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Abstracts of XIII Congress of Albanian Association of Heamatology

Albanian Association of Hematology, AAH
Congress XIII on 5, 6 November 2018, Plaza Hotel, Tirana, Albania.

content

CAR- T cell the new treatment in lymphoid neoplasia

A. Ivanaj, A. Cili, A. Perolla, P. Pulluqi, E. Calliku T. Caja, E. Pepa, R. Roxhani, T. Dedej

CAR T-cell therapy. A type of treatment in which a patient's T cells (a type of immune cell) are changed in the laboratory so they will bind to cancer cells and kill them. Blood from a vein in the patient's arm flows through a tube to an apheresis machine (not shown), which removes the white blood cells, including the T cells, and sends the rest of the blood back to the patient. Then, the gene for a special receptor called a chimeric antigen receptor (CAR) is inserted into the T cells in the laboratory. Millions of the CAR T cells are grown in the laboratory and then given to the patient by infusion. The CAR T cells are able to bind to an antigen on the cancer cells and kill them. In multicenter study, patients with refractory large B-cell lymphoma who received CAR T-cell therapy with axi-cel had high levels of durable response, with a safety profile that included myelosuppression, the cytokine release syndrome, and neurologic events. In the patients with ALL CAR T-cell therapy demonstrated very good response with a safety adviser site effects. CAR T-cell therapy is a safety and very promising treatment in lymphoid neoplasia.

Chronic myeloid leukemia 2018 update on diagnosis, therapy and monitoring

A. Cili, A. Perolla, E. Calliku, P. Pulluqi, T. Caja, A. Ivanaj

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1-2 cases per 100 000 adults. CML is characterized by a genetic translocation, t(9;22)(q34;q11.2), this rearrangement is known as the Philadelphia chromosome. The molecular consequence of this translocation is the generation of a BCR-ABL1 fusion oncogene, which in turn translates into a BCR-ABL1 oncoprotein.

Frontline therapy: Four tyrosine kinase inhibitors (TKIs), imatinib, nilotinib, dasatinib, and bosutinib are approved by the United FDA as first-line treatment of patients with newly diagnosed CML in chronic phase (CML-CP). Clinical trials with second generation TKIs reported significantly deeper and faster responses but this has not translated into improved long-term survival, because of the availability of effective salvage therapies .Patients who develop the T315I mutation display resistance to all currently available TKIs except ponatinib.

Treatment-free remission (TFR) has recently emerged as a goal of treatment in chronic myeloid leukaemia.The minimum eligibility criteria for a trial of TFR are not yet defined, but the available data support a MRD level of around a molecular response of 4·5 log for at least 2 years. Factors associated with a higher probability of TFR include low risk Sokal score, prior interferon treatment, longer total duration of imatinib treatment and higher numbers of natural killer cells at the time of imatinib discontinuation. Preliminary data suggest that the rate of TFR in patients treated with more potent tyrosine kinase inhibitors will probably be higher. The biology that underlies TFR is an area of active investigation.

The FDA's December 2017 Tasigna update, however, has some encouraging news for CML patients. The label now stipulates that Ph+ CML patients in the chronic phase may qualify to stop treatment with Tasigna altogether. However, you must take Tasigna for at least three years and achieve specific predetermined remission criteria before stopping treatment. More specifically, the updated FDA guidelines say patients must achieve a sustained deep molecular response of MR4.5 before stopping Tasigna sustained deep molecular response of MR4.5 before stopping nilotinib . The FDA also recently authorized a test that can detect this response in nilotinib therapy patients that achieve treatment-free remission.

Allogeneic stem cell transplantation although remains an important therapeutic option for patients with CML-CP who have failed at least 2 TKIs, and for all patients in CML advanced phases.

Earlier this year, Bin Zhang, MD, PhD, Associate Research Professor in the Department of Hematologic Malignancies Translational Science at City of Hope led a study published in *Nature Medicine* on a more effective, less toxic treatment for patients with CML involving miristen—a new drug developed at the facility—and TKIs (2018;24:450-462). We have reason to believe miristen makes TKIs more effective at killing the leukemia stem cells, so we treated mice with CML with different drug combinations and found those treated with miristen and TKI who had received stem cell transplants went into complete remission.

Miristen targets a type of microRNA that is expressed in leukemia stem cells, known as miR-126. We believe this RNA molecule plays an important role in the self-renewal and persistence of cancer-causing leukemia stem cells. By eliminating this molecule in the blood, there›s an opportunity to reduce the chance of cancer recurrence by eradicating the stubborn stem cells altogether.

Transplantation of the bone marrow cells collected from those treated with miristen and TKI resulted in no sign of leukemia in the healthy recipient mice, meaning all leukemia stem cells were eliminated.

A very rare case of transformation of a patient with Multiple Myeloma to NonHodgkin malignant lymphoma

A. Cili, L. Lacej, E. Pepa, R. Tozharaku, A. Ivanaj

A rare case of transformation of Multiple Myeloma to non-Hodgkin's lymphoma is presented. The patient presented in 2013 with mid-back and rib pain. In an abdominal CT performed, the patient resulted with osteolitic lesions in the vertebrae and hip bone. Bone marrow aspiration demonstrated a presence of 15% atypical plasma cells. He was diagnosed with stage III A Multiple Myeloma. After 5 years of remission from Multiple Myeloma he came back to the clinic with a scrotal mass that after the bipsy resulted to be a Large B Cell diffuse Lympohoma

Introduction

Multiple myeloma (MM) is the major malignancy of plasma cells. Although lymphomas are usually neoplasms of lymphatic tissues, substantial numbers of non-Hodgkin's lymphoma arise in other tissue.The transformation of Multiple Myeloma to non Hodgkin malignant Lymphoma is very rare. We report a case of a patient presented with this transformation and we discuss the possible pathogenetic mechanism of the two disorders.

Case report

A 32-year-old man presented in 2016 with mid-back pain and rib pain during the last 2 months. On examination he appeared normal.. Complete blood count revealed hemoglobin 8.0 g/dl,total protein of 10.5 g/dl. Abdominal CT revealed olsteolytic bone lesions in the vertebrae, scull and pelvis. Serum electrophoresis revealed a monoclonal peak in the gamma globulin region, identified IgA lambda on immunoelectrophoresis. Bone marrow aspiration smears revealed 15% o plasma cells. The patient was diagnosed with stage III A Multiple Myeloma. After treatment with eight cycles of chemotherapy according to VAD protocol the patient was discharged from the hospital in complete remission.

Two years later, in march 2018 the patient comes back to the consultation clinic a mass with an Biopsy examination showed Large diffuse B cell lymphoma Cd20 neg with positive CD45 ++- CD79a +++ and Ki67 80%. Bone marrow aspiration showed no presence of plasmatic cells.The patient was diagnosed with non Hodgkin malignant lymphoma We treated the patient according DHAP chemotherapy regimen . After the chemotherapy protocol we performed a CT scan cause we do not have access to PET/CT scan ,the patient was in complete remission .

Discussion

Multiple myeloma (MM) is the major malignancy of plasma cells. Although lymphomas are usually neoplasms of lymphatic tissues, substantial numbers of non-Hodgkin's lymphoma arise in other tissue,

The occurrence of both MM and NHL in our patient implies several possible pathogenetic mechanisms. First, one malignant disease may evolve from another. A comparison of the immunologic phenotype of both MM and NHL in a patient is needed to reach meaningful conclusions. On the other hand, the development of high grade malignant lymphoma in patient with chronic lymphocytic leukemia was first reported by Richter in 1928 and transformation to high grade lymphoma is now a well-known event in other low grade malignancies of the B cell lineage. The malignant transformation of MM has rarely been reported. During the last decade, patients with advanced MM survive longer due to intensified chemotherapy and improved supportive care. This increased survival has permitted the development and improved the chance of observing transformation of MM to high grade malignant lymphoma. It is possible that cytotoxic treatment per se may promote transformation. Another possible mechanism is that both malignancies are different manifestation of original neoplastic clone. Although it would be rare, a possibility of independent of two infrequent malignancies at one time exists.

This as the only case of MM patient transformation to NHML offers additional support to the theory of malignant transformation of MM to NHML. Opportunities to study and understand the unique natural history and evolutional dynamics for this transformation are rare. We would recommend further multicenter comparisons of slimilar cases in a broad effort to better define this complicated disease process.

Te dhëna epidemiologjike të mielomës multiple në Shqipëri

A. Çyrbja, T. Caja, A. Cili, A. Perolla, P. Pulluqi, E. Calliku, A. Ivanaj

Mieloma Multiple është një hemopati malinje e karakterizuar nga një proliferim neoplazik i një kloni të vetëm qelizash plazmocitare, që prodhojnë imunoglobulina monoklonale.

