MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

DISTANCE LEARNING CENTRE

DEPARTMENT OF "NEPHROLOGY, HEMATOLOGY AND GASTROENTEROLOGY"

PRACTICAL EXERCISES – THESES

FOR E- LEARNING IN NEPHROLOGY

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BALKAN ENDEMIC NEPHROPATHY

PART I – GENERAL NOTES ON THE DISEASE:

Definition. Balkan endemic nephropathy /BEN/ is a peculiar, pri-marily renal disease that is spread in certain regions of some countries on the Balkan Peninsula, namely Bulgaria, Romania and former Yugoslavia. The illness has a family characteristic, a long termed course without hypertension and nephrotic syndrome, and very often is combined with tumors of the urinary tract.

Epidemiology. ***In Bulgaria BEN is found out in the sub-Balkan districts of Vratza and Montana regions, exclusively among the village population.***

Etiology and Pathogenesis.

There are three hypotheses for clarifying the origin of BEN:

1. Hypothesis for an **infectious** etiology:

- Bacterial origin-definitely rejected.
- Fungal agents-not proved.
- Viral agents-isolated from urothelial tumours in patients having BEN but causality with the origin of the disease is still not proved.

2. Hypothesis for a slow developing **intoxication** of the organism, predominantly damaging the kidneys. Summarizing the results of toxicological investigations of water, soil, foodstuffs and organs from dead patients ascertains repeatedness mostly of manganese, followed by lead, cadmium, copper, cobalt, barium, aluminium, chromium. Most of those chemical elements are known as having a nephrotoxic effect.

Causal relationship between possible toxic substances and BEN has not been yet determinatively established.

3. **Genetic hypothesis** – approved by most of the authors nowadays.

Evidence of genetic origin of BEN:

- The family characteristics of the disease, supported by clinicogenealogical studies.
- Determination of a chromosome marker, namely shortened long shoulder of one of the homologs of the third chromosome couple.

It could be assumed that BEN is a genetically determined disease that is handed down in an autosomal-dominant way.

PART II – EXAMINING A PATIENT:

1. Asking basic questions – surname and first names, age, occupation, marital status, date of admittance to the hospital.

Particular attention must be paid to the place of birth and resi –

dence – an endemic region. Asking about either emigration from or immigration to an endemic place of living. Clarifying the duration of life in the endemic settlement.

2. Case history:

- Lack of an acute beginning of the complaint. The patient cannot fix the real start of the sickness.
- The appearance of manifested sufferings is characteristic for persons being in their fourth to sixth decade of age because of the slow, gradual and insensible course of the disease.
- Disorders of general nature – long-termed and transitory headache, inconstant weakness, loss of appetite, dryness and metal taste in the mouth, loss of weight.
- Disorders of local nature – a dull waist-pain, polyuria, nocturia, colourless urine.

In cases of urothelial tumours there might be reddening of the urine on account of hematuria. Elimination of a blood clot through the urinary tract may resemble a renal colic.

- Lack of anamnesis for high blood pressure and/or nephrotic disorders.

3. Family history:

- Relations that are diagnosed as having BEN.
- Born and living in an endemic region relations, known as being ill with tumours of the urinary tract.

4. Physical examination:

- Typical complexion – a copper-pale coloured face skin.
- Pale visible mucosae.
- Xanthochromia – pumpkin-yellowy colouring of the palms and the feet.
- Lack of high blood pressure. Hypertension may occur when chronic renal failure has taken place.
- None oedema of a nephrotic nature.
- Renal succussion might be bilaterally slightly positive.

PART III - MAKING THE DIAGNOSIS.

1. Discussing the findings of the case history and the data from the physical examination.

2. Laboratory tests that back up the diagnosis:

(a) urinalysis:

- proteinuria of a low degree, always below 1 g/l;

- sedimentation test of no leucocytes and bacteria;
- hematuria in case of an urothelial tumour;

(b) full blood count:

- either normo- or hypochromic anaemia which appears to be an early symptom of the disease and is presented even in patients with unaltered renal function;
- white blood cells-of normal value;

(**c) ESR** – possibly high on account of anaemia;

(d) in case of an advanced renal affection and e kidney failure there are relevant changes in blood levels of nitrogen waste products as well as acid-base imbalance and disorders in calcium-phosphorus metabolism.

3. Microbiological examination of urine – no bacteria found. If a significant bacteriuria is established, it is due to a superposed infection of the urinary tract.

4. Diagnostic methods for evaluating renal function:

(a) testing of the capacity for concentrating and diluting the

urine. Characteristic of BEN is a relatively early reduction of the kidney concentration ability. Hypostenuria is found out at the test of Zimnicki.

(b) Clearance of creatinine as an index of glomerular filtration. In the compensated stages clearance values are normal or slightly reduced.

(c) Clearance of p-amino-hippuric acid /PAH/ which in normal is approximately of 600 ml/min, in patients with BEN is reduced.

(d) Fraction of filtration /FF/ is of either normal or increased value. The data are indicative of impaired much more tubular than

glomerular function likely a chronic interstitial nephritis.

5. Methods of imaging the kidneys:

(a) Ultrasonography – shows symmetrical for both kidneys alterations such as considerably lessened sizes and reduced thickness of the cortex.

(b) Excretory venous urography – of importance at diag-nosing tumours in the renal pelvis, along the ureters or in the urinary bladder.

(c) CAT – takes place when data for tumour processes are present and excretory venous urography is contraindicated.

6. Special investigations:

- Of sera and urine aminoacids. There is typical for BEN constellation, namely hyperalaninemia and hyperprolinemia coupled with hyperalaninuria and hyperaminoglycinuria.

- Of Vitamin A and carotine metabolism which is also typically changed. The constellation is of hypocarotinemia, hypervitamin-A-emia and retinol binding protein of normal value.

- Of beta-2-microglobulin. Characteristic of BEN is hyperbeta-2-microglobulinemia.

- Chromosome marker.

- Renal biopsy - usually of importance for early diagnosing the disease at young people from an endemic region and for research purposes as well. The histomorphology is that of a chronic interstitial nephritis. Characteristic features of BEN at electron microscopy are the damages of the basal membranes of proximal and distal tubules like moth eaten defects. In some of the epithelial tubular cells vacuoles with osmiophilic particles in them are found, suspected to be viral fragments.

7. Principal diagnostic criteria:

(a) Specific for BEN – endemia, facility, appearance of the main symptoms lately in the real course of the illness, anaemia, typical constellation of amino acids, often combination with multifocal, bilaterally localized urothelial tumours that appear to be papillocarcinomas.

(b) Characteristic of BEN – typical complexion ("Indian facies"), xanthoderma of the palms and feet, symmetrically lessened size of the kidneys, lack of hypertension, proteinuria of a low degree, altered metabolism of carotenes and Vitamin A.

8. Differential diagnosis:

- Renal hypoplasia, especially bilateral.
- Chronic glomerulonephritis.
- In cases of present tumours – with nephrolithiasis, tuberculosis of the urinary tract.

PART IV – TREATMENT AND MANAGEMENT:

1. Nutritionally-complete balanced diets if renal function is not impaired.
2. No limiting of sodium chloride in food because of the lack of high blood pressure.
3. In case of chronic renal failure – according the relevant stage.
4. Surgical treatment of tumors.