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.
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 $\text{AST}=248\text{UI/l}$, oxalate aminotransferase $\text{ALT}=342\text{UI/l}$.)
MATERIAL AND METHODS

- yGT=121,
- alkaline phosphatase=20 UI/l
- indirect bilirubin=2,32mg/dl,
- total bilirubin=3mg/dl,
- AgHBs+, viremia= 6millions units,
- liver biopsy with histopathology examination confirmed active chronic hepatitis.
Histopathology examination of the liver  HE stain - Piece meal necrosis
MATERIAL 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.
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.
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.
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.
After that the patient developed a syndrome of progressive azotized retention uremia.

- creatinemia = 5,08 mg/dl
- urea = 402 mg/dl
- hiperpotasemia = 6,5 mEq/l
- pH = 7,0 - severe metabolic acidosis
- anuria in 24 hours 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.
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 PEGYLATED 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.
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 were 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 Pegylated 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 monitor very carefully the kidney function with the azotized parameters every day if the patient follow the protocol of therapy with Pegylated 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.
4. This has been noted most commonly with Pegylated 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).
5. Other mechanisms of renal injury reported with interferon use include acute tubular necrosis, acute interstitial nephritis, and even hemolytic-uremic syndrome.
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 recognize the problem of these patients are not solved yet and we do not have to give false hope to our patients.
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.
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.
Finally, the question is if the factors of the workplace could be considered in causing this disease?
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