Mieloma Multiple është përshkruar për herë të parë në vitin 1848 nga Otto Kahler. Në vitin 1845 doktor William Macintyre nga Londra vuri re që një grup të sëmurësh kishin dhimbje kockore dhe ndryshime urinare. Pas një viti, në 1846 doktor Henri Bence - Jones, duke analizuar urinat e këtyre të sëmurëve, zbuloi se ata paraqitnin vargje të lehta urinare. Si rezultat i zhvillimeve të mëvonshme, në 1929 u tregua që këta pacientë kishin ndryshime në mielogramë. Në 1937 u vunë re ndryshime në elektroforezën e proteinave. William në vitin 1953 tregoi se në imunoelektroforezë ka një Pik monoklonal, duke përcaktuar diagnozën e monoklonalitetit të një imunoglobine.

Mieloma Multiple përbën 1% të të gjithë neoplazive dhe është neoplazia e dytë hematologjike më e shpeshtë pas Limfomave duke zënë 10% të malinjancave hematologjike, me incidencë vjetore 4.3 raste në 100000 burra te bardhe, 3 raste ne 100000 gra të bardha në Shtetet e Bashkuara të Amerikës dhe me vlera të përafërta epidemiologjike dhe në Europë. Haset në të gjitha racat, në racën e zezë është dy herë më e shpeshtë se në atë kaukaziane. Përsa i përket prekjes gjinore, më e shpeshtë është në seksin mashkull, me raport mashkull:femër = 1.4:1.

Mosha mesatare e prekur është 66 vjeç, me prekje më të shpeshtë të grupmoshës 61-80 vjeç. Vetëm 2% e pacientëve me mielomë janë më pak se 40 vjeç.

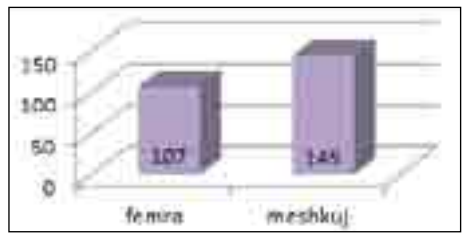
Manifestohet klinikisht me simptomat: lezionet litike kockore, hiperkalcemia, disfunksioni renal anemia, të lidhura me infiltrimin e plazmociteve në palcën e kockave dhe në organet e tjera. Për vendosjen e diagnozës, kriteri kryesor diagnositk

është prania e më shumë se 10 % plazmociteve në palcën e kuqe të kockave. Në varësi të rezultateve të imunoelektroforezës së proteinave dallohen disa tipe: në 67% te rasteve konstatohen IgG, IgM dhe IgA Mieloma Multiple, të cilat në varësi të vargjeve të lehta të prodhuara, nëngrupohen si Kappa ose Lambda, ndërsa në 33% vërehen Mielomat Multiple me vargje të lehtë, oligosekretore dhe asekretore.

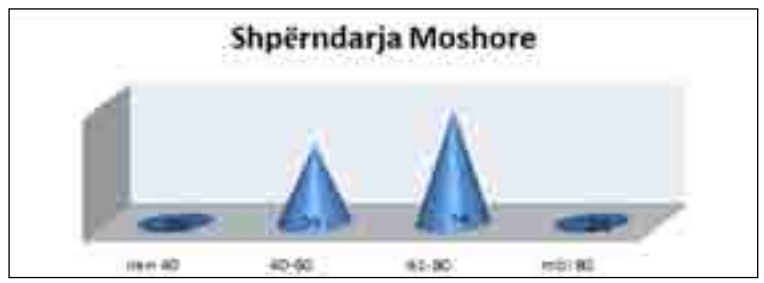
Në sajë të përdorimit të skemave të reja të trajtimit, me preparate me mekanizëm të ndryshëm veprimi, transplantit allogjenik dhe terapisë post transplant, është mundësuar përmirësimi i cilësisë së jetës dhe zgjatja e mbijetesës së pacienteve.

Në këtë studim vlerësohen të dhënat epidemiologjike për vendin tonë të kësaj patologjie, gjatë periudhës kohore Janar 2013-Dhjetor 2017, ku janë përfshirë 252 raste të diagnostikuar me Mielomë Multiple në Shërbimin e Hematologjisë në Qendrën Spitalore Universitare «Nënë Tereza».

U vlerësua **përkatësia gjinore**, ku u konstatua një predominim i seksit mashkull me shpërndarje përkatësisht 58% në seksin mashkull dhe 42% në seksin femër.



U analizua **shpërndarja sipas grupmoshës**, e paraqitur në grafikun më poshtë, ku u konstatua se në 252 pacientë të marrë ne shqyrtim, 142 prej tyre, ose 56% i përkasin grupmoshës 61-80 vjeç, 99 pacientë ose 39% i përkasin grupmoshës 40-60 vjeç, 6 pacientë janë nën 40 vjeç, që përbëjnë 3% dhe 5 pacientë ose 2% janë mbi 80 vjeç.



Vendlindja, sipas rrethit, është një karakteristikë tjetër që u analizua në studim. Siç është paraqitur dhe në grafikun me poshtë, vihet re probabilitet më i lartë shpërndarje në qendrat e populluara urbane, sikurse është Tirana dhe Fieri apo me problematika në zhvillimin teknologjik të prodhimit si Elbasani për shkak të metalurgjikut.

Konkluzione

Nga studimi i realizuar u konstatua qe 142 pacientë, ose 56% i përkasin grupmoshës 61-80 vjeç, 99 pacientë ose 39% i përkasin grupmoshës 40-60 vjeç, 6 pacientë janë nën 40 vjeç, që përbëjnë 3% dhe 5 pacientë ose 2% janë mbi 80 vjeç. Gjithashtu u konstatua një predominim i seksit mashkull me shpërndarje përkatësisht 58% në seksin mashkull dhe 42% në seksin femër. Raporti M:F 1.4:1. Përsa i përket shpërnarjes gjeografike vihet re probabilitet më i lartë shpërndarje në qendrat e populluara urbane, sikurse është Tirana dhe Fieri, apo Elbasani për shkak të problematikave në zhvillimin teknologjik të prodhimit.

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Treatment of Mantle Cell Lymphoma

A. Hate, A. Cili, A. Perolla, T, Caja, P. Pulluqi, E. Calliku, A. Pushi, A. Ivanaj

Mantle cell lymphoma (MCL) is a B-cell non-Hodgkin lymphoma with typically aggressive behavior. The genetic signature is the chromosomal translocation t(11;14)(q13;q32) resulting in overexpression of cyclin D1. Asymptomatic newly diagnosed MCL patients with low tumor burden can be closely observed, deferring therapy to the time of disease progression. Although MCL classically responds to upfront chemotherapy, it remains incurable with standard approaches. For patients in need of frontline therapy, the initial decision is whether to proceed with an intensive treatment strategy or a non-intensive treatment strategy. In general, given the unfavorable risk-benefit profile, older MCL patients should be spared intensive strategies, while younger and fit patients can be considered for intensive strategies. The bendamustine and rituximab (BR) regimen is becoming an increasingly popular treatment option among the elderly population, with improved progression-free survival (PFS) and acceptable side-effect profile. Although rituximab maintenance after R-CHOP improves survival outcomes in elderly patients, no clinical trial to date has shown statistical significance to support the use of rituximab maintenance after BR induction in older patients. In young and fit patients with MCL, an intensive strategy to maximize the length of first remission has emerged as a worldwide standard of care. With current high-dose cytarabine-containing immunochemotherapy regimens followed by autologous stem cell transplantation, the median PFS has exceeded 7 years. In the relapsed or refractory (R/R) setting, reduced intensity conditioning allogeneic hematopoietic stem cell transplantation may offer the highest likelihood of long-term survival in young R/R MCL patients, at the cost of increased risk of non-relapse mortality and chronic graft versus host disease. Novel agents targeting activated pathways in MCL cells, such as bortezomib, lenalidamide, ibrutinib and temsirolimus are now available for the management of R/R disease.

Next-generation sequencing - a new era in hematological malignancies

A. Perolla, P.Pulluqi, A.Ivanaj, E.Calliku, A.Cili, T.Caja

In order to determinate an accurate order of nucleotides in our chromosomes and in our genome a new era of DNA exploration has been developed, and this is DNA sequencing. The knowledge of DNA sequences has accelerated medical researches and is applied in a large number of fields. In the early 1970 DNA sequencing has been done using two dimensional chromatography but now, several new methods of DNA sequencing is been developed. Next-generation sequencing (NGS), the massively parallel sequencing technology enables the medical researchers to perform explorations at a level never achieved before. NGS is a revolution in the study of hematological malignancies and is filling the gap of unknown pathways and to uncover specific ways of treatment. There are a lot of studies and publications based on this "new era" technology bringing the need of this technology to be part of the clinical routine. The aim of NGS is the discovery of the genetic mutations in the hematological neoplasms, and to be able to create the best individualized target therapy for the hematological patients. NGS incudes different methods that make possible the exploration of the whole human genome but Whole Genome Sequencing (WGS), the sequencing of all exons with Whole Exome Sequencing (WES) and Sequencing of messaging RNA are the most important methods used.

