Original case report
ACUTE RENAL FAILURE AFTER THERAPY WITH INTERFERON

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OBJECTIVES

The main objective of this clinical case presentation is to attract attention about the **dangerous and unexpected side effects of therapy with Interferon** in context of patients with **active chronic hepatitis with virus B or C positive**, which follow this protocol of therapy.

OBJECTIVES

The summary of the urine and **the evaluation of kidney function** are absolutely necessary before start this therapy. We must to be carefully to **protect the kidney** about the **side effects of drugs.**

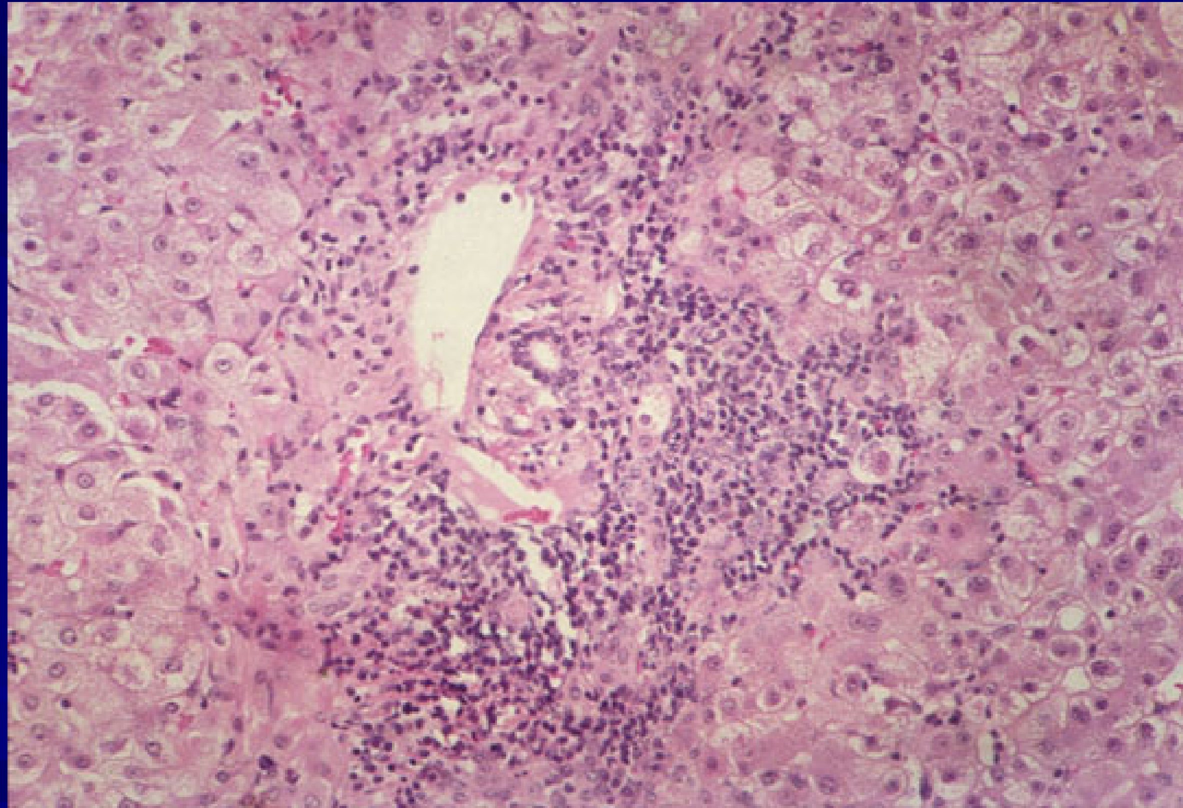
MATHERIAL AND METHODS

I present the clinical case of a patient age 48 years old who was hospitalized for the diagnosis of **active chronic hepatitis with virus B positive** with **increase value** of the **liver enzymes: glutamate amino transferase AST=248UI/l, oxalate aminotransferase ALT=342UI/l)**

MATHERIAL AND METHODS

- **γGT=121**,
- alkaline phosphatase=20 UI/l
- **indirect bilirubin=2,32mg/dl**,
- **total bilirubin=3mg/dl**,
- **AgHBs+**, **viremia= 6millions unites,**
- **liver biopsy** with histopathology examination confirmed **active chronic hepatitis**.

HISTHOPATHOLOGY EXAMINATION OF THE LIVER



Histopathology examination of the liver HE stain - Piece meal necrosis

MATHERIAL AND METHODS

The summary of the urine:

- **urobilinogen positive**
- **proteinuria+**

The value of:

- urea=32mg/dl,
- creatinine=0,9mg/dl,
- Cl creatinine=105ml/min

All other lab tests was normal range.

