). Although tonic convulsions rarely
complicate uræmia, yet a tetanic type is recognized. The cases of uræmia of Thomas, Weiss, d'Aran, de Hauser, Rauth, and Jaccoud exhibited trismus. Avrard relates a case in which convulsions on one side and contractures on the other were combined. Jaccoud places on record three cases of spasmodic contractures of the forearm and cervico-dorsal flexors, producing opisthotonos. Convulsions and contractures have coincided upon one side of the body, and a case of flaccid hemiplegia was transformed by uræmia into hemiplegia with convulsions and contractures (Raymond).

Rigidity of the neck, rarely absent in meningitis, cannot be excluded from the symptomatology of uræmia (cases of Jaccoud,11 Kussmuller,12 Rose,13 Weiss,14 Coheu,15 and Thomas). The hands, usually free in tetanus, are involved in uræmia. Retraction of the head is also caused by rheumatism,14 diseases in the medulla, aneurism of basilar artery, brain tumors in the posterior fossa, peripheral irritation, tender cervical glands, and abdominal disturbances.

Paralyses in uræmia are infrequent, so that Lesègue, Lecorché, and Talamoa deny their existence. They are chiefly transitory hemiplegias. The cases assigned are cerebral edema, capillary hemorrhage, softening, apoplexy, inflammatory foci, or cortical overstimulation by toxins. Some instances of hemiplegia are the following: Cases of Fuché,29 Baginsky,30 Addy (with aphasia, amnesia, and deafness31), Paetsch,32 Churchillo,33 Imbert-Gourbeyre,34 Rego (aphasia35), Lequima,36 Raymond,37 Charpeatière,38 Thomas,6 Blackhall, Leichtenstern, Simpson, Townsend, Rosenstein, Chauffard, and Mutenesse. Paraplegia seems to have occurred but twice.39 Jaeckel in four hemiplegias found facial paralysis twice and one crossed oculomotor paralysis, with no post-mortem lesion except edema cerebri. Other combinations are: aphasia with facial paralysis (Dieulafoy37); glossoplegia,38 neuralgia, myosis, spasticity of arm, right facial paralysis and right hemiplegia.41 Dunin's cases exhibited the following focal symptoms: Case 1, unilateral spasm; 2, unilateral spasm with aphasia; 3, aphasia, both internal recti paralyzed, diplopia, nystagmus.

The following histories illustrate the difficulties met in equivocal cases:

CASE I.—Woman, aged forty years; delirious; pulse 90 to 120; fairly continuous temperature, ranging between 101.9° and 102.6°; tongue dry and coated brown; glazed pharynx; respirations 30; diffuse bilateral moist mucous rales, with signs of hypostasis over the lower lobes behind and at base; pulse not tense; second aortic tone slightly accentuated; arteries somewhat tortuous and rigid. The urine is ammoniacal, 1015, albuminous, but contains considerable pus and micrococci, yet no casts warranting a diagnosis of cystitis; the amount cannot be obtained on account of involuntary evacuations. There is divergent strabismus due to paralysis of the left internal rectus; there is ptosis on the left
side and right hemiplegia, complete save for the upper facial twig. The paralyses were present five days ante mortem. Clinical diagnosis—meningitis and cystitis. Autopsy—edema of the brain; no meningitis; no cerebral lesion; arterio-sclerosis; diffuse hrmachitis with hypostasis; diffuse pyelonephritis secondary to cystitis; hence uraemia.

CASE II.—Married woman, thirty-three years old; denies syphilis and abortions; mind wanders, and her accounts of the previous history and present illness are unreliable. No edema; no leucoderma; no eruption; slight alopecia; pharynx and mouth negative; pulse, temperature, and respiration normal; reflexes somewhat exaggerated; sensation normal except some slight general hyperesthesia, especially over tibia. The left abduces and left oculomotor nerves and the lower half of the right facial nerve are paralyzed; power in the extremities is apparently normal, but the mental condition makes voluntary muscular tests difficult. The urine shows hyaline and granular casts and abundant albumin, still no additional lesion in the cranium is suspected from the multiple nerve-affectons, and a process at base of cranium, probably syphilis, is diagnosed. Antisyphilitic treatment futile; sudden death. Autopsy—chronic parenchymatous nephritis, with the usual microscopic and microscopic findings; left heart dilated, but not hypertrophied; brain absolutely negative; hence no cerebral lesion, but uraemia.

CASE III.—Man, aged forty years; admitted to Cook County Hospital in delirium, without any history; marked arterio-sclerosis; tortuous braclials; atheromatous plaques on radials; pulse 90, tense, regular, quick; no temperature; left heart distinctly dilated; apex in left vertical nipple-line strong and heaving; the second aortic tone loud and metallic; urine heavily loaded with albumin, but no casts nor formed elements found. The diagnosis lies between uraemia and meningitis. No rigidity of neck, no ear disease, no temperature, no focal symptoms; retina negative. Because of the cardio-vascular changes and albuminuria I diagnosticated uraemia. Autopsy—marked universal arterio-sclerosis; atheroma aortae; hypertrophy and dilatation of the left ventricle and to a less degree of the right; kidneys and other viscera wholly negative; no diffuse purulent meningitis over base and convexity originating from an empyema of the sphenoid sinuses. (V. s., regarding value of cardio-vascular signs in the diagnosis of uraemia.)

CASE IV.—A case closely resembling delirium tremens, with history of recent and ancient alcoholic excesses. Urine 1018, acid, much albumin, 1500 to 1800 cm. per diem; moderate number of hyaline, granular, and epithelial casts; history of previous masuace and ascites; left ventricle hypertrophied and dilated; pulse very tense with inappropriate sphygmographic tracings; headache, delirium, sopor, and vomiting; no convulsions, but two sudden lapses into coma, with temporary recovery; neuro-retinitis hemorrhagica; suddenly a paralysis of the right and a paresis of the left rectus internus, lasting four days, causing diplopia, disappearing for three days, recurring with right ptosis. Death. Clinical diagnosis—secondary contracted kidney, cardiac hypertrophy, and dilatation; edema of brain. Autopsy confirmed clinical diagnosis; the cerebral edema being very pronounced. There were no gross brain lesions.
BIBLIOGRAPHY.

1. Leube: Specielle Diagnose innerer Krankheiten.
5. Landots: Die Uremie.

Citation 5, S. 120.
8. Strümpell: Arch. der Halkunde, 17 Jahrgang, 1876, S. 40.
16. Strümpell; Arch. f. Halkunde, 1876.
27. Bourdillat: Gaz. de Hôp., 1856, 38.
32. Dieulafoy: Gaz. de Hôp., 1867.
35. Traité de Méd. (Charcot-Bouchard), Guinon, t. vi. p. 574.
42. Chauffard: Arch. gén. de Méd., 1857.
44. Van Vyre: Arch. méd. Belges, 1876.
46. Bourdillat: Gaz. de Hôp., 1866.
47. Legroux: L'Encéphale, 1883, Nu. 1.