Whole Genome Sequencing: uses two methods of preparation of the DNA libraries, one is called "paired-end sequencing" where are sequenced about 100 bp starting from the 400 bp endings of the DNA fragments. Using this method we can identify unique nucleotide variants (SNV), the insertions and deletions, but also the copy numbered changes. This method uses small quantities of DNA for the generation of the libraries and this is a big advantage when used in the hematological malignancies where the quantity of DNA is low or sometimes very low. The second method is the preparation of the DNA libraries using "mate -pair sequencing". This method is based on the generation of big fragmentations of DNA from 1 to 10 kb of length and this can be used for simultaneous detection of the mutations, structural abnormalities and also of the copy-numerical changes. But this method has an enormous disadvantage related to the big quantity of DNA needed to create the libraries being so limited od use for only a little number of tumors.

Whole-Exome-Sequencing (WES): is largely used for the study of the exons, called also the codifying genomes, and for the study of untranslated areas (regions). This method is based on the enrichment of exons areas and after that is passed in the next step, of the target sequencing. The Exome represents only 1,4% of the whole genome, so samples can be weld and sequenced together during one procedure of the machine. The weak point of WES is related with the incapacity of the enriched kits used for the whole exome. According to all this has been performed a lot of cohort studies for the hematological neoplasms. As expected the genes *TP53, ATM* and *RAS* has been confirmed as mutated in a variety of hematological malignancies. Also a whole new group of mutated genes and defective pathways has been discovered as a cause of hematological malignancies using NGS. Some of them were only mutated genes and some othes represented defective pathways leading to the hematological neoplasms. This discoveris are the start of creation of new effective and individualized target therapies for the hematological diseases.

***Keywords**: Next genome sequencing, DNA sequencing, Exome , Genome , Mutations*

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"Next-generation sequencing - a new era in hematological malignancies"

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5. Bowers J, Mitchell J, Beer E, et al. Virtual terminator nucleotides for next-generation DNA sequencing. Nat Methods 2009;6:593–595

Leukemia Akute Limfoblastike, te dhena epidemiologjike per periudhen 2008-2018 ne Shqiperi

A. Papa, A. Cili, P. Pulluqi, A. Perolla, T. Caja, E. Calliku dhe A. Ivanaj

Hyrje:
Leukemia Akute Limfoblastike eshte nje lloj tumori ne te cilin ndodh proliferimi malinj I prekursoreve qelizor hemopoetike I linjes limfoide.Eshte malinjanca me e shpeshte midis leukemive ne femijeri ,gati 75-80% te rasteve.Ne vendet e zhvilluara incidence me te larte ka ne moshen 2-5 vjec. Ne te rriturit eshte nje leukemi e rralle,ne US llogaritet nje incidence gati 1.6/100,000 banore, ka nje kulm ne 15-24 vjec dhe nje kulm te metejshem pas 50 vjec.Persa I perket etiologjise ajo eshte e panjohur,mund te permendim disa faktore predispozues si ekspozimi ndaj rrezatimit jonizues,trajtimi I meparshem me kimioterapi,crregullimet gjenetike,prania e nje vellai ose motre me LAL etj.Klasifikimi morfologjik sipas FAB I ndan LAL ne 3 nentipe,L1,L2,L3, kurse sipas WHO ndahen ne LAL-B dhe LAL –T.

Qellimi:
Te njihemi me incidencen dhe prevalencen,te dhenat gjinore dhe nentipet e LAL-se ne Shqiperi pergjate gati 10 viteve.

Metodat:
Jane marre ne studim te gjitha te dhenat ne rregjistrat e pacienteve te Sherbimit te Hematologjise dhe Imunologjise per periudhen nga viti 2008 deri 2018. Ne kete studim jane futur vetem pacientet e diagnostikuar me LAL ,qe jane diagnostikuar dhe shtruar ne Sherbimin e Hematologjise , nga mosha >14 vjec e lart.

Rezultatet:
U pa se ne vitin 2008 ne sherbimin e Hematologjise ishin shtruar ne total 49 (100%) paciente me LAL nga te cilet 28 raste (58%) ishin raste te reja,nga keto te fundit 19 meshkuj e 9 femra.

Ne vitin 2009 ishin shtruar 61(100%) paciente nga te cilet 33(54%) raste te reja(22 meshkuj dhe 11 femra).

Ne vitin 2010 ishin shtruar 60(100%) paciente nga te cilet 33(55%) paciente ishin raste te reja (17 meshkuj e 16 femra).

Ne vitin 2011 ishin shtruar 38(100%) paciente nga te cilet 19(50%) paciente ishin raste te reja(11 meshkuj e 8 femra).

Ne vitin 2013 ishin shtruar ne total 30(100%) paciente nga te cilet 13(43%) raste ishin raste te reja(10 meshkuj e3 femra).

Ne vitin 2015 ishin shtruar ne total 42(100%) paciente nga te cilet 23(54.7%) raste te reja (12 meshkuj e 11 femra).

Ne vitin 2016 ishin shtruar 28(100%) paciente me LAL nga te cilet 16(57%) paciente ishin raste te reja(5 meshkuj e 11 femra).

Ne vitin 2017 ne sherbimin e Hematologjise ishin te shtruar 27(100%) paciente ne total nga te cilet 16(59%) ishin raste te reja(8 meshkuj e 8 femra).

Ne vitin 2018(deri ne muajin tetor) ishin shtruar ne total 22(100%) paciente nga te cilet 14(63.6%) raste te reja(11 meshkuj e 3 femra).

Gjithashtu ne kete studim u pa edhe shperndarja e LAL-ve sipas nentipeve nga periudha 2010 deri 2018.Ekzaminimi I Imunofenotipit leukocitar,te realizuar ne palce kockore apo gjak periferik,I eshte mundesuar ne total 84(100%) pacienteve nga te cilet 53 (63%) paciente rezultuan me LAL nentipi B, 14 (16.7%)paciente rezultuan me LAL nentipi T, 14 (16.7%) paciente rezultuan me LAL nentipi Bifenotipik , 1(1.2%) pacient rezultoi me LAL nentipi T/NK dhe 2 paciente me LA te padiferencuar.

Persa I perket shperndarjes gjinore u vu re se ne 195(100%) paciente te diagnostikuar me LAL per here te pare ,ne periudhen 2008 deri 2018, nder ta 115 (59%) ishin meshkuj dhe 80(41%) ishin paciente femra.

Konkluzioni:

Leukemia Akute LImfoblastike eshte nje patologji malinje qe ze nje vend shume te rendesishem ne malinjitet ne Shqiperi,me nje incidence dhe prevalence qe

ndryshon relativisht nga viti ne vit.Ne studimin qe iu be incidences lidhur me gjinine u vu re se ka incidence me te larte ne gjinine mashkullore se femerore. Tipi me I shpeshte I LAL –ve ne Shqiperi rezultoi tipi me limfoblaste B(63%).

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Acute Lymphoid leukemia in Albania, retrospective study.

Genta Smaja, A. Cili, T. Caja, P. Polluqi, A. Perolla, E. Calliku, and A. Ivanaj

Background

The incidence of acute lymphoid leukemia is increasing worldwide. In our country, there are no reports clearly describing the incidence of this malignancy or the reports are incomplete. ***Aim***: In this study, our main aim is to investigate the number of the new cases of the disease in adults during the period of time 2013-2017 in Albania. We can say that by investigating the number of the new cases in QSUT during this period, we have investigated the number of new cases in Albania because QSUT is the biggest hospital center in Albania. ***Materials and method***: This is a cohort retrospective study and we reviewed all the data from patients'records and hospital register, protecting the patient confidenciality in accordance with Helsinki declaration. We have analyzed the patient based on their demographic, diagnostic and therapeutic characteristics, followed by a statistical analysis to predict the disease's prognosis using SPSS and MedCALC software. ***Conclusions:*** We came to a final result that the incidence of acute lymphoblastic leukemia in adults in our country is about 0.6-1/100000 per year. Male to female ratio is 1.4/1. The age-group with the biggest number of new cases was 60-69 years old. Most of the new cases come from big cities and urban areas. The mean age was about 48.7 years old. Total DFS is 16.3 months. The most common treatment regimen used in our country is Rossi-Ferrini, followed by Hyper CVAD, CALBG and AEIOP 95'. We also tried to find a statistical difference between the regimens used, but there was no significant difference, probably due to the small number of the sample we have studied. We came to another conlusion that there is a significant statistical difference between age differences and WBC at presentation and DFS (disease free survival). DFS for age above 60 is 7 months comparing with 10 months for patients under 60 (p=0.09).

As for WBC number, DFS is 6 months for WBC>30,000/μL and 12 months for WBC <30,000/μL (p=0.07).Finally we can say that these two factors mentioned above are really important prognostic factors for this malignancy.

Key words : acute lymphoid leukemia,incidence, retrospective study,prognosis

The Registers of chronic diseases in Albania

Albana A. Fico, Alban Ylli, Elizana Petrela, Bajram Dedja

The most frequent diseases, which started to massively affect the health of Albanians during the end of 20th century and that now, in the new century, are the major threat to public health, have been traditionally called “chronic diseases” or even “degenerative diseases”.

These terms had their limits in describing the group of diseases of interest here, with tuberculosi, syphilis or AIDS showing a ”chronic” development, while heart attack or stroke

being ”acute” manifestations of the blood circulation diseases. Furthermore, the term ”degenerative disease” is too broad and misleading, with its underlying conotation of the unstopable process of human body geting old and frail.