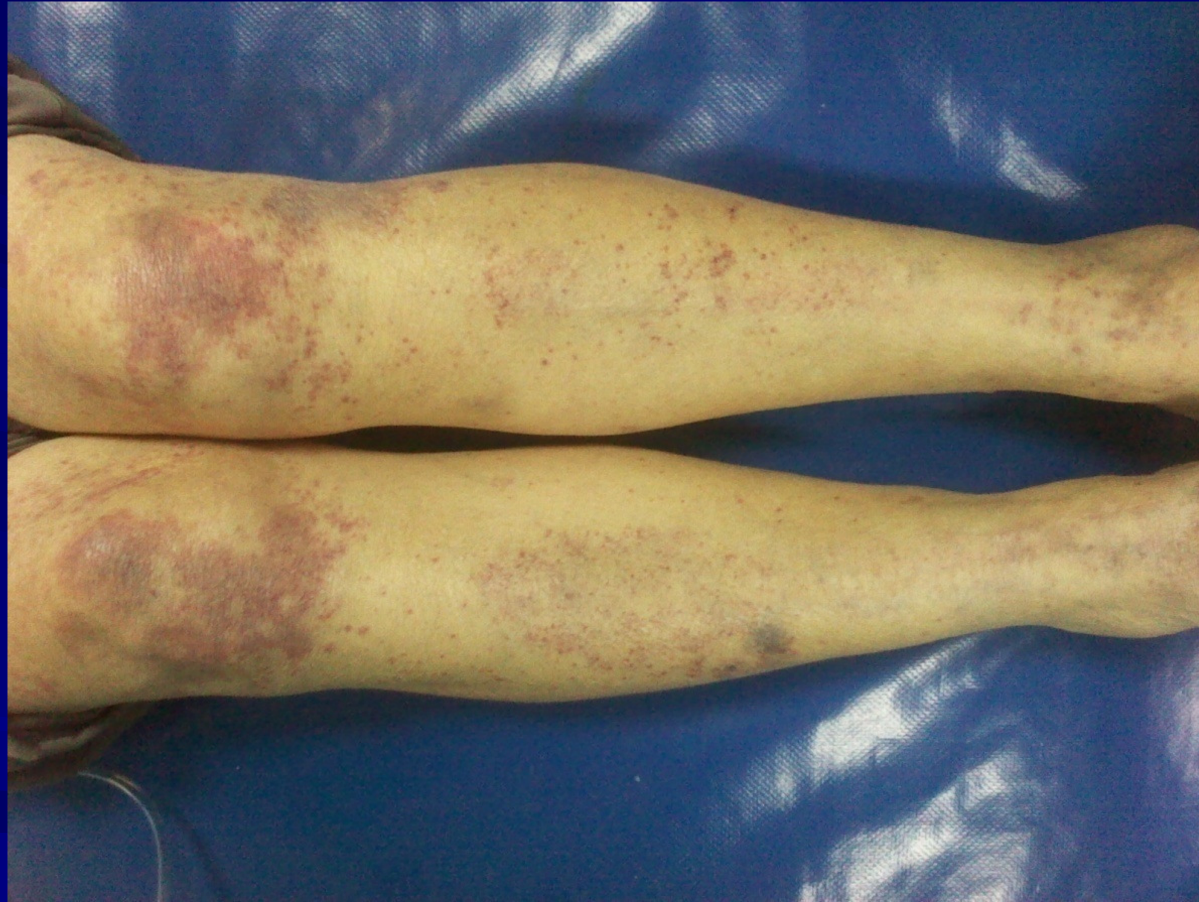
THERAPY

The patient follow the protocol of therapy with **Pegylat @Interferon 3MU 3 times/week during three weeks**. The patient tolerated good the therapy without any problem except in the third week of therapy.

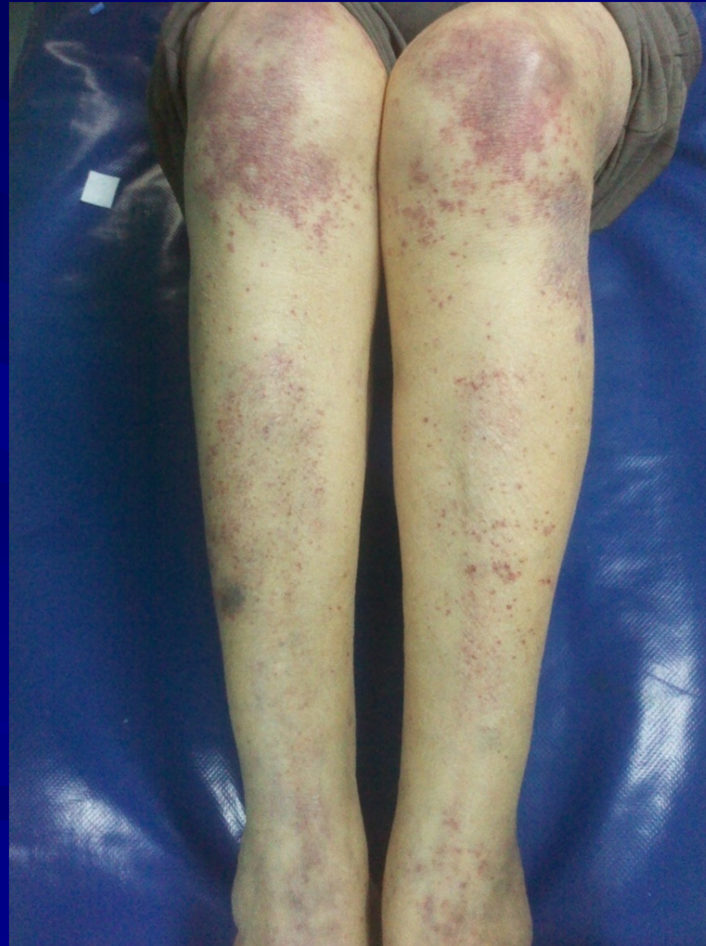
EVOLUTION

In the **third week of therapy** with @Interferon 3MU 3 times/ week the patient presented the apparition of a **palpable rash (purpura)** at **the lower limbs** shown in the images below:

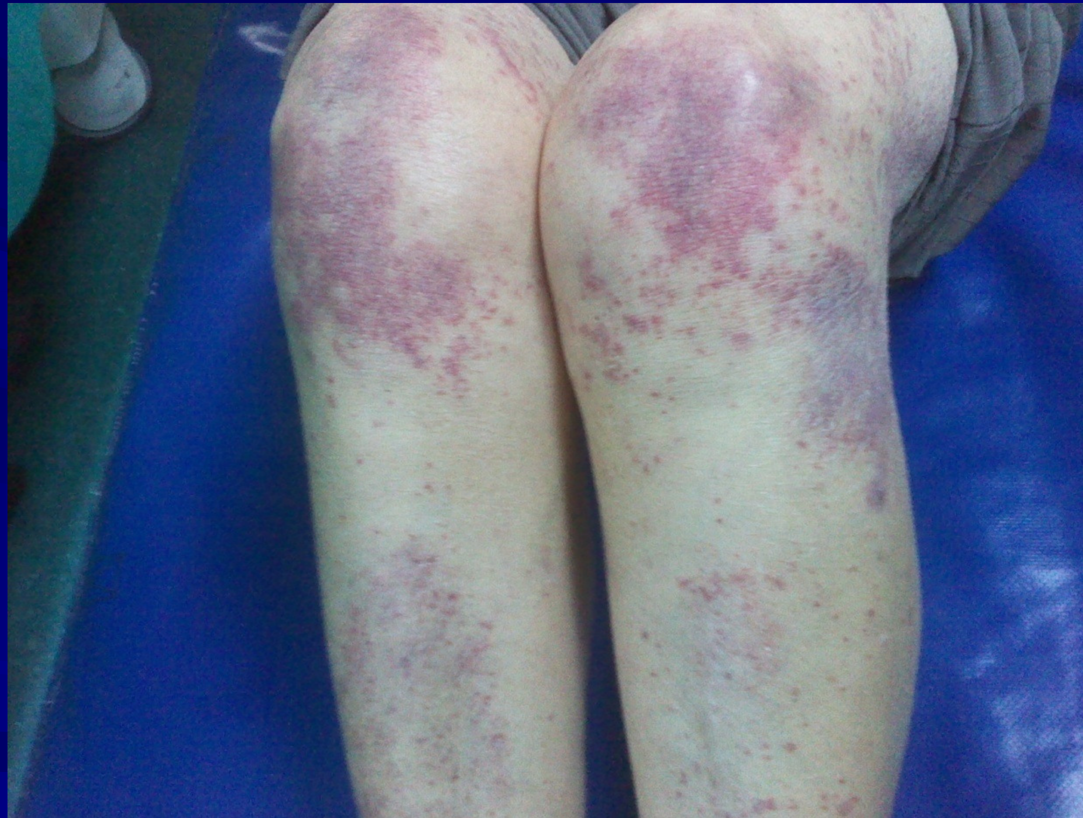
THE PALPABLE RASH (PURPURA) AT THE LOWER LIMBS



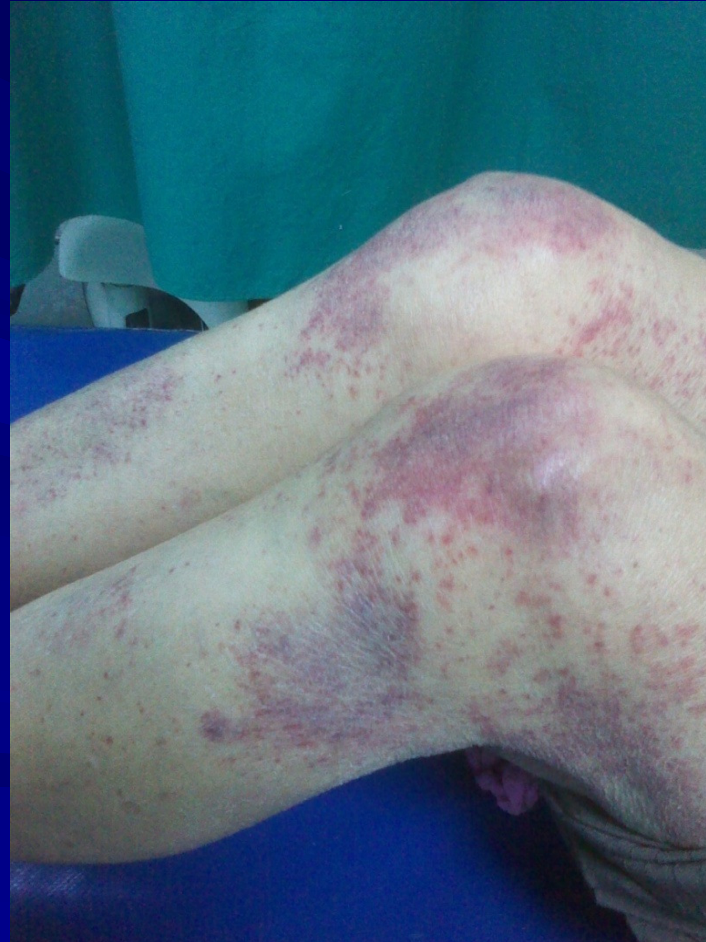
THE PALPABLE RASH (PURPURA)