”Non infective diseases” (NCD) is the term most widely accepted as the appropriate name for the group of diseases which dont get typically trasmited by means of direct contact or by various vectors. It is not the ideal term for diseases which have a infective agent at the basis of their pathogenesis, such as rheumatismal heart disease or cancer of cervix, but it is generally efective for describing together in a category, from a public health point of view, health problems such as ischemic heart diseases, hypertension, cerebrovascular diseases, tumors, diabetes, chronic obstructive lung diseases etc. Although, these diseases have important specifics and diferences among them, their control strategies, or the organisation of an health system for them have a lot in common.

The monitoring process or the survveillance of NCDs is the systematic and continous collection of data and their analyses for providing the due insight on their time and space distribution, their health impact and burden in society, as well as their risk factors and socio economic determinats.

NCD monitoring also provide information on health system capacities and efectiveness in facing them. NCD monitoring is indinspensable in setting up health programs, developing health-related policies and documenting potential progress in NCD prevention and control.

The NCD monitoring system in Albania should has three principal components:

1. Monitoring for exposure to risk factors
2. Monitoring health outcomes (NCD related mortality and morbidity rates)
3. Evaluation of NCD-related health system response capacities

Treatment of acute myeloid leukemia based on citogenetics and molecular biology

Polikron Pulluqi, Tatjana Caja, Adela Perolla, Alma Cili, Elsuarta Calliku, Marsela Shani, Xheni Ngjela, Anxhela Papa, Adela Buzo dhe Arben Ivanaj

AML is the most common type of leukaemia in adults, accounting for approximately 25% of leukaemia diagnoses, with an estimated 351,965 cases worldwide.

About half of AML patients will die annually.

Detection of molecular and cytogenetic abnormalities is critical in AML.

Evaluation of molecular mutations may be important for risk assessment and prognosis to help manage the disease.

European LeukemiaNet recommendations propose screening at diagnosis for various mutations, including NPM1, CEBPA, RUNX1, TP53, ASXL1, and FLT3 ITD and TKD2

Based in clinical examination, molecular genetic testing, prognostic score is decided which will be the best treatment for AML.

The most successful induction therapy in treatments of AML was and is three days of an anthracycline, daunorubicine 60 mg/m^2 /day and seven days of cytarabine 100 mg/ m^2 /day, referred as "7+3" regimens. Complete remission is achieved in 60- 80% of younger adults and in 40-60% of older adults > 60 years. High rate of CR is not converted in survival for patients. Remission duration is about 13 months and survival about 21 months.

Consolidation therapy after CR, widely used, is HiDAC, cytarabine 2000-3000 mg/ m^2 every 12hrs, days 1,3,5. There are some studies about results of intermediate dose of cytarabine 1000- 1500 mg / m^2. These studies have showed that there is no convincing evidence in superiority of HiDAC (cytarabine 3000 mg/ m^2

AML patient´s survival has improved with 3+7, but AML still shortness the survival of patients.

The 5-year survival rate in patients with AML is about 19%.

New drugs are presented in treatment of AML, addition of a third drug to 3+7 backbone.

New drugs

CPX-351: A liposomal formulation of cytarabine and daunorubicine encapsulated at a 5:1 molar ratio(1 ui= 1 mg ARAC and 0.44 mg DNR). This combination has long half-life > 24hrs, It has preferential uptake in leukemic blasts and accumulation in bone marrow.

Comparing CPX-351 (100 units/m^2 D1,3,5) with "7+3" cytarabine 100 mg/ m^2 /day, D1-D7, plus DNR 60 mg/m^2 / day, D1-D3 resulted that CPX-351 is superior in OS, increased CR+Cri response (47,7%vs. 33.3%, p=0.016) and CPX-315 arm has lover 60 days mortality (13% vs.21%).

Vosaroxin is the first in class anticancer quinolone derivative that acts by intercalates DNA, and by inhibited topoisomerase. It showed no significant OS advantage, but it showed OS benefit limited to elderly pts. Vosaroxin is evaluated in addition to HiDAC in consolidation, also in place of antracycline during induction and in combination with HMA in elderly fit pts.

Target therapy

Gemtuzumab Ozogamicine was the first targeted antibody-drug conjugate tu be approved in the USA for AML in 2000 and was reapproved in 2017 for treatment of AML newly diagnosed CD33-positive AML. **Vadastuximab talirine**- Anti CD33 as monotherapy in older patients showed CR 54%, and 0% mortality rate on 30 days, and15% on 60 days.

Vadastuximab talirine plus 3+7 was used in 44 previously untreated younger AML pts and showed 78% CR rate of which 75% had negative MRD. Others medicaments as anti CD 44, Anti-CD123 monoclonal antibodies are under study.

Venetoclax *a BCL2 inhibitors(anti-apoptotic proteins)* is in study for treatment of AML.

3+7 is backbone chemotherapy for treatment of AML discussion is how to incorporate new agents in AML treatment based in clinical situation and especially in genotype. For example if AML has genotype FLT3 is added **midostaurin** to 3+7. FLT3 mutations are present in 30% of AML patients, 23%: internal tandem duplication and 7% point mutation in tyrosin kinase domain. These mutations constitutively activate FLT3. FLT3-ITD associated with increased frequency of relapse, short survival. "RATIFY" a randomized study showed results of first line chemo ± midostaurin in FLT3 mutated AML. One arm: 1-2 cycles of induction "3+7" + midostaurin 50mg PO BID D8-21. Consolidation up to 4 cycles: Cytarabine 3 gr/m^2 over 3h q12h D1,3,5+ midostaurine 50mg PO BID D8-21. Maintenance (12 cycles) midostaurin 50mg PO BID D1-28.

The other arm was the same but instead of midostaurine was used placebo. CR was 59% for midostaurine arm and CR 54% for placebo arm. **OS of midostaurine arm was longer than placebo arm(midostaurin 74.4, placebo 25.6) p=.009**

Actually are in studies second generation of FLT3 inhibitors as Quizartinib(AC220), Crenolanib, Gilterinib.

IDH1 and IDH2 mutations are found in 16% of AML cases, IDH1 mutation 7.5% and IDH2 mutations 8.5%. There are 2 medications that are approved as mutant IDH1, 2 inhibitor: **Enasidenib(AG-221)** approved by FDA august 2017. **Ivosidenib (AG-120)** was approved in July 2018 for patients with relapsed/ refractory IDH1- positive AML. Both these medication are safe and are good tolerated. Both inhibitors induce differentiation. CR rate is 18% and overall response rate 36%.

Anemic syndrome in patients with Inflammatory Bowel Disease

Skerdi Prifti, Marsela Sina, Adea Kocollari

Anemia is the most common extra-intestinal manifestation and complication of inflammatory bowel disease (IBD). It has an important effect on the ability to work and on health related quality of life (QoL). Anemia is the major cause of increasing hospital admissions in IBD patients. The presence of the anemia correlates directly with the disease activity due to the fact that hemoglobin levels form part of a widely used disease activity index.

Anemia has a complex and multifactorial pathogenesis. In most cases it is a combination of iron deficiency anemia (IDA) and anemia chronic disease (ACD). Other causes may include vitamin B12 and folate deficiency, pro-inflammatory cytokines effects, medication toxicity, myelosuppression or hemolysis.

Iron deficiency is the most common cause of anemia in IBD patients. It can be related to ''absolute" iron deficiency, due to low dietary intake and also blood loss from ulcerated mucosa, especially in ulcerative colitis. The iron deficiency can also be related to reduce iron absorption, especially in Crohn's disease of the upper GI tract. The ''functional" iron deficiency, a particular condition of iron deficiency, is related to the regulation of systemic iron homeostasis by hepcidin.

Initial exams for anemia in IBD should consist of hemoglobin and full blood counts. The determination of erythrocyte mean corpuscular volume (MCV) and of mean corpuscular Hb (MCH), are important to distinguish between microcytic, normocytic and macrocytic anemia. The reticulocyte count can differentiate between regenerative or hypo-generative anemia. In most cases, total store of body iron with serum-ferritin (ferritin) and the iron available in the bone marrow with transferring saturation (TfS), is sufficient to differentiate between IDA and ACD. Anyway in the presence of inflammation a normal ferritin level does not rule out iron deficiency, therefore TfS should also be measured. Patients in clinical remission should be monitored for anemia at least every 6 to 12 months, while patients with active disease, every 3 months or at even shorter intervals depending on the iron levels.

In conclusion, the pathogenesis of anemia in patients with IBD is complex. The prompt diagnosis and eventual treatment is essential in order to improve patient's quality of life and the disease prognosis as well.

"The hematologic complications in patients treated with antithyroid drugs".

Prof. Agron Ylli, Th. Fureraj, V.Hoxha, G. Husi, M.Kermaj, R.Sanxhaku, E. Hoxha

Antithyroid drugs are widely used to treat hyperthyroidism, especially Graves' disease, but they tend to cause agranulocytosis, which increases the mortality rate. Agranulocytosis is a rare but serious complication of antithyroid drug therapy, and an up-to-date understanding of this topic is important. Both direct toxicity and immune-mediated responses have been described as possible mechanisms. Some major susceptibility loci have recently been identified, which may lead the diagnosis of agranulocytosis into a genomic era. Onset is acute and patients present with symptoms and signs of infection together with high fever. Clinical suspicion is pivotal and should prompt blood sampling. An absolute neutrophil count of <500/μl in the presence of antithyroid drugs establishes the diagnosis. The causative drug should immediately be stopped to prevent further damage. Treatment includes broad-spectrum antibiotics and granulocyte-colony stimulation factor in selected patients. Later, patients will need definitive treatment for hyperthyroidism, usually with radioactive iodine or surgery. The best way to avoid the mortality associated with antithyroid drug-induced agranulocytosis is patient education

Cellular cardiomyoplasty into infracted swine's hearts by retrograde infusion through the venous coronary sinus: An experimental study.

Prof. Edvin Prifti

OBJECTIVES:
The aim was to create a model of myocardial infarction with a borderline myocardial impairment which would enable evaluation of the retrograde cellular cardiomyoplasty through the venous coronary sinus in a large animal model.

MATERIALS AND METHODS:
Fifteen (study group) and 10 juvenile farm pigs (control group) underwent distal left anterior descending artery ligation. One month later the study group animals underwent sternotomy and a murine myoblastic line C2-C12 was injected at a constant pressure of 30mmHg, into the coronary venous sinus. Thirty days later all animals that survived from both groups underwent transthoracic echocardiography and 99Tc scintigraphy and were later euthanized and specimens were taken for microscopic evaluation.

RESULTS:
Cardiac output decreased significantly after ligation ($p<0.001$) and increased significantly after cardiomyoplasty ($p<0.001$). In all animals, the surgical induction of myocardial infarction caused a marked decline in the echocardiographic values of cardiac function; however, the cardiac function and dimensions were significantly improved in the study group after cardiomyoplasty versus the control group. All animals undergoing cardiomyoplasty demonstrated a significant reduction of the perfusion deficit in the left anterior descending artery territory,

instead such data remained unchanged in the control group. The histological examination demonstrated the engrafted myoblasts could be distinguished from the activated fibroblasts in the scar tissue because they never showed any signs of collagen secretion and fiber buildup.

CONCLUSIONS:
In conclusion, the venous retrograde delivery route through the coronary sinus is safe and effective, providing a significant improvement in function and viability.

"Current treatment for ITP"

Elsuarta Calliku MD

Zbulime te medha e hapa te shpejte jane bere ne fushen e Hematologjise keto vitet e fundit dhe po ashtu kjo eshte pare edhe ne trajtimin e PTI. Nga Idiopatike ne Imune , kjo ka sjelle pa dyshim nje trajtim gjithnje e me te mirepercaktuar.

Trajtimi I PTI kerkon ne vetvete te kuptohet sakte patofiziologjia e kesaj semundjeje dhe trajtimi i personalizuar mbeshtetur ne moshen , numrin e trombociteve kuadrin klinik, kohezgjatjen, stilin e jeteses, konsideratat ekonomike etj. , duhet te jete menyra me e mire e trajtimit te kesaj patologjie.

Trajtimi ii PTI ndahet ne ate terapeutik dhe ne ate kirurgjikal. Nderkohe qe ai terapeutik klasifikohet ne preparatet linje e pare apo linje e dyte, kirurgjikali ka ne vetvete splenektomine.

Opsionet terapeutike ne linje te pare mbetet kortikosteroidet , imunoglobulinat IV dhe Rh anti-D.

Por ne rastet qe nuk pergjigjen mund te kalohet ne trajtimin me Rituzimab , ciklofosfamid, azatioprim, dhe danazol.

Ne 2008, u vune ne perdorim dy agoniste te receptoreve te trombopoietines: romiplostin (Nplate) dhe eltrombopag (Promacta). Ne gusht 2015, FDA e shtriu indikacionin e perdorimit te eltrombopag edhe per pacientet kronike me PTI ne moshen 1 vjec dhe me te medhennj si dhe tek ata qe nuk kishin patur nje pergjigjie te duhur me terapite e tjera mjekesore apo nga splenektomia.

Eksperiencat e kufizuara me keta agjente jane premtuese megjithate studime te tjera jane ende ne vijim e te tjera do te duhet te realizohen ne te ardhmen

Epidemiologjia e Leukemise Limfoide chronike ne vitet 2013-2017

M.Shani, P.Pulluqi, T.Caja, A.Cili, E.Calliku, A.Perolla, Xh.Ngjela dhe A. Ivanaj.

Leukoza Limfoide Chronike perkufizohet si hemopathi pasoje e prishjes se mekanizmave te apoptozes, e cila konsiston ne grumbullimin e limfociteve monoklonale B ,me karakteristika imunofenotipike te vecanta,ne gjakun periferik,palcen e kockes dhe indin limfoid. Leukoza limfoide chronike dhe small cell limfoma mendohet te jene e njejta patologji B-malinj dhe ndryshojne ndermjet tyre vetem sa i takon menyres se invadimit te gjakut dhe limfonodujve.Brenda spektrit LLC-SCL rreth 10% e rasteve prezantohen si SCL dhe 90%si LLC.Leukoza limfoide chronike eshte nje crregullim heterogjen si nga pikepamja klinike dhe ajo biologjike.

Qëllimi : përcaktimi I incidences , të dhënat demografike per periudhen 2013-2017 te LLC.

Per kete qellim jane perdorur te dhena te marra nga Sherbimi i Statistikes QSUT, te dhena te mbledhura nga Regjistri i semundjeve malinje ne QSUT.

LLC eshte forma me e shpeshte brenda spektrit te leukemive ne vendet perendimore.Ne USA mendohet te kete rreth 4.2 raste te reja ne vit per 100.000 banore.Po ne USA perllogariten rreth 15000 raste te reja ne vite dhe pothuaj 4500 vdekje ne vit te cilat I atribuohen kesaj patologjie.

Prane sherbimit te Hematologjise per vitet 2013-2017 jane trajtuar ne total 496 raste te diagnostikuar me LLC,nga te cilet 138 femra (27.82%)dhe 358 meshkuj (72.17%).Mosha mesatare e te prekurve ishte 65.5 vjec nderkohe qe tek meshkujt ishte 65.47 vjec dhe te femrat 65.58 vjec.

	Femra	Meshkuj	Total
Stad 0	17(12.31%)	36(10.05%)	53(10.6%)
Stad I	17(12.31%)	45(12.5%)	62(12.5%)
Stad II	70(50.7%)	174(48.6%)	244(49.1%)
Stad III	31(22.46%)	94(24.41%)	125(25.2%)
Stad IV	3 (2.17%)	9(2.51%)	12((2,41%)

Gjate viteve 2013-2017 u diagnostikuan ne total 213 raste te reja me LLC ose mesatarish 43 raste te reja ne vit, nga te cilat 90 femra dhe 123 meshkuj,mosha mesatare e te cileve ishte 56.3 vjet per meshkujt dhe 54.9 vjet per femrat.

Gjate kesaj periudhe u verejten raste te diagnostikuara ne moshat 42-46 vjec mosha keto jo tipike per Leukozen Limfoide Chronike. Raportimi I rasteve ne mosha te reja me simptomatologji te paket duket se eshte nje fenomen ne rritje,pasoje kjo e egzaminimeve rutine me te shpeshta.

Lidhur me kohen e diagnostikimit te pathologjise, per vitet 2013-2017 haset nje shtim I rasteve te diagnostikuar hershem (stadet 0,I,II sipas Rai)te cilat zene ne total 59.3% e raste te reja te diagnostikuar per kete periudhe.

Lidhur me alternativat e trajtimit, rreth 72% e rasteve te vleresuara per trajtim moren terapi ne linje te pare sipas skemes Fludarabine-Endoxan-Rituximab, ndersa pjesa tjeter u trajtuan me terapi alternative si CVP, CHOP,Leukeran .

New era of target therapies and immunotherapies in solid tumours

Erion DOBI M.D. Ph.D.

In recent years, target therapies and especially immunotherapy has revolutionized and changed the standard of care in patients with solid tumeurs. Immune checkpoint inhibitors, fundamentally those that act by blocking the programmed cell death receptor-1 (PD-1) and its ligand the programmed cell death ligand-1 (PD-L1) have emerged as novel treatment strategies in solid tumors, demonstrating undoubted superiority over chemotherapy in terms of efficacy. There is consensus that PD-L1 expression on tumor cells predicts responsiveness to PD-1 inhibitors in several tumor types. Hence PD-L1 expression evaluated by immunohistochemistry (IHC) is currently used as a clinical decision-making tool to support the use of checkpoint inhibitors in patients with solid tumeurs.

However, these therapies are ineffective in a significant percentage of patients, and some initial responders eventually develop resistance to these therapies with relapsed disease. The mechanisms leading to both primary and acquired resistance to PD-1/PD-L1 inhibition are varied and can be both multifactorial and overlapping in an individual patient. As the mechanisms of resistance to PD-1/PD-L1 blockade continue to be further characterized, new strategies are being developed to prevent or reverse resistance to therapy, leading to improved patient outcomes.