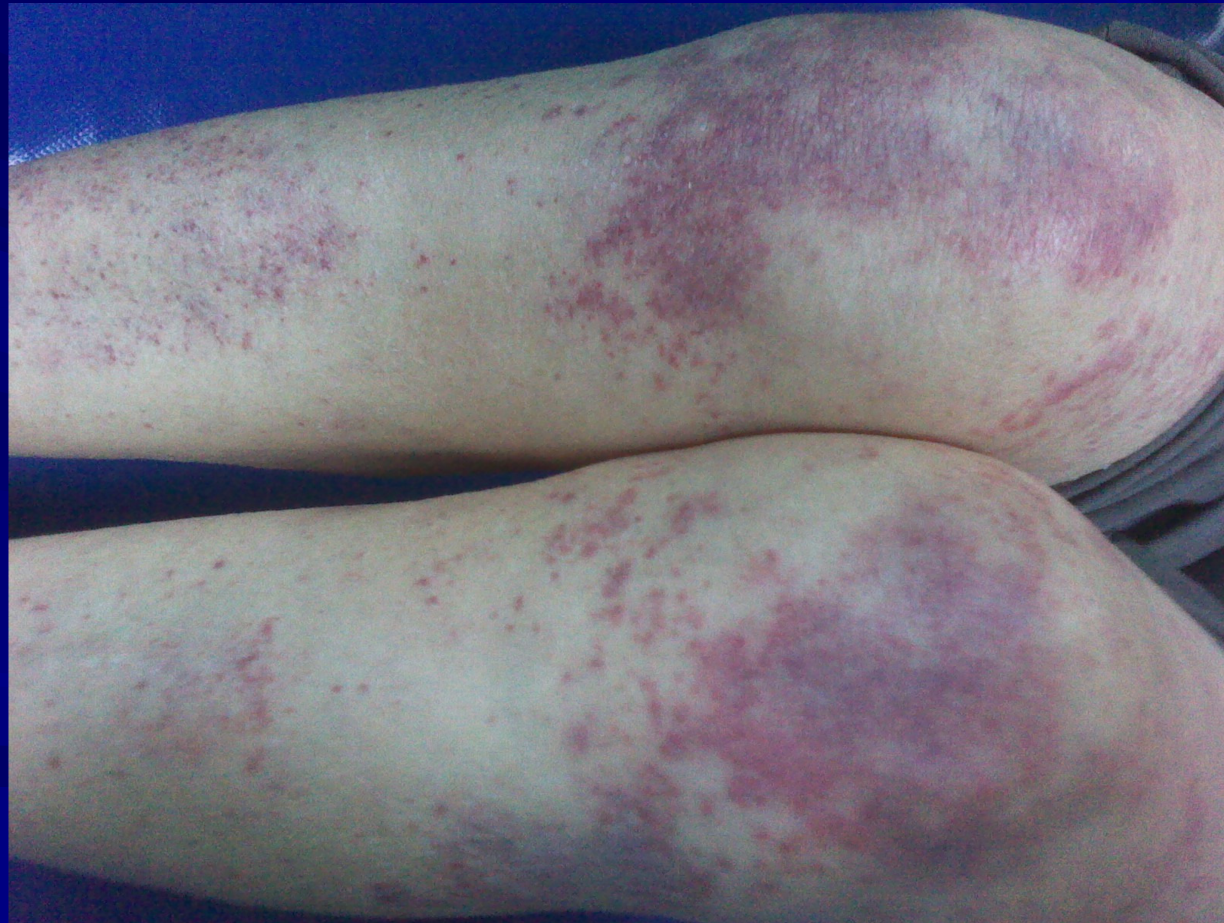
THE PALPABLE RASH (PURPURA) ON THE KNEES



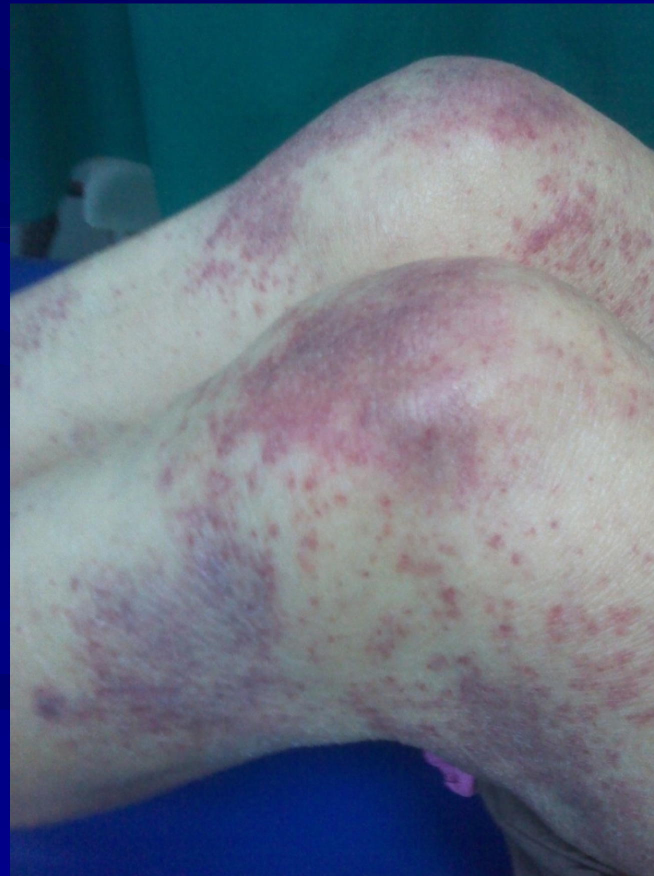
THE PURPURA LATERAL INCIDENCE



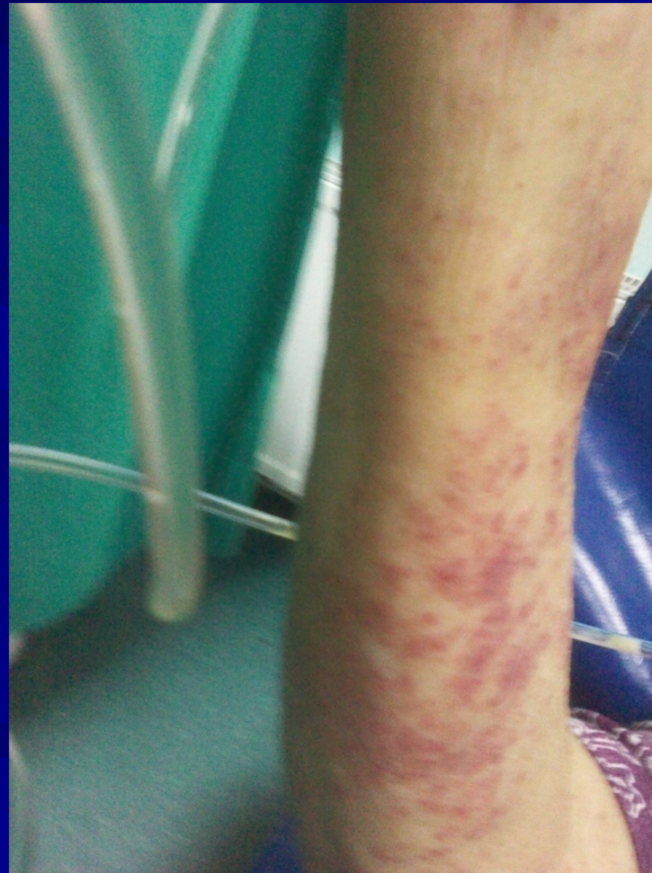
THE PALPABLE RASH (PURPURA)



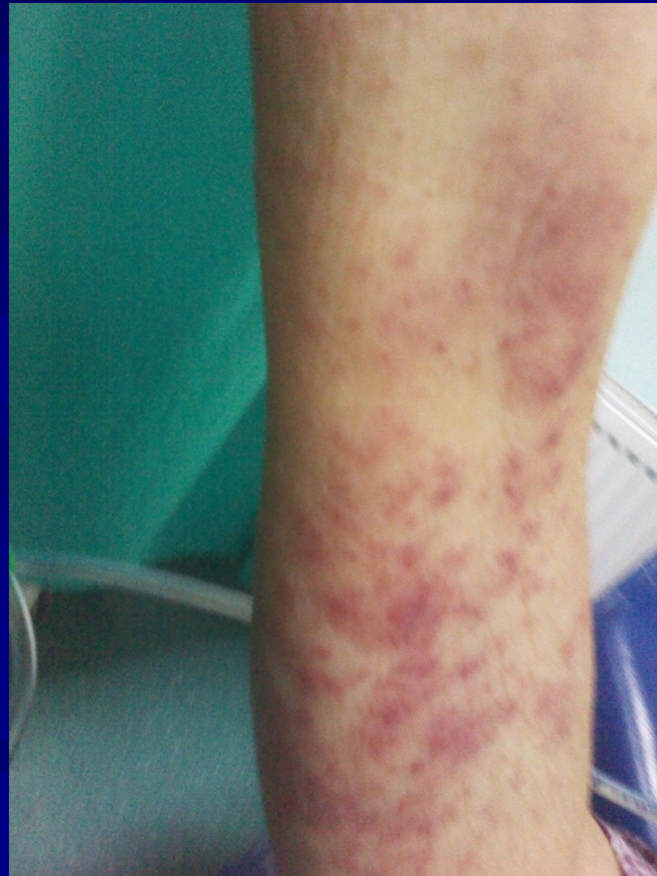
THE PALPABLE RASH (PURPURA) LATERAL INCIDENCE



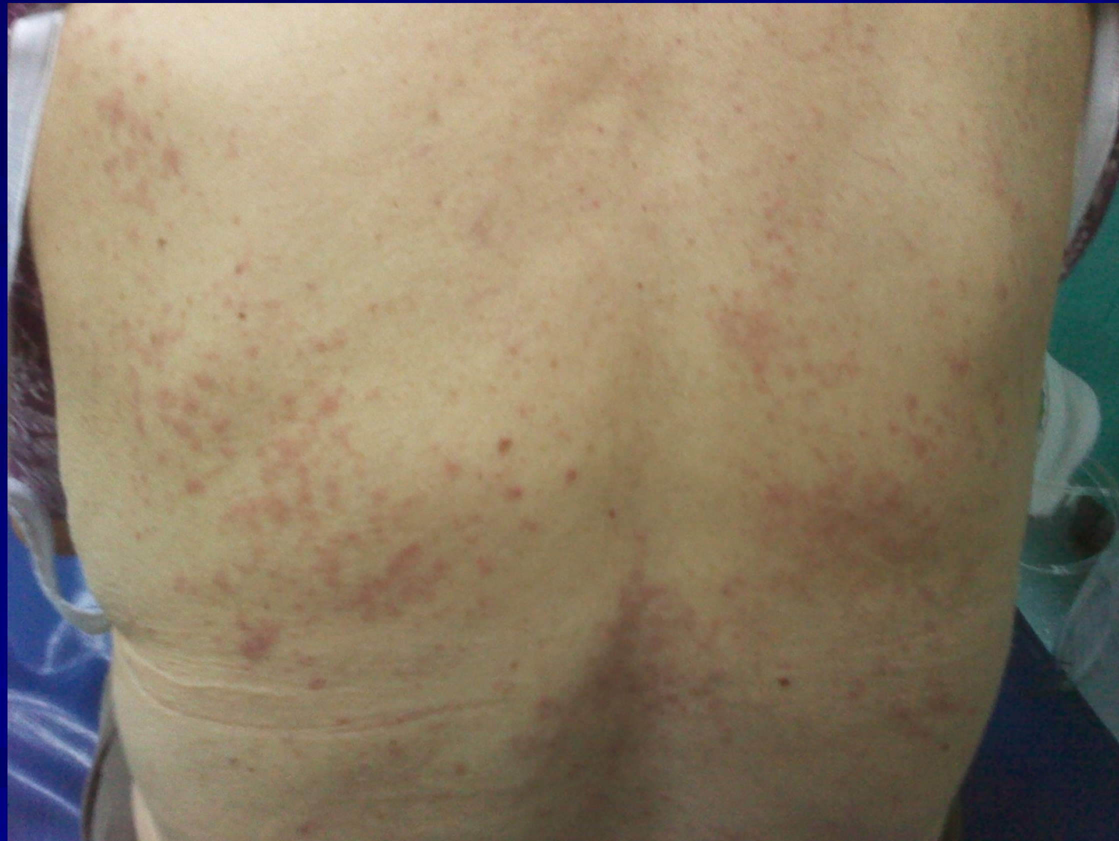
THE PURPURA
THE RIGHT ARM



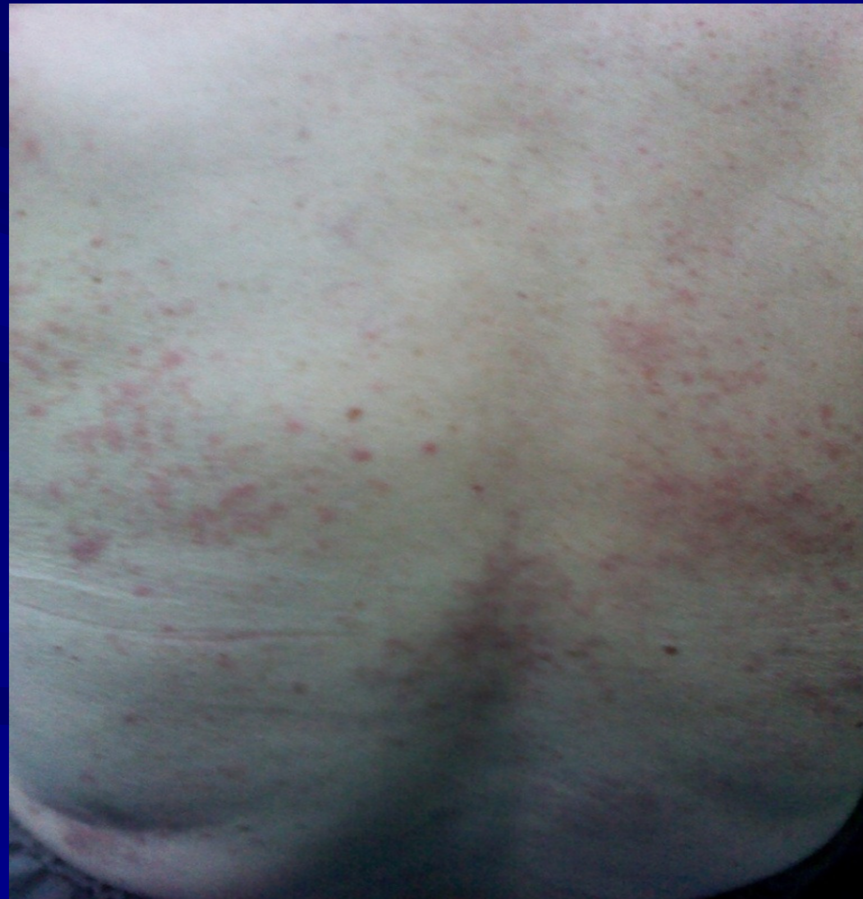
THE PURPURA
THE RIGHT ARM



THE PURPURA
THE POSTERIOR THORAX



THE PURPURA THE POSTERIOR THORAX AND LUMBAR AREA



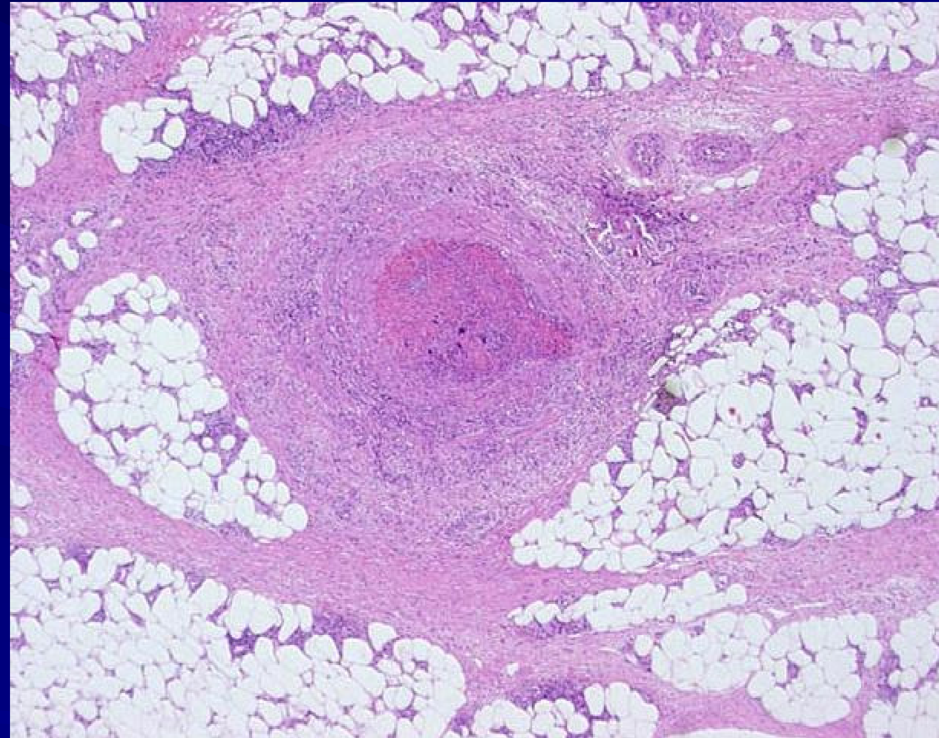
THE PLATELETS LEVEL

The platelets level was in **normal range =286 000/L.** In this condition I excluded that the decrease level of platelets could be the cause of purpura and also **the purpura was palpable** and this appear only in context of the **systemic vasculitis** so a **skin biopsy** was performed .

SKIN BIOPSY