Despite this progress made in this field, further investigations needs to be realised in order to evaluate the implication of other factors tumour's environment.

All these researches emphasize the urgent need that we have to better identify the tumors characteristic related to higher benefit of these targeted treatments.

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Chronic Lymphocytic Leukemia: From Genes to Treatment

Gianluca Gaidano

Molecular genetics and diagnostics. Approximately 80% of chronic lymphocytic leukemia (CLL) patients carry at least one of four common chromosomal alterations, namely deletion 13q14, deletion 11q22-23, deletion 17p12 and trisomy 12. In addition, the typical genome of CLL carries ~2000 other molecular lesions. More than 40 recurrently mutated driver genes have been identified and can be integrated into a small set of pathways. These include microenvironment-dependent signaling through NOTCH (*NOTCH1*, *FBXW7*), inflammatory receptors (*MYD88*), MAPK-ERK (*BRAF*, *KRAS*, *NRAS*, *MAP2K1*) and NF-κB pathways (*BIRC3*, *TRAF3*, *NFKBIE*), as well as intracellular programs such as DNA damage and cell cycle control (*ATM*, *TP53*, *SAMHD1*, *POT1*), chromatin modification (*HIST1H1E*, *CHD2*, *ZMYM3*), transcription (*EGR2*, *IRF4*, *BCOR*, *MED12*), and ribosomal processing (*XPO1*, *SF3B1*, *RPS15*). Based on the mutation status of immunoglobulin heavy chain variable *(IGHV)* genes, 60% carry mutated and 40% unmutated *IGHV* genes. Knowledge of CLL genetics has translated into the availability of prognostic and predictive biomarkers. In the clinical practice, predictive biomarkers (del17p, *TP53* mutation, *IGHV* mutation status) impact on clinician's choice since they can inform CLL treatment decisions.

Treatment of elderly patients. For decades monotherapy with chlorambucil was the standard therapy for elderly and/or comorbid patients. Chlorambucil is well tolerated, but rarely induces long lasting remissions resulting in significantly reduced life expectancy in the elderly. With more intensive combination regimens becoming standard in younger and/or physically fit patients, concomitant diseases and physical fitness play a major role for the selection of treatment. Individual clinical assessment of a CLL patient remains so far the standard in the routine practice, but use of comorbidity scores such as Cumulative Illness Rating Scale (CIRS) and complex geriatric assessment (CGA) may provide additional valuable

information on the frailty of the patient. The combination of chlorambucil plus a CD20 antibody (rituximab, ofatumumab, obinutuzumab) has become the new standard first line therapy for elderly patients because of long progression free survival rates in comparison to chlorambucil monotherapy. B-cell receptor (BCR) inhibitors, namely ibrutinib and idelalisib, are now available for CLL patients with genetically high risk disease or relapsed disease. BCR inhibitors as well as BCL2 inhibitors are evaluated in frontline therapy of elderly CLL patients. Notably, the selection of the optimal treatment in elderly CLL patients requires knowledge of *TP53* status in the leukemic clone.

Treatment of young patients. Fludarabine, cyclophosphamide and rituximab (FCR) is the most effective chemoimmunotherapy regimen for the management of CLL, and represents the current standard for untreated patients who are young and in good physical conditions and who are devoid of *TP53* disruption. Though the majority of patients receiving FCR as frontline therapy are destined to relapse, a subgroup of cases may experience durable first remission. In the new scenario of targeted agents for CLL, affordable treatment strategies should be patient-risk oriented as well as cost-effective and resource-saving. On these bases, there is an increasing interest in identifying *a priori* patients who may maximally benefit from FCR. Patients with mutated *IGHV* genes and without deletion of *TP53* and *ATM* may achieve durable remissions after first-line FCR and experience an expected survival similar to that of the general population.

Treatment of TP53 disrupted patients. *TP53* codes for a central regulator of the DNA-damage-response pathway and, when functional, triggers CLL cell apoptosis in response to chemotherapy. *TP53* may be disrupted in CLL by deletions, mutations or a combination of both. In order to perform a comprehensive evaluation of the **TP53** gene status, it is recommended to assess both the presence of chromosome 17p13 deletion by FISH and of **TP53** mutations by gene sequencing. *TP53* assessment is recommended at the time of treatment requirement, and should be retested at each relapse requiring treatment since *TP53* disruption may become evident over time during the clinical course. Because of the well established association with chemorefractoriness, detection of *TP53* disruption at the time of treatment requirement is an indication for choosing BCR inhibitors. The BCL2 inhibitor venetoclax, as single agent or in combination with anti-CD20 antibodies, has documented high efficacy in this setting.

Treatment relapsed/refractory patients. Relapsed/refractory CLL patients currently have several treatment options, that should be tailored according to the timing of relapse and the molecular genetics of the disease. Options include chemoimmunotherapy in late relapses, and new drugs targeting components of the B cell receptor (Bruton tyrosine kinase in the case of ibrutinib; PI3 kinase delta in the case of idelalisib in combination with rituximab) or the BCL2 protein (venetoclax). Several trials are exploring the best sequence of novel agents as well as the potential of combination strategies. In this context, the role of allogeneic stem cell transplantation is decreasing.

Treatment of Richter transformation. Richter syndrome (RS) is the development of an aggressive lymphoma in patients with a previous or concomitant diagnosis of CLL. It is difficult to propose a standard and optimized approach for these patients. However, at least in the diffuse large B-cell lymphoma (DLBCL) variant of RS, some suggestions can be made based on the available literature: *i)* adopt a biopsy policy for CLL patients; *ii)* carefully monitor CLL cases harbouring risk factors for RS transformation; *iii)* in the presence of a clinical suspicion of RS transformation perform a ^{18}FDG PET/CT and tailor the open biopsy of the index lesion according to its results; *iv)* if the biopsy reveals an aggressive lymphoma, establish its clonal relationship with CLL by *IGHV*-rearrangement analysis; *v)* if the CLL and RS are clonally unrelated, treat the disease as a *de novo* DLBCL; *vi)* if the CLL and RS are clonally related, encourage participation in prospective studies. If such studies are not available, the following approach can be considered: *i)* treat with an induction regimen, namely R-CHOP or, alternatively, OFAR (oxaliplatin, fludarabine, cytarabine, rituximab) if the patient had received prior anthracycline-containing chemotherapy; *ii)* consolidate young and fit patients with autologous or reduced intensity conditioned allogeneic stem cell transplant.

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Learning objectives

After attending this presentation, the participant will be able to:

- have knowledge of TP53 status by FISH and understand that DNA sequencing is required for choosing CLL treatment in both young and elderly patients,
- know the combination of chlorambucil plus a CD20 antibody is standard first line therapy for elderly unfit CLL patients devoid of TP53 disruption,
- know that FCR is standard treatment for young fit CLL patients devoid of TP53 disruption,
- know that BCR inhibitors are the treatment of choice for TP53 disrupted patients,
- understand that treatment of relapsed/refractory patients includes multiple options that should be tailored according to the timing of relapse and the genetics of the disease, and
- understand that no standards of care are yet available for Richter syndrome, though immunochemotherapy induction followed by stem cell transplantation is an option for clonally related patients.

Rezultatet e mjekimit me DHAP- R ne linje te dyte ne te semuret me DLBCL

Eralda Pepa, A. Cili, R. Roxhani, T. Caja, A. Perolla, P. Pulluqi, E. Calliku dhe A. Ivanaj

Obiektivi: qellimi i studimit eshte te vleresoje trajtimin e Limfomave non hodgkin me kemioterapi sipas skemes DHAP si linje e dyte ose e trete e mjekimit dhe prognozen mbas 6 muaj mjekim ne nje shtrirje kohore nga viti 2015-2018.

Metoda: Per kete studim jane perdorur te dhena te marra nga Sherbimi i Statistikes QSUT,eshte punuar me te dhena te mbledhura nga Regjistri i semundjeve malinje ne QSUT, kartelat e sherbimit te Hematologjise.

Rezultati: Gjate periudhes 2015-2018 ne Shqiperi jane trajtuar per here te pare 27 paciente me diagnoze Limfome magligne Non Hodgkin me kemioterapi sipas skemes DHAP , nga te cilet 16 rezultuan te seksit mashkull (59%) dhe 11 te seksit femer (41%).

Verehet nje incidence me e larte ne grupemoshat 50-78 vjec me 85%% te rasteve dhe ne grupmoshat 37-45 vjece me 15% te rasteve.

Nga 27 raste te marra ne studim 15(56%) rezultojne me tipin Diffuze Large B Cell Lymphoma (DLBCL), 4(14.8%) me Lymphome Splenike, 4(14.8%) me Small Cell Lymphoma(SCL), 2 (7.4%) Lymphome T Angioblastike, 1 (3.7%) MALT Lyphoma.

Ne stadin e IIA 2(7.4%) ne Stadin e IIB 2(7.4%) raste ne Stadin e IVA 6(22.2%) raste ne stadin e IVB 17(62%).