The histopathology examination with **fibrinoid necrosis of the vessel wall** with surrounding **perivascular lymphocytic infiltrates,** confirmed safe the diagnosis **polyarteritis nodosa.**

THE HISTOPATHOLOGY EXAMINATION POLYARTERITIS NODOSA



STAIN: HEMATOXYLIN AND EOSIN
MAGNIFICATION:X40
The **fibrinoid necrosis of the vessel wall** with surrounding **perivascular lymphocytic infiltrates**

SPECIFIC TEST

ANCA test was performed in this condition **(p ANCA was positive)** and also confirmed the diagnosis of **systemic vasculitis polyarteritis nodosa.**

EVOLUTION

After this event **in the third week** after the therapy with **@Interferon 3MU 3 times/week** the **nephritic syndrome** was accented:

- **proteinuria=30mg/dl**,
- **hematuria=20mg/dl.**

EVOLUTION

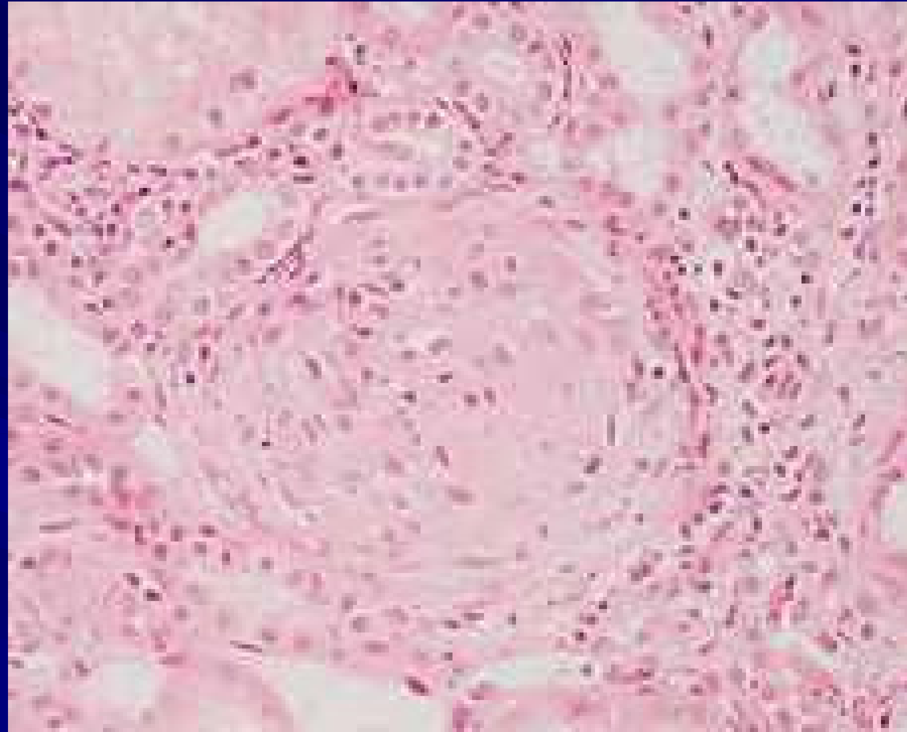
After that the patient developed a **syndrome of progressive azotized retention uremia.**

- **creatinemia=5,08 mg/dl**
- **urea=402mg/dl,**
- **hiperpotasemia=6,5mEq/l,**
- **pH=7,0-severe metabolic acidosis**
- **anuria in 24hours** so an **acute renal failure**

EVOLUTION

This is happened in context of **systemic vasculitis** with **secondary nephropathies** and **in context of the therapy with Pegylat @ Interferon** hence an imposition of **dialysis (three times)** for the normalization of the azotized parameters and revue the normal diuresis of the patient.

THE KIDNEY BIOPSY



- Photomicrograph of a **kidney biopsy** from the patient revealed **crescentic glomerulonephritis** showing prominent fibro cellular crescent formation and moderate **mesangial proliferation** in a **glomerulus.** Hematoxylin and eosin stain

THE FINAL DIAGNOSIS

- ***POLIARTERITIS NODOSA.***
- ***ACTIVE CHRONIC HEPATITIS VIRUS B POSITIVE.***
- ***SECONDARY SUBACUTE GLOMERULO NEPHRITIS IN CONTEXT OF SYSTEMIC VASCULITIS.***
- ***ACUTE RENAL FAILURE AFTER THERAPY WITH PEGYLAT@ INTERFERON***

THERAPY

Cyclophosphamide regimen was administered intravenous **pulse therapy** with intravenous **cyclophosphamide (15 mg/kg)** administered at weeks zero, two, and four, and then every three weeks **for three doses and until a stable remission has been achieved with good evolution of the patient.**

RESULTS AND DISCUSSIONS

The patients with **active chronic hepatitis virus B or virus C positive** is possible to have a **systemic vasculitis** in the context of the disease **without clinical manifestations (subclinical) unknown** and **with secondary nephropathy** in this context

RESULTS AND DISCUSSIONS

with **minimal nephritic syndrome** manifested with:

- **isolated proteinuria**
- **isolated hematuria** or
- **proteinuria and hematuria** identify after summary urine examination was performed or
- **undetectable(unknown).**

RESULTS AND DISCUSSIONS

If the patient had this result with **nephritic syndrome** after urine examination before start the therapy with Interferon for active chronic hepatitis with virus C or B positive, **the patient has risk** to develop during the protocol of therapy, **unexpected, acute renal failure**

RESULTS AND DISCUSSIONS

with **severe evolution** of the patient with **rapid progressive azotes retention syndrome** and is **necessary dialysis to save the patient’s life.**

RESULTS AND DISCUSSIONS

During the period in which therapy with **Pegylat @ Interferon was discovered** everybody believed that this **represented the solution for chronic viral B and C hepatitis** with the view of removing the virus from the body thanks to this protocol.

RESULTS AND DISCUSSIONS

But after **the standard protocols of therapy where applied** in medical practice it was observed that **a small proportion of the patients responded very well** to the therapy, a second portion had an **incomplete response** to the therapy and many others have **no responsible** to this therapeutic protocol.

RESULTS AND DISCUSSIONS

After **the therapy with Pegylat @ Interferon** appeared to be **a partial amelioration of the disease** as the analyzed blood test showed **a decrease in the level of cytolyses liver enzymes (ASAT, ALAT)** glutamate aminotransferase and oxalate aminotransferase - and **decreased viremia** but **the virus B or C remained in the body of the patient.**

RESULTS AND DISCUSSIONS

This has a price very important **side effects** we can’t neglect and a significant number of patients **did not tolerate this complete protocol of therapy** and this must to be **stopped or reduced** for a shorter period of time compared to the standard protocols administered and currently used in the medical practice.

CONCLUSIONS

1. We must to **monitories very carefully the kidney function** with **the azotized parameters every day** if the patient **follow the protocol of therapy with Pegylat @Interferon** for active chronic virus B or C hepatitis

CONCLUSIONS

because in context of **unknown (subclinical) systemic vasculitis** with **a secondary glomerulonephritis** the patient is possible to **develop sudden and unexpected an acute renal failure** and **dialysis is necessary** to save the patient life.

CONCLUSIONS

2. With **the increasing use of interferon's,** has come the realization that they **can have renal side effects** in some patients.

CONCLUSIONS

3. A variety of mechanisms of injury have been reported, though most attention has focused on **the ability of interferon therapy to cause proteinuria and nephritic syndrome.**

CONCLUSIONS

4.This has been noted most commonly with **Pegylat @Interferon therapy**, though in many of the **patients with hepatitis B or C** it may be **difficult to be certain whether or not**

CONCLUSIONS

the development of nephritic syndrome comes from the interferon therapy or a direct hepatitis-mediated renal injury such as MPGN.(membranous proliferative glomerulonephritis).

CONCLUSIONS

5.Other mechanisms of **renal injury** reported **with interferon use** include **acute tubular necrosis**, **acute interstitial nephritis**, and even **hemolytic-uremic syndrome**.

CONCLUSIONS

6.Occasionally, **tubulo reticular structures as seen on electron microscopy of a kidney biopsy** can be a clue as to the diagnosis of **interferon-induced renal injury.**

CONCLUSIONS

7.We must have the courage to recognized **the problem of these patients are not solved yet** and we do not have to **give false hope to our patients.**

CONCLUSIONS

8. This **actual schemes** and protocols of treatment which **are far from ideal**, more than that followed by **serious side effects**, this **should serve as an alarm signal.**

CONCLUSIONS

9. I believe with strong opinion that **this therapeutics protocols must be reevaluated** in the medical practice.

CONCLUSIONS

10. Also other doctors must be encourage to relate other clinical observations from their medical practice about **the side effects of therapy with Interferon.**

CONCLUSIONS

11. The balance between the risks and benefits I believe should be seriously reevaluated.

CONCLUSIONS

12.The kidney is **one of the most precious organ from the body,** worked like a veritable filter, and we must to be very carefully **to protect the kidney** about the **side effects of drugs.**

THANK YOU

FLOWER FOR YOUR