Rezulton nga 27 paciente, 9(33.3%) kane bere remision komplet te semundjes, 8(29.6%) kan bere remision parzial, 1(3.7%) ka deshtuar nga mjekimi dhe 9(33.3%) kane bere exitus.

Konkluzioni: Limfoma malinje Non Hodgkin eshte nje neoplazi malinje e indit limfatik, e cila e mere origjinen nga linfocitet (B dhe T), me lokalizim primitiv ne linfonoduj dhe me ralle mund te shfaqet ne zonat extra-nodale(lekure, gjendrat esocrine, gonadet, aparati gastro-intestinal, sistemi nervor central)

Ne studimin tone vihet re incidence me te larte te meshkujve ne raport me femrat. Mosha mesatare eshte 62 vjec. Vihet re predominim i variantit Difuze Large B Cell Limfoma me 56%. 62% e pacienteve te cilet jan trajtuar me kemioterapi siapas skemes DHAP jane ne stadin IVB.

Ne 27 pacienete te trajtuar me DHAP ne vitet 2015-2018 vetem 9(33.3%%) prej tyre kane bere remision komplet te semundjes, 8(29.6%) remision parcial, 1(3.7%) deshtim nga mjekimi, 9(33.3%) kane bere exitus.

Fjalet kyce: Lmpphoma Maligne non Hodgkin, Limfocit, Difuze Large B Cell Lymphoma, Mantel Cell Lymphoma, Small Cell Lymphoma, Lymphoma T Angioblastike, remision komplet, remision parcial, deshtim.

Current treatment for Immune Thrombocytopenia

Elsuarta Calliku (Jusufaj) MD, Marsela Shani, Adela Perolla MD, Prof. Polikron Pulluqi, Alma Cili MD, Ass.Prof. Tatjana Caja dhe prof. Arben Ivanaj

Background : Immune thrombocytopenia (ITP) is a hematologic disorder characterized by isolated thrombocytopenia with no evident clinical cause present in the organism. Most of the cases seem to be related with antibodies against platelets. Normal values for adults are between 150000-450000 per mm.

Values of platelets below 50.000 per mm risk for traumatic hemorragies, meanwhile values below 20.000 per mm have the risk of spontaneous hemorragies.

According to American Society of Hematology (ASH) the incidence of ITP is calculated up to 50-100 new cases per 1.000.000 persons.

Study : In Hematology service, Mother Teresa University Hospital, have been treated 349 cases with ITP for the period between 2014-2017,or in total 2.9% of all hemopathies treated in this period.

Results: In nowdays the pathogenesis of ITP is not considered anymore idiopathic but autoimmune because of the antiplatelet antibodies found present in around 60% of the cases. In most of the cases they belong to IgG class against glycoprotein IIb-IIIa or Ib-IX of the thrombocitic membrane. Platelet coating with these antibodies makes them clogged by splenic macrophages leading to their secuestration.

The clinic is dominated by hemorrhagic phenomena whose roughness correlates with the number of platelets. Platelets under 10,000 increase the risk of hemorrhage in the large cavities of the body like the brain, the eye, the abdomen or the pulmonary cavity.

Treatment options include corticotherapy, IVIg, splenectomy, Rituximab,TPO-RA-s and in other specific cases Azathioprine,Cyclosporine,Cyclophosfamide,Danazol,Mychophenalate and Vincristine.

Current evidence supports alternatives to splenectomy for second line management of patients with persistently low platelet counts and bleeding. Long-term follow up data suggest both efficacy and safety,in particular for the thrombopoietin receptor agonists (TPO-RA) and the occurrence of late remissions.

Follow up of patients who have undergone splenectomy for ITP reveals significant potential risks that should be discussed with patients and may influence the clinician and patient choice of second line agent Novel therapeutics are in development to address ongoing treatment gaps.

Keywords: ITP, current, treatment, novel therapy

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Limfoma Hodgkin ne Shqiperi. Epidemiologjia (vitet 2008-2018) dhe trajtimi me skemen ABVD te kimioterapise

Resmije Tozharaku, A. Cili, T. Caja, P. Pulluqi, A. Perolla, E. Carlliku, E. Pepa dhe A. Ivanaj

Limfoma malinje Hodgkin eshte nje neoplazi e cila prek indin limatik, e mer origjinen nga proliferimi monoklonal i limfocitet B, karakterizohet nga rritja ne dimensione e limfonodujve periferik dhe prezencen e qelizave tipike Reed-Sternberg .

Qellimi

Qëllimi I studimit tonë është që të përcaktohet incidenca vjetore, të dhënat demografike,të dhëna lidhur me gjininë dhe moshën e pacientëve të diagnostikuar me Limfomën Hodgkin në Shqiperi nga viti 2008 deri në vitin 2018.Tipi histiologjik qe predominon si dhe prognoza e pacienteve te trajtuar me skemen ABVD te kimioterapise.

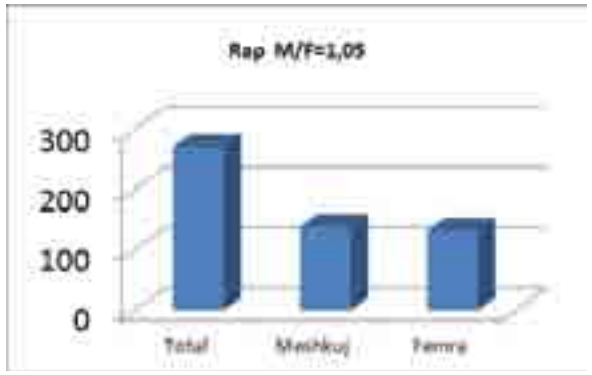
Metodat

Per kete qellim jane perdorur te dhena te marra nga Sherbimi i Statistikes QSUT,eshte punuar me te dhena te mbledhura nga Regjistri i semundjeve malinje ne QSUT, kartelat e sherbimit te Hematologjise dhe kartelat e sherbimit te Onkologjise.

Zhvillimi

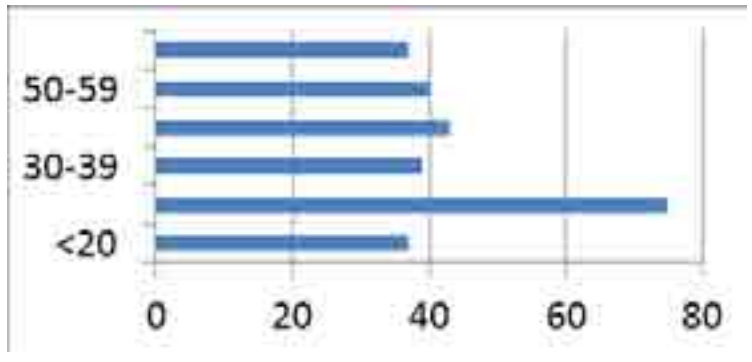
Gjate periudhes 2008-2018 ne Shqiperi jane diagnostikuar dhe trajtuar per here te pare 271 paciente me Limfoma Hodgkin.nga te cilet 139 rezultuan te seksit mashkull (51%) dhe 132 te seksit femer (49%).Raporti M/F =1.05.Incidenca me e

larte eshte ne vitin 2012 me 1.14 raste per 100000 banore.Tab1.Shperndarja sipas gjinise



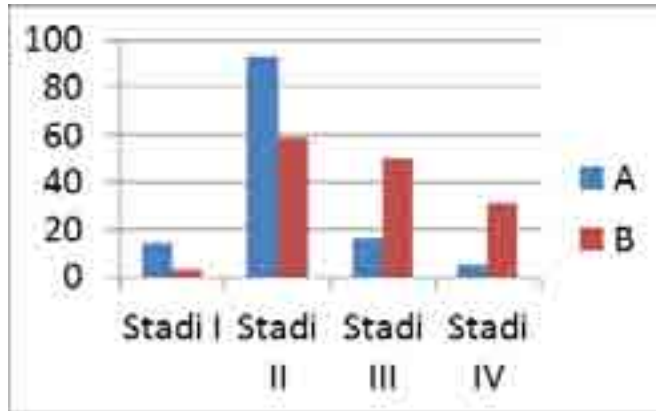
Shperndarja sipas grupemoshes eshte si ne grafikun me poshte.Ku verehet nje incidence me e larte ne grupemoshat 20-29 vjec me 28% te rasteve.Ndersa sipas shperndarjes Gjeografike verehet predominim i rasteve ne Tirane me 30% dhe 10% ne rrethin e Korces,pjesa tjeter e shperndare ne gjithe territorin e Shqiperise.

Tab 2.Shperndarja sipas grupemoshes



Nga 271 raste te marra ne studim ne momentin e diagnostikimit 14(5%) rezultojne ne stadin e IA,3(1%) ne Stadin e IB,93(35%) raste ne Stadin e IIA,59(22%) raste ne stadin e IIB,16(6%) ne stadin e IIIA,50(18%) ne stadin e IIIB,5 (1%) ne stadin e IVA dhe 31(12%) raste ne stadin e IVB ne

Tab3.Shperndarja sipas stadit te semundjes



3ee3eeTab.4 Shperndarja sipas variantit Histologjik.

Vihet re predominim i variantit Klasik Skleroze nodular me 63% te rasteve kurse pjesa tjeter eshte e shperndare ne kete menyre: Varianti nodular me predominim limfocitar 4% te rasteve,Varianti klasik me celularitet miks 22% te rasteve,Varianti klasik me predominim limfocitar 8% te rasteve dhe Varianti klasik me deplecion limfocitar 3% te rasteve.

Mjekimi ne linje te pare per pacientet e diagnostikuar me Limfoma Hodgkin ne Shqiperi eshte skema ABVD e kimioterapise.

Ne 271 pacient te diagnostikuar pergjate periudhes 10 vjecare te studimit ne vitet 2008-2018 vetem 6 (2%) prej tyre nuk kane filluar mjekim.Nderkohe pjesa tjeter ka filluar mjekim me skemen ABVD.Nder ta 211 pacient(78)% kane bere Remision Komplet te semundjes(zhdukje te limfonodujve me CT-scan ne mungese

te PET-CT)ndersa 40 (15%)pacient kane filluar mjekim ne linje te dyte me skemat BEACOPP,MINE,Gemsar+Cysplatin ,dhe vetem 14 (5%)pacient kane bere exitus gjate mjekimit ne linje te pare.

Konkluzioni

Pergjate viteve 2008-2018 ne Shqiperi rezultuan 271 pacient te diagnostikuar me Limfoma malinje Hodgkin.

Incidenca me e larte verehet ne vitin 2012 me 1.14 raste per 100000 banore,dhe incidenca me e larte ne grupemoshat 20-29 vjec.Raporti M/F=1.05

Nga rastet e mara ne shqyrtim ne momentin e diagnostikimit predominon stadi i IIA me variantin histologjik klasik ,nentipi sklerozes nodulare.

Mjekimi ne linje te pare i pacienteve me Limfoma hodgkin vazhdon te mbetet skema ABVD e kimioterapise ,rreth 78% e pacienteve kane bere Remision Komplet te semundjes nga te dhena e CT-skanerit (ne mungese te PET-CT).

Surgery role in the treatment of abdominal NHML

Prof. Arvin Dibra

Non-Hodgkin lymphomas a diverse group of blood cancers derived from lymphocytes that have a significant variability in their agressivity. Today's protocols of treatment rarely consider surgery as a treatment because of the efficacy of chemotherapy, biological therapy, radiotherapy and hematopoietic stem cell transplantation. Surgery mostly can have place in confirming or refuting a doubt of the radiological diagnosis through biopsy, removing symptomatic limited disease from an affected organ and in splenectomy for primary splenic lymphoma. Some times emergency surgery for acute complications of NHL in abdomen provides palliation and diagnosis. Actually there is no consensus to the optimal treatment for symptomatic limited disease affecting an organ and timing of chemotherapy preoperatively.

Ndryshimet midis Mielomes Multiple sekretore dhe jo sekretore ne Kosove nga viti 2017 deri 2018

A.Ukimeraj, V.Cavolli, E.Ismani, Sh. Sadiku

Hyrje. Mieloma Multiple eshte nje cregullim malinj I cili karakterizohet nga prezenca klonale e qelizave plazmatike ne palcen kockore , te cilat cojne ne ndryshime hematologjike, insuficience renale, dhe demtime kockore. Mieloma Multiple eshte patologjia malinje hematologjike e dyta nga frekuenca ne bote. Zakonisht karakterizohet nga prodhimi monoclonal ne sasi te medha te nje imunoglobuline varg te rende ose te lehte ose vetem prej vargjeve te lira. Megjithate nje perqindje e vogel e mielomave multiple karakterizohen nga prodhimi I paket I nje imunoglobuline ose nga mungesa totale e prodhimit te tyre. Keto myeloma quhet myeloma oligosekretore ose josekretore.Mielomat e verteta josekretore nuk sekretojne aspak imunoglobuline apo vargje te lehta. Ne vendin tone u studiuan 33 raste me mielome multiple te diagnostikuara ne dy vitet e fundit 2017 dhe 2018. U vune re se midis dy llojeve te mielomave kishte ndryshime ne nivelin e sedimentit, hemoglobines , prekjeve renale dhe vatrave osteolitike.

Metodat. Nga 33 raste 23 u diagnostikuan si mielome sekretore dhe 9 raste si mielome josekretore. Eshte matur niveli I sedimentimit, niveli I hemoglobines, prekja renale dhe demtimet osteolitike kockore ne te dy llojet e mielomave.

Rezultatet. Nga 23 raste me mielome sekretore, ne 16 prej tyre u vu re nje sedimentim mbi 100, ne 6 raste nje sedimentim midis vlerave 80-100, dhe vetem ne nje rast vlera e sedimetit ishte 50.Ne 9 raste me mielome josekretore ne 2 raste u vu re nje sediment mbi 100 dhe ne 5 raste te tjera sedimenti ishte midis vlerave 12 dhe 60. Ne 23 raste me mielome sekretore 7 prej tyre ishin pa vatra osteolitike. Ne 9 raste me mielome josekretore vetem ne 2 prej tyre nuk kishin vatra osteolitike. Ne te 23 rastet me mielome sekretore te gjitha ishin me hemoglobin nen 100g/dl. Ne 9 raste me mielome josekretore 6 ishin me hemoglobin mbi 100g/dl dhe 3 me hemoglobin normale. Ne 23 raste me mielome sekretore vetem 3 nuk kishin prekje renale. Ne 9 raste me mielome josekretore vetem 2 kishin prekje renale.

Perfundimi. Nga ky studim eshte vene re se myeloma sekretore karakterizohet me vlera me te larta te anemise, sedimentit dhe prekjeve renale, dhe me me pak prekje kockore. Ndersa myeloma jo sekretore karakterizohet nga vlera jo shume te ulura te hemoglobines, nga nje sediment jo I larte , me me pak prekje renale dhe me me shume prekje kockore .

Leukemia akute mieloblastike. Te dhena epidemiologjike

Xh. Ngjela, A. Cili, A. Perolla, P. Pulluqi, T. Caja, E. Calliku, dhe A. Ivanaj

Hyrje

Leukemia mieloblastike akute eshte nje semundje malinje klonale e palces se kockes ne te cilen prekursoret hematopoetike jane te frenuar ne etapat e para te zhvillimit dhe jane te karakterizuara nga prania e nje numri te shtuar te qelizave te papjekura ne palcen e kockes dhe ne gjak.

Ne faktoret etiologjike qe mund te permenden jane: sindromat familjare, prania e rrezatimeve, ekzistenca e semundjeve te tjera hematologjike si psh.; mielodisplazia apo leukemia mieloide kronike, faktoret gjenetike, si dhe ekspozimi ndaj drogave. Gjithsesi leukozat akute mieloblastike paraqiten ne menyre te menjehershme dhe dramatike tek nje person I cili ka qene me pare I shendetshem.

Klinikisht pacientet paraqiten me shenjat e leukopenise (temperature e larte); anemise(lodhje, dobesi , kepute) si dhe shenjat e trombocitopenise(hemorragji gingivale, apo petekie dhe ekimoza.). Keto shenja vijne si rezultat I invadimit te palces se kockes nga qeliza te papjekura: blaste. Ne disa forma te vecanta te leukemive mieloblastike paraqiten edhe elemente te vecante te klinikes si psh: ne leukemine promielocitare verehe shenjat e koagulimit intravaskuar te diseminuar ndersa ne leukemine akute monocitare verehn shenjat e infitrimit leukemik si psh infiltrim gingival.

Qellimi

Ne kete prezantim do te jepen te dhena mbi rastet me leukemi akute mieloblastike te diagnostikuar ne kliniken e hematologjise prej vitit 2015-2016.

Metoda

Ky eshte nje studim retrospektiv kohort ku te dhenat jane marre nga regjistrat e hematologjise. Gjate ketyre dy viteve jane paraqitur 136 raste me LAM.

Rezultatet

Sipas etiologjise eshte vene ne re se vetem 6 raste (4.4%) kane ndodhur ne paciente paraprakisht me mielodisplazi dhe leukemi mieloide kronike. Nga te dhenat te mbledhura numri I femrave te prekura eshte 63 (46,4%), ndersa numri I meshkujve te prekur eshte73 (53,6%). Verehet seT irana eshte qyteti me me teper raste 51 (37.7%), me pas Fieri dhe Durresi me 11 raste secila(8%) , Elbasani me 10 raste (7.4%) si dhe vetem tre raste te huaj ; ku nje pacient ka qene nga Kosova, nje nga Polonia dhe nje iraniane. Mosha mesatare e pacienteve te prekur eshte 54,7 vjec.

Ne 84% te rasteve pacientet kane qene pa semundje shoqeruese nderkohe qe ne 16% kane pasur semundje te tjera shoqeruese. Vetem 6 raste kane qene paraprakisht te diagnostikuar me MDS.

Pacientet jane trajtuar ne menyre specifike sipas skemes “7+3 “ si dhe ata te paraqitur me leukemi akute promielocitare kane marre trajtim specific me ATRA pervec skemes” 7+3” si dhe kane marre trajtim suportiv ne trajtimin e KID.